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Hemodynamic response of children with attention-deficit and hyperactive disorder (ADHD) to emotional facial expressions ☆

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ABSTRACT

Children with attention-deficit/hyperactivity disorder (ADHD) have difficulty recognizing facial expressions. They identify angry expressions less accurately than typically developing (TD) children, yet little is known about their atypical neural basis for the recognition of facial expressions. Here, we used near-infrared spectroscopy (NIRS) to examine the distinctive cerebral hemodynamics of ADHD and TD children while they viewed happy and angry expressions. We measured the hemodynamic responses of 13 ADHD boys and 13 TD boys to happy and angry expressions at their bilateral temporal areas, which are sensitive to face processing. The ADHD children showed an increased concentration of oxy-Hb for happy faces but not for angry faces, while TD children showed increased oxy-Hb for both faces. Moreover, the individual peak latency of hemodynamic response in the right temporal area showed significantly greater variance in the ADHD group than in the TD group. Such atypical brain activity observed in ADHD boys may relate to their preserved ability to recognize a happy expression and their difficulty recognizing an angry expression. We firstly demonstrated that NIRS can be used to detect atypical hemodynamic response to facial expressions in ADHD children.

1. Introduction

Social cognitive deficits have been reported in school-aged children with attention-deficit hyperactivity disorder (ADHD). ADHD is characterized by inattention, hyperactivity and impulsivity, and has recently become one of the most commonly diagnosed developmental disorders in children (American Psychiatric Association, 2000). Inattention, hyperactivity, and impulsive behavior in children with ADHD can result in social problems (for review, Nijmeijer et al., 2008; Uekermann et al., 2010). Children with ADHD experience seriously disturbed peer relations and tend to be excluded from peer activities (Hoza et al., 2005; Landau & Moore, 1991; Owens, Hinshaw, Lee, & Lahey, 2009).

Children with ADHD have been reported to have other social cognitive impairments besides inattention, hyperactivity and impulsivity. Although we still have limited knowledge about basic face processing in children with ADHD, Tye et al. (2013) demonstrated, as far as we know, the first study to investigate the face-inversion effect and gaze processing in children with ADHD using ERP. They found that the ADHD children showed a reduced face inversion effect on P1 latency compared to TD children. Yuill and Lyon (2007) demonstrated that children with ADHD performed as well as younger controls on a non-emotional task when examiners helped children inhibit impulsive responding. However, in the same study, children with ADHD still showed impairments in the emotion understanding task that required them to choose facial photographs corresponding to emotional descriptions. Furthermore, children with ADHD and its common comorbid disorder (oppositional defiant disorder; ODD) showed significantly lower performance on an emotional understanding task than typically developing (TD) children or children with autistic

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disorder (Downs & Smith, 2004). These studies indicate ADHD children's possible cognitive difficulty in emotion understanding.

School-aged children with ADHD have been found to have impaired recognition of emotional expression (Cadesky, Mota, & Schachar, 2000; Corbett & Glidden, 2000; Pelc, Kornreich, Foisy, & Dan, 2006; Sinzig, Morsch, & Lehmkuhl, 2008; Williams et al., 2008). Previous studies examined the recognition accuracy of children with ADHD using facial expressions of basic emotions such as anger and happiness (Cadesky et al., 2000; Corbett & Glidden, 2000; Kats-Gold, Besser, & Priel, 2007; Pelc et al., 2006; for review, Dickstein & Castellanos, 2012). In these studies the ADHD children recognized angry expressions less accurately than the TD children, yet recognized happy expressions as accurately as the TD children (Kats-Gold et al., 2007; Pelc et al., 2006; Williams et al., 2008, but see also Cadesky et al., 2000). Pelc et al. (2006) asked ADHD children and TD children to identify the emotions portrayed in facial photographs of anger, happiness, disgust and sadness. Compared with the TD children, the decoding accuracy of the ADHD children was equivalent for happiness and disgust, but significantly lower for anger and sadness. Pelc et al. attributed ADHD children's difficulty in recognizing angry expressions to both the complex dynamics of the self-perception of anger and to a "distorted empathy" in ADHD children. Guyer et al. (2007) supported this attribution, although they found that adolescents (who were 12-years or older) with ADHD or conduct disorder performed face-emotion labeling tasks similarly to control participants, and concluded that preadolescent ADHD children could have greater difficulty recognizing facial emotions than older ADHD children. Based on these studies and the aforementioned literature reporting that school-aged ADHD children have experienced angry expressions from their peers more often than TD children (Hoza et al., 2005; Landau & Moore, 1991), we can suppose that their biased experience may result in them processing angry expressions and happy expressions differently.

