Reduced Prefrontal Hemodynamic Response in Adult Attention-Deficit/Hyperactivity Disorder as Measured by Near-Infrared Spectroscopy

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Abstract

Aim: Recent developments in near-infrared spectroscopy have enabled non-invasive clarification of brain functions in psychiatric disorders. In pediatric attention-deficit/hyperactivity disorder, reduced prefrontal hemodynamic responses have been observed with near-infrared spectroscopy repeatedly. However, there are few studies of adult attention-deficit/hyperactivity disorder by multi-channel near-infrared spectroscopy. Therefore, in this study, we used multi-channel near-infrared spectroscopy to examine the characteristics of prefrontal hemodynamic responses during the Stroop color-word task in adult attention-deficit/hyperactivity disorder patients and in age- and sex-matched control subjects.

Methods: Twelve treatment-naïve adults with attention-deficit/hyperactivity disorder and 12 age- and sex-matched healthy control subjects participated in the present study after giving consent. We used 24-channel near-infrared spectroscopy to measure the oxyhemoglobin changes at the frontal lobes of participants during the Stroop color-word task. We compared the oxyhemoglobin changes between adults with attention-deficit/hyperactivity disorder and control subjects by t-tests with Bonferroni correction.

Results: During the Stroop color-word task, the oxyhemoglobin changes observed in the attention-deficit/hyperactivity disorder group were significantly smaller than those in the control group in channels 11, 16, 18, 21, 22, 23 and 24, correspond to the prefrontal

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cortex. At channels 16, 21, 23 and 24 of the attention-deficit/hyperactivity disorder group, there were negative correlations between the symptomatic severity and the oxy-Hb changes.

Conclusion: The present study suggests that adults with attention-deficit/hyperactivity disorder have reduced prefrontal hemodynamic response as measured by near-infrared spectroscopy.

Keywords: adult attention-deficit/hyperactivity disorder, functional neuroimaging study, near-infrared spectroscopy, prefrontal hemodynamic response, Stroop color-word task

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in children and adolescents with high pervasiveness into adulthood. The prevalence of ADHD in adulthood is estimated at approximately 4% [1, 2]. The symptoms are often severe and may cause serious difficulties in the daily life of affected individuals [3]. Given the great morbidity associated with the disorder, including [4].persistent neuropsychological impairments determining theunderlying neurobiology of ADHD is of great importance. Recent reviews of data from neuroimaging, neuropsychological, genetic, and neurochemical studies have generally implicated frontostriatal network abnormalities as the likely cause of ADHD. However, recent findings have suggested that, for some individuals, ADHD may not arise until adolescence or adulthood and may therefore be associated with different risk factors and outcomes than childhood ADHD [5, 6].

Studies have shown that ADHD is characterised by multiple functional and structural neural network abnormalities including most prominently fronto-striatal, but also fronto-parieto-temporal, fronto-cerebellar and even fronto-limbic networks. Evidence from longitudinal structural imaging studies has shown that ADHD is characterised by a delay in structural brain maturation. In a meta-analysis of functional imaging studies in children and adults, Hart et al [7] found ADHD-related hypoactivation in the right inferior frontal cortex, supplementary motor area, anterior cingulate cortex, and

striato-thalamic areas when pooling studies on inhibition, and found ADHD-related hypoactivation in the right dorsolateral prefrontal cortex, posterior basal ganglia, and thalamic and parietal regions when focusing on attention tasks. In another meta analysis focused on timing tasks, including studies in both children and adults, Hart et al [8] found ADHD related hypoactivation in the cerebellar vermis, left inferior prefrontal cortex and insula, and left supramarginal gyrus extending into left superior temporal and postcentral gyri. Lee et al [9] reported that children with clinical ADHD show reduced orbitofrontal regional cerebral blood flow on single photon emission computed tomography (SPECT) scans. Functional magnetic resonance imaging (fMRI) also shows dysfunction in the prefrontal cortex in children with ADHD [10, 11]. Other work shows hypoperfusion in orbitofrontal regions by SPECT scans of both children and adults with clinical ADHD [12.14]. Studies of adult ADHD patients using positron-emission tomography (PET) have found glucose metabolism reduction in the premotor cortex and the superior prefrontal cortex [15]. Additionally, one study of adult ADHD patients using PET showed significantly increased dopamine active transporter binding in the right caudate [16].

However, functional brain imaging methodologies, such as PET, SPECT, and fMRI have the disadvantage of requiring large apparatuses, which precludes their use in a bedside setting for diagnostic and treatment purposes. Additionally, these functional brain imaging methodologies do not offer high temporal resolution. By contrast, multi-channel near-infrared spectroscopy (NIRS) systems have recently been developed to allow non-invasive and bedside functional mapping of the cerebral cortex, with high temporal resolution [17-19].

Multi-channel NIRS enables the noninvasive detection of neural activity near the surface of the brain using near-infrared light [20, 21]. It measures alterations in hemoglobin (oxy-Hb) deoxygenated hemoglobin (deoxv-Hb) oxygenated and concentrations in micro-blood vessels on the brain surface. Local increases in the concentration of oxy-Hb and decreases in the concentration of deoxy-Hb are indicators of cortical activity [21, 22]. In addition, changes in the concentration of oxy-Hb have been associated with changes in regional cerebral blood volume, using a combination of PET and NIRS measurements [23, 24]. NIRS is a neuroimaging modality that is particularly suitable for use in psychiatric patients for several reasons [25]. First, the subject can be examined in a natural sitting position, without any surrounding distraction. Second, the cost is much lower than other neuroimaging modalities. Third, because NIRS is relatively insensitive to motion artifact, it can be applied to experiments that might cause some motion of the subjects such as vocalization. Fourth, the setup is very easy. Fifth, the high temporal resolution of NIRS is useful in characterizing the time course of prefrontal activity of psychiatric disorders [26, 27]. Accordingly, NIRS has been used to assess brain functions in many psychiatric disorders, including schizophrenia, depression, bipolar disorder, obsessive-compulsive disorder, post traumatic stress

disorder, dementia, pervasive developmental disorders, and ADHD [25-35].