The neural basis of ADHD children's processing of emotional expression is also different from that of TD children. When ADHD children observed a neutral expression and rated the intensity of a fearful expression, their left amygdala hyperactivated relative to that of the TD children (Brotman et al., 2010). Marsh et al. (2008) reported that when ADHD children implicitly processed a fearful expression in the gender-judgment task, their amygdala responded to a fearful expression as strongly as those of TD children, but that their posterior cingulate cortex and middle frontal gyrus hyperactivated for an angry expression. While the amygdala is recruited for the 'amygdala network' that is involved in triggering emotional responses to detected social stimuli, the posterior cingulate cortex and the superior temporal sulci (STS) are involved in the 'mentalizing network' (Kennedy & Adolphs, 2012). The STS is well-known to play important role in processing biological motion and dynamic facial movement (Allison, Puce, & McCarthy, 2000; Pelphrey, Morris, McCarthy, & Labar, 2007). Also, STS is responsible for recognizing facial expression that inherent in even static image of facial expression (Andrews & Ewbank, 2004; Engell & Haxby, 2007; Narumoto, Okada, Sadato, Fukui, & Yonekura, 2001; Said, Moore, Engell, & Haxby, 2010). The ERP study has revealed atypical neural response in the temporal region around the STS in ADHD children to an angry expression, but typical neural response to a happy expression (Williams et al., 2008). However, the spatial location of brain activity cannot be accurately drawn with ERP. To further investigate the neural activity around the STS, we can use near-spectroscopy (NIRS), which has a much more reliable spatial resolution than ERP.

In this study, we used NIRS to investigate the neural basis of school-aged ADHD children's processing of facial expressions. NIRS has several clear advantages for studying children with developmental disorders (Ernst, Schneider, Ehlis, & Fallgatter, 2012; Fukuda, 2009; Ichikawa et al., 2014). Compared to other neuroimaging techniques such as fMRI, NIRS is completely silent, providing a non-intrusive environment and requiring less stabilization of the body and head. NIRS has been utilized in revealing the brain activity of ADHD children for executing cognitive tasks (Ehlis, Bähne, Jacob, Herrmann, & Fallgatter, 2008; Monden et al., 2012; Weber, Lütschg, & Fahnenstich, 2005). These studies measured the hemodynamic response in the prefrontal area. However, as mentioned above, the most important region in processing facial expressions is the occipital temporal area, including the superior temporal sulcus (STS) (Andrews & Ewbank, 2004; Said et al., 2010). Our group previously applied NIRS to measure the brain activity in the bilateral occipital temporal area overlying the STS of 6- to 7-month-old infants while they viewed facial expressions and found face-related cerebral hemodynamic response (Nakato, Otsuka, Kanazawa, Yamaguchi, & Kakigi, 2011). For typically developed adults, it has been reported that the processing of facial expression occurs dominantly in the right hemisphere (Etcoff, 1984; Gainotti, 2012; Nakamura et al. 1999; Tsuchiya, Kawasaki, Oya, Howard, & Adolphs, 2008).

To investigate the neural basis of ADHD children's recognition of facial expression, we used NIRS to measure the hemodynamic responses of ADHD children and TD children to the facial expressions of happiness and anger. This is the first attempt to reveal the hemodynamic response in the bilateral occipital temporal area of ADHD and TD children to facial expressions using NIRS.

2. Methods

2.1. Participants

The participants were 13 Japanese boys (mean age, 10 years 0 months; SD = 1 year 3 months, range, 8–12 years) with ADHD (5 combined, 6 inattentive, and 2 hyperactive/impulsive subtype) and 13 typically developing (TD) boys (mean age, 9 years 8 months; SD = 1 year 3 months; range, 8–12 years)[1]. An additional five boys with ADHD and two TD boys participated, but were excluded from the final analysis because they either failed to look at the face stimuli for more than three trials during the presentation of faces (two ADHD boys), or exhibited large body movements during the experiment (the three other ADHD boys and the two TD boys).

All diagnoses were based on the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR) and were made by two pediatric neurologists. Averaged ADHD-Rating Scale scores were 30.9 (SD = 11.7; range, 8–52) for the ADHD boys and 12.3 (SD = 5.9; range, 6–25) for the TD boys. Seven of the ADHD boys received methylphenidate, one received atomoxetine and the other five ADHD boys were not medicated. It is unclear whether medication affects the recognition of facial expression in ADHD children. Two previous papers reported that medication did not improve the recognition of facial expression in ADHD children (Schwenck et al., 2013) or slightly normalized it (Williams et al., 2008), although these other studies did not test the effect of medication (Cadesky et al., 2000; Da Fonseca, Seguier, Santos, Poinso, & Deruelle, 2009; Miller, Hanford, Fassbender, Duke, & Schweitzer, 2011; Pelc et al., 2006). In this study, because we found a consistent tendency of hemodynamic

[1] According to the Wechsler Intelligence Scale of Children-Third Edition (WISC-III), the IQ scores of 11 of the ADHD boys and 12 of the TD boys were assessed. The full IQ scores of these boys were over 75. When the missing IQ scores of two ADHD and one TD boy were replaced by means of their clinical group respectively, the full IQ scores of the ADHD participants (mean = 108.38; SD = 5.8) were significantly lower than those of the TD boys (mean = 89.8; SD = 12.8), $t(24) = 4.78$, $p < .000$. However, the performance IQ, which was related more to emotion recognition ability than full IQ (Buitelaar, Wees, van der Swaab-Barneveld, & van der Gaag, 1999), was not significantly different between the ADHD (mean = 92.2; SD = 12.4) and TD groups (mean = 99.5; SD = 8.6), $t(24) = 1.75$, $p = .09$.

response irrespective of medication (see footnote 2 of Section 3.1), we included the hemodynamic data from boys with and without medication in our data analysis.

This study was approved by the Ethical Committee of the Dokkyo Medical University Koshigaya Hospital (hosp-k 24016) and by the Ethical Committee of Chuo University (2012-8). Written informed consent was obtained from the participants and their parents. The experiments were conducted according to the Declaration of Helsinki.

2.2. Stimuli and design

The same stimuli were used as in Nakato et al. (2011). The sequence of stimuli presentation consisted of a test period and a baseline period (Fig. 1A).

The stimuli for the test period consisted of color images of five Japanese females each posing neutral, happy, and angry facial expressions, obtained from the Facial Information Norm Database (FIND) (Watanabe et al., 2007) with permission. There were two conditions: the happy face condition and the angry face condition. In each condition, an image of one of the five female models was chosen randomly for each trial and repeatedly shown 10 times.

In the same manner as Nakato et al. (2011), we presented a neutral face for 400 ms followed by a happy or an angry face for 400 ms so that such successive presentation of faces was perceived as a dynamic expression that changed from neutral to either happy or an angry. We adopted the apparent motion presentation in order to enable children to perceive the facial expressions more easily. Ambadar, Schooler, and Cohn (2005) demonstrated that a facial expression was recognized with greater accuracy when it was presented with apparent motion (89%) than when it was static (63%).

The sizes of the stimuli were approximately 13×10 deg for the faces and 3.5×3.5 deg for the blinking black dots. The total duration of each test period was fixed at 10 s. The order of the conditions was counterbalanced across the boys.

Each test period followed a baseline period of at least 20 s. The duration of the baseline period was controlled by the experimenter. The hemodynamic responses obtained from viewing a blank screen were used as a baseline.

2.3. Procedure

Each boy was tested while sitting in a chair and facing a computer screen approximately 50 cm away. The boys watched the stimuli passively while their brain activity was measured, and they were allowed to watch the stimuli for as long as they were willing. Their behavior was recorded on videotape during the experiment.

2.4. Recording

We used the Hitachi ETG-4000 system (Hitachi Medical, Chiba, Japan) to measure the hemodynamic changes in oxyhemoglobin (oxy-Hb), deoxyhemoglobin (deoxy-Hb), and total-Hb concentrations from 24 channels with .1 s time resolution. Twelve channels were assigned for the measurement of the right temporal area and 12 channels for the left (Fig. 1B). Two wavelengths of near-infrared light (695 and 830 nm) were projected through the skull. The intensity of the NIR light illumination at each channel was .6 mW.

The NIRS probes (Hitachi Medical) contained nine optical fibers (3×3 arrays) with five emitters and four detectors. The distance between the emitters and detectors was set at 3 cm. Each pair of adjacent emitting and detecting fibers defined a single measurement channel.

We set the probes at the bilateral temporal area centered at T5 and T6 according to the International 10–20 system (Jasper, 1958), since these posterior regions of the temporal lobe are thought to be especially important for face perception (Kanwisher, Mcdermott, & Chun, 1997; Puce, Allison, Asgari, Gore, & McCarthy, 1996). This location of the probes was the same as that of our recent studies (Nakato et al., 2011). When the probes were positioned, the experimenter checked to see if the fibers were touching each boy's scalp correctly. The channels were rejected from the analysis if adequate contact between the fibers and the boy's scalp could not be achieved because of hair interference.

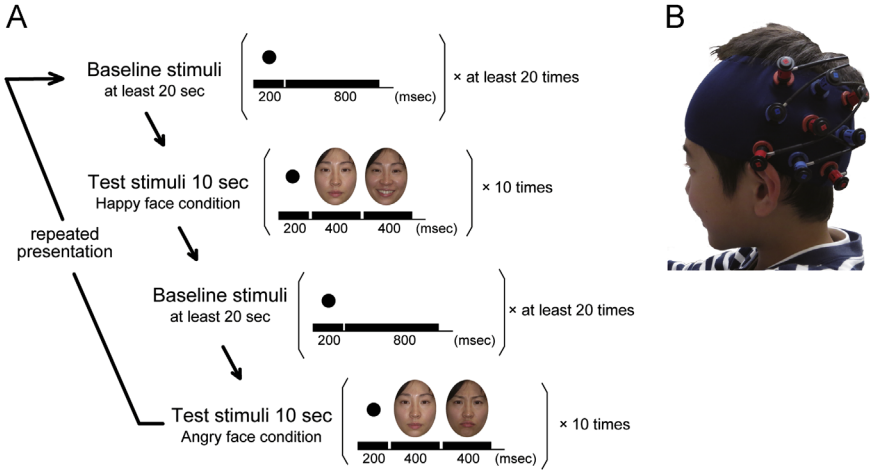

Fig. 1. (A) Experimental conditions and stimuli sequence. Each trial consisted of a test period and a baseline period. The test period consisted of two conditions in which faces were presented: the happy face condition and the angry face condition. The duration of the test period was fixed for 10 s. In the happy face condition, a happy facial expression was presented for 400 ms following a neutral face presented for 400 ms. In the angry face condition, an angry facial expression was presented for 400 ms following a neutral face presented for 400 ms. In each condition, prior to the presentation of each face, a fixation point (a blinking black dot) was presented for 200 ms. During the baseline period, instead of the presentation of faces, the monitor screen was filled with a white uniform blank. The blank screen was presented for a duration of 800 ms, and a 200 ms inter-stimulus interval was filled with the same fixation point (a blinking black dot) as the test period. The presentation order of test conditions (happy and angry face conditions) was counterbalanced across the boys. To attract and retain the attention of the boys, both the face stimuli and the blank were accompanied by a beeping sound. Two different sounds were used for the face stimuli and the blank, and these sounds were used in both the happy and angry face conditions. The relation between the sounds and the visual stimuli was counterbalanced across the boys (see also Supplementary material). (B) Location of the probe on a boy's head. The fibers were placed on the left and right temporal areas centering at T5 and T6 of the International 10–20 system (Jasper, 1958). The distance between the fibers was set at 3 cm.

2.5. Data analysis

Before performing the data analysis, we monitored the videotape which recorded the boys' behavior to evaluate valid trials for the statistical analysis. We excluded a trial from the analysis when either of the following occurred: when accumulative looking time within the trial did not reach 5 s, or when movement artifacts were detected by the analysis of sharp changes in the time series of the raw NIRS data. In the ADHD group, the mean number of rejected channels was .53 under the happy condition (.19 channels due to movement artifacts, and .34 channels due to inadequate contact between fibers and the scalp) and .56 under the angry condition (.20 channels due to movement artifacts, and .36 channels due to inadequate contact between fibers and the scalp). In the TD group, the mean number of rejected channels was .2 under the happy condition and .28 under the angry condition, both due to movement artifacts. Finally, each subject contributed an approximately equal number of channels to the analysis (for happy condition, mean 23.6, SD .57, $t(24)=1.55$, $p=.14$, *n.s.*; for angry condition; mean 23.6, SD .64, $t(24)=1.16$, $p=.26$, *n.s.*). We conducted a 2×2 ANOVA on the number of channels contributed by each subject with group (ADHD versus TD) as a between-participant factor and condition (happy face versus angry face) as a within-participant factor and found no significant main effect or interaction in the number of channels between the ADHD and TD groups.

The raw data of oxy-Hb, deoxy-Hb, and total-Hb from the individual channels were digitally band-pass-filtered at .02–1.0 Hz to remove noise from the heartbeat pulsations or any longitudinal signal drift (Monden et al., 2012; Nakato et al., 2011). Then the raw data of each channel were averaged across the trials within a subject in a time series of .1 s time resolutions from 3 s before the test period onset to 10 s after the test period offset. From the time series of raw data of oxy-Hb, deoxy-Hb, and total-Hb, we calculated *Z*-scores at each time point to examine deviations of hemodynamic response to the presentation of faces from the baseline period where the blank was shown. The *Z*-scores were calculated separately for oxy-Hb, deoxy-Hb, and total-Hb in the happy and angry face conditions for each channel. The *Z*-scores were calculated using the following formula:

$$d = (x_{test} - m_{baseline})/s$$

x_{test} represents the averaged raw data at each time point during the test period and $m_{baseline}$ represents the mean of averaged raw data during the baseline period. s represents the SD of the baseline period. The "baseline" used to calculate the *Z*-score was the period of 3 s immediately before the beginning of each test period, which reflected the activation during the observation of the white uniform blank. Then the *Z*-scores obtained from the 12 channels within each measurement area were averaged in order to increase the signal-to-noise ratio. Although the raw data of NIRS were originally relative values and could not be averaged directly across subjects or channels, the normalized data such as the *Z*-scores could be averaged regardless of the unit (Matsuda & Hiraki, 2006; Schroeter, Zysset, Kruggel, & Von Cramon, 2003; Shimada & Hiraki, 2006).

Consistent with a previous study (Boynton, Engel, Glover, & Heeger, 1996) and our own previous studies using NIRS (Nakato et al., 2011), we found that a response peak lags a few seconds behind stimulus onset (see Fig. 2). Therefore, we performed statistical analyses against the mean *Z*-scores from 5 to 15 s after the face stimulus onset. A two-tailed one-sample *t*-test against a chance level of 0 (baseline) was conducted for the mean *Z*-score during the 5–15 s of the test trials in both temporal areas.

3. Results

3.1. Group comparison

We obtained hemodynamic responses from 26 boys who looked at the stimuli for more than three trials in both the happy and angry face conditions. The mean number of trials was 4.54

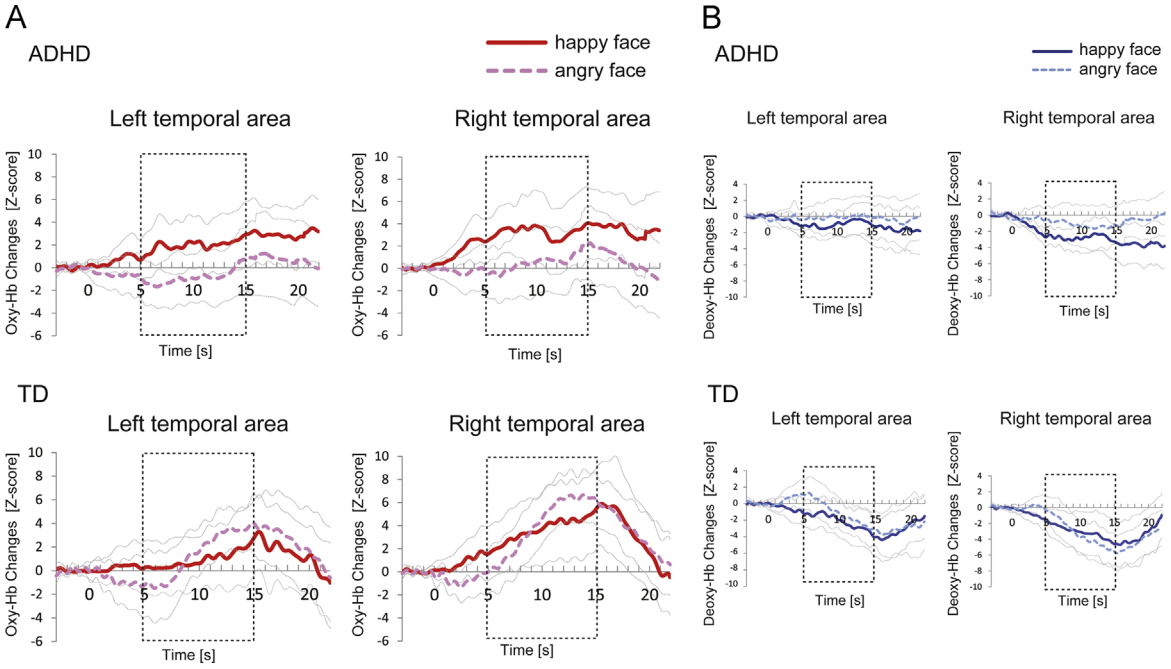

Fig. 2. The time-course of the average change in oxy-Hb (panel A) and deoxy-Hb (panel B) concentrations during the happy and angry face conditions. In each panel, the left and right columns show the data obtained from the left and right temporal areas, respectively. The graphs indicate the data for the mean *Z*-score in the happy face condition (a dark solid line) and the angry face condition (a dark broken line). Gray lines indicate 95% confidence intervals in the happy face condition (a pale solid line) and the angry face condition (a pale broken line). Zero on the horizontal axis represents the beginning of the test period and 10 on the horizontal axis represents the end of the test period. The area between 5 and 15 indicates the zone for the statistical analysis.

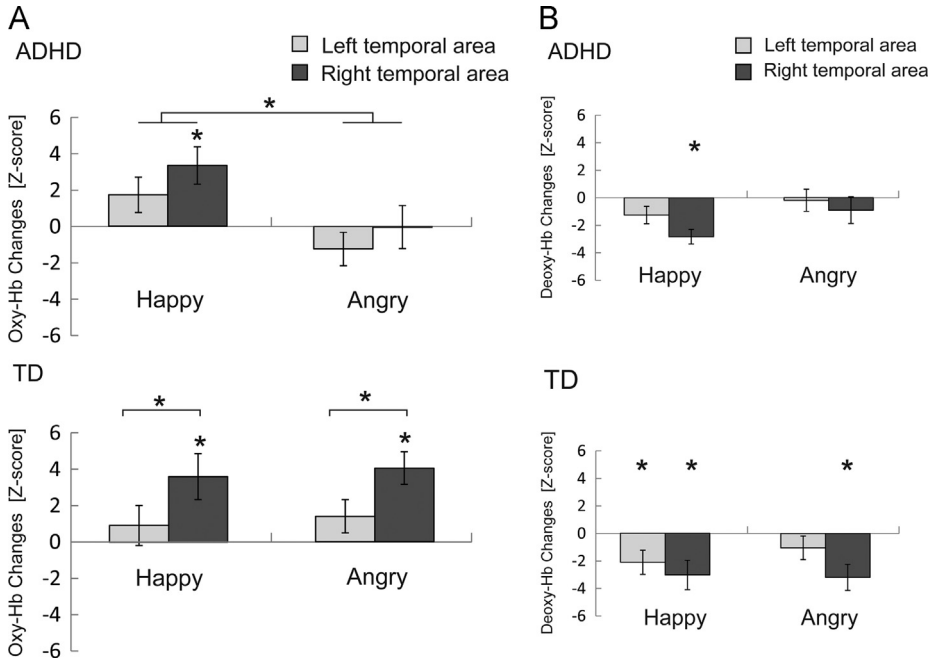

Fig. 3. Mean *Z*-score of oxy-Hb (panel A) and deoxy-Hb (panel B) change from 5 to 15 s of the trial. In each panel, the vertical lines in the graphs represent 1 *SEM*. In the ADHD group, ANOVA with condition (happy face versus angry face) and measurement area (right versus left) revealed a significant main effect of condition. The concentration of oxy-Hb in the right temporal area increased significantly only for happy faces (a darker bar) compared to the chance level of 0 (*$p < .05$). In the TD group, ANOVA with condition and measurement area revealed a significant main effect of measurement area. The concentration of oxy-Hb in the right temporal area increased significantly for both the happy (a darker bar) and angry faces (a pale bar) compared to the chance level of 0 (*$p < .05$).

(SD = 1.04) for the happy face condition and 4.62 (SD = .86) for the angry face condition for the ADHD boys, and 4.15 (SD = .90) for the happy face condition and 4.00 (SD = .82) for the angry face condition for the TD boys. Finally, each subject contributed an approximately equal number of trials to the analysis (for happy condition, mean 4.26, SD .92, $t(24) = 1.07$, $p = .30$, *n.s.*; for angry condition; mean 4.35, SD .89, $t(24) = 1.59$, $p = .13$, *n.s*). We conducted a 2×2 ANOVA on the number of trials contributed by each subject with group (ADHD versus TD) as a between-participant factor and condition (happy face versus angry face) as a within-subject factor and found no significant main effect or interaction in the number of trials between the ADHD and TD groups.

Fig. 2 shows the time course of the average change of the oxy-Hb and deoxy-Hb concentrations during the presentation of the happy and angry faces. The grand-averaged data obtained by all 13 subjects of each subject group were shown to examine the general tendency of inter-hemispheric difference.

Fig. 3 shows the mean *Z*-score from 5 to 15 s of the trial in the left and right temporal areas. We obtained the data of oxy-Hb and deoxy-Hb and analyzed them separately.

To compare the differential oxy-Hb concentration between the ADHD and TD groups, a $2 \times 2 \times 2$ ANOVA was conducted with: (i) group (ADHD versus TD) as a between-participant factor, (ii) condition (happy face versus angry face) as a within-subject factor, and (iii) measurement area (right versus left) as a within-subject factor. This analysis revealed a significant interaction between group and condition, $F(1,24) = 5.152$, $p = .03$, partial $\eta^2 = .18$ and a significant main effect of measurement area, $F(1,24) = 12.01$, $p = .002$, partial $\eta^2 = .33$. The other main effect and the other interactions were not significant, $p > .10$. For deoxy-Hb concentrations, the ANOVA revealed a significant main effect of measurement area, $F(1,24) = 4.58$, $p = .04$, partial $\eta^2 = .16$. The other main effect and the other interactions were not significant, $p > .10$.

As a follow-up test, we tested the effect of condition by independent two-sample *t*-tests on oxy-Hb concentration of ADHD and that of TD. We found that ADHD children showed increased oxy-Hb concentration for happy faces similarly as TD children did, $t(24) = .20$, $p = .84$, $r = .04$, while for angry faces they showed less oxy-Hb concentration than TD children did, $t(24) = 3.97$, $p = .001$, $r = .63$. For deoxy-Hb concentrations, the ANOVAs did not reveal any significant effect or interaction, $p > .10$.

Furthermore, as we originally aimed to illustrate the differential hemodynamic lateralization between the groups, we conducted 2×2 ANOVAs respectively with: (i) condition (happy face versus angry faces) and (ii) measurement area (right versus left) as within-subject factors. For the oxy-Hb concentrations of the ADHD boys, this analysis revealed only a significant main effect of condition, $F(1,12) = 6.53$, $p = .03$, partial $\eta^2 = .35$; no other main effects or interactions were significant[2]. On the other hand, for the oxy-Hb concentrations of the TD boys, only a main effect of measurement area was significant, $F(1,12) = 11.74$, $p = .01$, partial $\eta^2 = .49$; no other main effects or interactions were significant. For deoxy-Hb concentrations, the ANOVAs did not reveal any significant effect or interaction, $p > .10$.

To examine the possibility that there was differential activity for the presentation of faces compared with the baseline, we conducted a two-tailed one-sample *t*-test on the *Z*-scores against a chance level of 0 (baseline) for each condition and measurement area (happy-right, happy-left, angry-right, and angry-left). Multiple comparisons were corrected using a false discovery rate (FDR), $q = .05$. The analysis revealed that the ADHD boys showed significant hemodynamic response only to the happy face condition. Their increase of oxy-Hb and decrease of deoxy-Hb in the right hemisphere were significant, oxy-Hb; $t(12) = 3.25$, $p = .01$, deoxy-Hb; $t(12) = -5.32$, $p = .00$, but not

[2] To confirm that the medication of MPH did not induce any intra-group variation within the ADHD group, a $2 \times 2 \times 2$ ANOVAs was conducted on the oxy-Hb concentration with: (i) medication (with versus without MPH) as a between-participant factor, (ii) condition (happy face versus angry face) as a within-subject factor and (iii) measurement area (right versus left) as a within-subject factor. This analysis revealed no significant main effect or interaction for the medication, while only the main effect of condition was significant, $F(1,11) = 8.951$, $p = .012$, partial $\eta^2 = .45$.

in the left hemisphere, oxy-Hb; $t(12)=1.76$, $p=.10$, deoxy-Hb; $t(12)=-1.98$, $p=.07$. On the other hand, the TD boys showed significant hemodynamic response to both the happy face and angry face conditions only in the right hemisphere. The oxy-Hb of the TD boys was significantly increased in the right hemisphere for the happy face condition, $t(12)=2.846$, $p=.02$, and for the angry face condition, $t(12)=4.506$, $p=.00$. In addition, deoxy-Hb decreased significantly in the right hemisphere for both the happy face condition, $t(12)=-2.84$, $p=.02$, and the angry face condition, $t(12)=-3.36$, $p=.01$, and in the left hemisphere for the happy face condition, $t(12)=-2.41$, $p=.03$.

3.2. Individual differences in peak latency

To further investigate group differences between the ADHD and TD groups, we compared the mean and variance of the individual differences in peak latency of the hemodynamic responses. Fig. 4 shows the individual data for the oxy-Hb time course averaged across the trials. First, we conducted two-tailed two-sample *t*-tests on the peak latencies for each condition and hemisphere; however, we did not find any significant differences. Next, we conducted Levene's tests for equality of variances and found that the peak latency had a significantly broader deviation for the ADHD group than for the TD group in the right temporal area under both the happy face condition, $F=8.14$, $p=.01$, and the angry face condition, $F=6.87$, $p=.02$. The individual difference in the latency of peak hemodynamic response deviated with broader temporal range in the ADHD group, while that of the TD group gathered at 14–17 s after stimuli onset. Because we did not find any difference in the number of trials and channels contributed by participants from each group, we could conclude that the variance of peak latency was not caused by a difference in the amount of data acquired from the ADHD and TD groups.

4. Discussion

In the present study, we used NIRS to investigate the neural basis of the recognition of facial expression in boys with ADHD. We measured and compared the hemodynamic responses to facial expressions of happiness and anger in ADHD boys and typically developing (TD) boys. We found different responses in oxy-Hb to the faces between those two groups. The ADHD boys showed a significantly greater increase in the concentration of oxy-Hb only for the happy faces compared with baseline. By contrast, the TD boys showed a significant increase of oxy-Hb for both the happy and angry faces compared with baseline only in the right temporal area. The significantly increased brain activity observed in the ADHD boys for happy expressions relates to both their preserved ability to recognize happy expressions and their difficulty recognizing angry ones.

The brain activity of the ADHD boys significantly increased only for the happy expression, while that of the TD boys significantly increased for both expressions. The similar responses of the ADHD and TD boys to the happy expression may be related to the ADHD boys' preserved behavioral response to expressions of happiness. Previous studies have demonstrated that the recognition of happy expressions remains normal in ADHD children, while the recognition of negative expressions is impaired (Kats-Gold et al., 2007; Pelc et al., 2006; Williams et al., 2008).

Furthermore, the ADHD boys did not show increased hemodynamic response to angry faces in either the right or left temporal area, while the TD boys showed significantly increased brain activity consistently in the right temporal area for both conditions compared with baseline. The TD boys showed right hemispheric dominance in processing facial expressions, consistent with the typically developed adults (Etcoff, 1984; Gainotti, 2012; Nakamura et al., 1999; Tsuchiya et al., 2008). Yet while right hemispheric dominance in TD children as young as school-age has been observed and successfully measured by NIRS, ADHD children have failed to show right hemispheric lateralization to angry faces. This finding is consistent with Williams et al. (2008) study which demonstrated that temporal region of ADHD children did not respond to angry faces. Contrary to Marsh et al. (2008), which demonstrated hyperactivity in the posterior cingulate cortex (PCC) and middle frontal gyrus (MFG), we did not found greater activation in the STS compared with baseline. The STS is the area

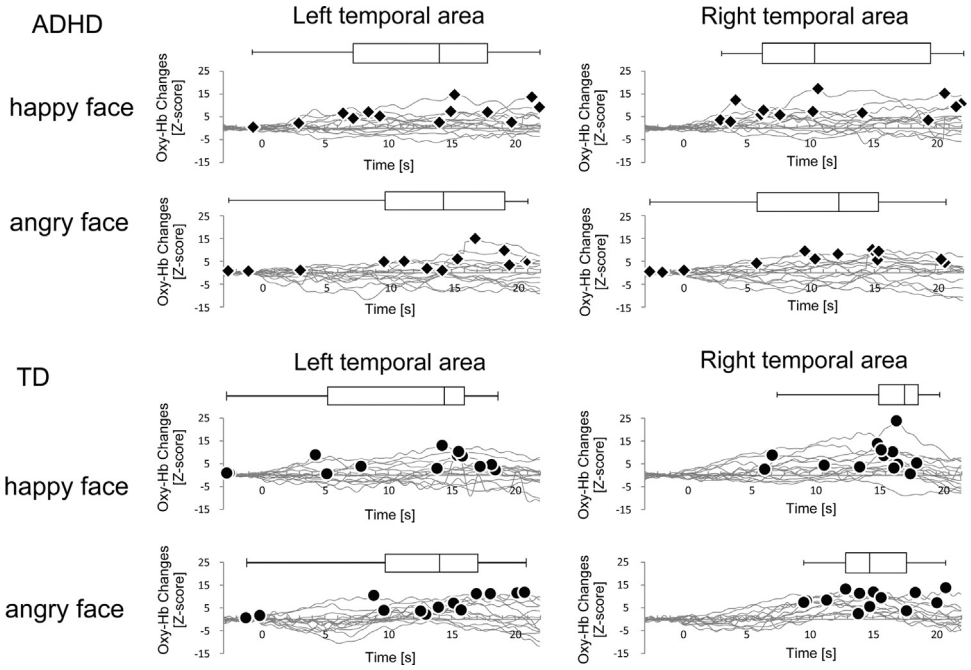

Fig. 4. The time course of oxy-Hb change in individual subjects. In each graph, line plots indicate the *Z*-score of individual data averaged across trials. Markers (of diamonds for the ADHD group and circles for the TD group) on each line indicate the peak of the concentration of oxy-Hb. The box plot displays the distribution of individual peak latency.

responsible for facial expression recognition (Andrews & Ewbank, 2004; Engell & Haxby, 2007; Narumoto et al., 2001; Said et al., 2010), while the PCC and MFG are reported to be activated by emotionally salient stimuli (Maddock, 1999). Although we did not concurrently measure the STS, the PCC and the MFG, the non-activation in the STS might reflect impairment in the recognition of angry expressions, while the hyperactivation in the PCC and MFG might reflect a stronger emotional reaction to angry faces in ADHD children compared with TD children.

It is interesting to note that the individual differences in the peak latency of the hemodynamic response in the right temporal area showed significantly broader variance in the ADHD group than in the TD group. The TD group showed increased hemodynamic response to both happy and angry faces in the right hemisphere and displayed the peak between 13 and 18 s after the beginning of the test period. Since the faces were presented repeatedly for 10 s, the hemodynamic response should have been repeatedly induced and accumulated. At the stimulus offset, the cumulative increase of oxy-Hb stopped and the peak was appeared. On the other hand, the ADHD group also showed increased hemodynamic response to happy faces compared with baseline in the right temporal area. However, as depicted in Fig. 4, the individual peak of the hemodynamic responses of the ADHD group was broadly and equally distributed from 5 to 20 s (happy face condition) after the beginning of the test period. Some of the ADHD children showed the peak of the hemodynamic responses around 5 s after stimuli onset and others showed the peak around 20 s after stimuli onset. Although we do not know if ADHD children processed the happy face in a different manner than TD children and we cannot exclude the possibility that the differential number of trials or channels may contribute to such differences between groups, we can suppose that some ADHD children respond to the happy face earlier while others respond later than TD children. The differential peak latency might imply differential neural processing and instability in the right hemispheric dominance when processing facial expressions.

The findings of the present study demonstrate atypical brain activity in the lateral occipito-temporal area around the STS in children with ADHD who are viewing emotional expression. Previous fMRI study has investigated the amygdala's response to facial expressions in children with ADHD (Brotman et al., 2010; Marsh et al., 2008). Although both the amygdala and the STS play important roles in the neural model of face processing (Gobbini & Haxby, 2007; Haxby, Hoffman, & Gobbini, 2000), each seems to be recruited for a different social brain network. The amygdala is a center of the "amygdala network" that is involved in triggering emotional responses to detected social stimuli; while the STS is part of the 'mentalizing network' that is involved in understanding other people's emotional states, intentions, and beliefs (Kennedy & Adolphs, 2012, for review). Our finding is that atypical hemodynamic response around the STS to emotional expression may be related to ADHD children's difficulty in decoding facial expression.

The limitations of this study should be discussed. First, NIRS is most effective if one's area of interest is close to the cortical surface. It is difficult for NIRS to detect the deeper regions of the brain cortex such as the amygdala, although the depth resolution of NIRS is dependent on the optical properties of the tissue (Fukui, Ajichi, & Okada, 2003). The present study is, as far as we know, the first attempt to use NIRS to measure the occipital temporal areas in school aged-children and we cannot evaluate the feasibility of using NIRS from only the present results. However, we have previously demonstrated that NIRS can detect differential hemodynamic response to happy and angry faces (Nakato et al., 2011) and in this study could also detect the response to different emotional faces. The second limitation concerns the sampling of participants. We included ADHD boys with and without medication. This sampling could have possibly brought a contamination effect from the medication to the present study which affected the variability of the peak latency of the hemodynamic response, although, as we mentioned in footnote 2 of Section 3.1, the MPH medication did not affect the averaged amount oxy-Hb concentration in the ADHD group. Furthermore, only boys were included in this study. Because the prevalence of girls with ADHD is two to three times lower than that of boys in the US (e.g., Ramtekkar, Reiersen, Todorov, & Todd, 2010), we did not have a sufficient sample of girls exhibiting symptoms of ADHD (Kats-Gold et al., 2007). Lastly, using a passive viewing task, we did not examine the participants' behavioral performance of facial expression recognition. We did not explicitly ask participants to judge the facial expressions, and we have no idea whether or not the ADHD children in this study had any difficulties in facial expression recognition. Thus, we can hardly conclude that the atypical hemodynamic response of the ADHD children reflects an impaired ability to recognize facial expression. Although this is the first study to demonstrate possible differences in hemodynamic response to facial expressions, in future study it would be helpful to investigate the relation between behavioral performance and cerebral hemodynamic response in the recognition of facial expressions.

The present study demonstrated differential brain activity between ADHD and TD children in response to facial expressions of happiness and anger. This result indicates that atypical neural responses to emotional expressions emerge in ADHD children from school-age. The ADHD children showed significantly increased oxy-Hb only for happy faces compared with baseline, which supposedly relates to their preserved recognition of happy expressions. On the other hand, the TD children showed a significantly increased concentration of oxy-Hb only in the right temporal area regardless of the expression; such right hemispheric dominance for processing facial expression is common in typically developed adults. Our results indicate that the neural basis of ADHD children's processing of emotional expressions differs from that of TD children. This atypical neural basis for processing emotional expressions might be responsible for ADHD children's later impairment in social recognition and the establishment of peer-relationships.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.neuropsychologia.2014.08.010.

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