In pediatric ADHD, reduced prefrontal hemodynamic responses have been observed with NIRS. Negoro et al [35] examined reduced prefrontal hemodynamic response in ADHD children as measured by NIRS and determined cerebral hemodynamic changes in response to the Stroop color-word task in 20 children with ADHD and 20 healthy ageand sex-matched controls. They showed that the oxy-Hb changes in the ADHD group were significantly smaller than those in the control group in the inferior prefrontal cortex during performance of the Stroop color-word task.

The Stroop color-word task is one of the most commonly used tools for determining attentional problems. It is also a test of executive function and working memory. The Stroop color-word task measures mainly a person's selective attention and an effect of interference. Previous review and meta-analysis revealed abnormal Stroop interference in ADHD [36]. Thus, it is significant to examine the characteristics of prefrontal hemodynamic responses in adults with ADHD using NIRS during the Stroop color-word task. In addition to these reasons, we used the Stroop color-word task for the following reasons. First, the inferior frontal gyrus has been described as one of the regions most strongly related to Stroop interference [37]. Second, in the NIRS study using the same task, Okada et al [29] concluded that the word reading task and incongruent color naming task produced suitable prefrontal brain activation in healthy adults.

Based on previous studies which showed dysfunction of the prefrontal cortex by other

neuroimaging modalities, we could predict that adults with ADHD had reduced prefrontal hemodynamic responses. However, there are few studies by multi-channel NIRS to examine prefrontal hemodynamic responses in adult ADHD. In the present study, we hypothesized that adults with ADHD would have reduced prefrontal hemodynamic responses as measured by NIRS. Therefore, in this study, we used multi-channel NIRS machines to examine the characteristics of prefrontal hemodynamic responses during the Stroop color-word task in adult ADHD patients and in age- and sex-matched control subjects.

Methods

Participants

Twelve subjects (4 males and 8 females), aged 21-47 years and diagnosed with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) [38], were compared with 12 age-, sex-, and intelligence quotient (IQ)-matched healthy control subjects (4 males and 8 females), aged 20-46 years (Table 1).

The subjects with ADHD, who had no history of previous psychiatric disorder treatment, consulted one of the experienced psychiatrists at the Department of Psychiatry of Nara Medical University with a chief complaint of attention deficit, hyperactivity, or impulsiveness. They underwent a standard clinical assessment comprising a psychiatric evaluation, a standard diagnostic interview, and the taking of a medical history by the experienced psychiatrist. Two experienced psychiatrists confirmed the diagnosis of ADHD in accordance with the DSM-5 [38], and confirmed the presence of ADHD symptoms prior to the age of 12. Intellectual level was assessed with the Wechsler Adult Intelligence Scale–Third Edition by the psychologist, and patients whose full-scale IQ (FIQ) scores were below 70 were excluded. In addition, we excluded patients who presented a comorbid psychiatric disorder defined by the DSM-5, a neurodevelopmental disorder (including autism spectrum disorder), a neurological disorder, a head injury, a serious medical condition or a history of substance abuse/dependence; two patients with autism spectrum disorder and two patients with bipolar disorder were excluded. Finally, 12 subjects with ADHD, who had no previous medication, were enrolled in this study.

Healthy control subjects were recruited via local print advertising. They also underwent a standard clinical assessment comprising a psychiatric evaluation, a standard diagnostic interview, and the taking of a medical history by the experienced psychiatrist. Intellectual level was assessed with the Wechsler Adult Intelligence Scale-Third Edition by the psychologist. Finally, 12 healthy control subjects, who did not have confirmed ADHD and who had no current or past history of psychiatric or neurological disorder, were enrolled in the present study as well.

All subjects were right-handed and Japanese. This study was approved by the Institutional Review Board at the Nara Medical University. Written informed consent

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was obtained from all subjects before the study.

Assessment of ADHD symptoms

The Conners' Adult ADHD Rating Scale-Investigator Rated (CAARS-Inv): Screening Version was used to evaluate ADHD symptoms in the participants. The CAARS-Inv: Screening Version is a 30-item, investigator-rated scale that measures the severity of ADHD symptoms. Each item is measured on a four-point scale ranging from 0 (not at all, never) to 3 (very much, very frequently), and separate scores can be derived for the Inattention subscale (9 items), the Hyperactivity/Impulsivity subscale (9 items), and the ADHD Index subscale (12 items). The CAARS-Inv total score is the sum of the Inattention subscale score and the Hyperactivity/Impulsivity subscale score, with possible scores ranging from 0 to 54.

ADHD subjects underwent assessment on the CAARS-Inv (Table 1) on the same day as the NIRS element of the study. As shown in Table 1, the mean CAARS-Inv total score was 28.42 (SD, 8.11), ranging from 16 to 48.

Stroop Color-Word Task

The traditional Stroop task comprises a word reading task, an incongruent color naming task and a color naming task. Here, however, we reproduced the Stroop task according to an alternative method that has been previously described [39]. The Stroop color-word

task consisted of two pages: each page had 100 items in five columns of 20 items each and the page size was 210×297 mm. On the first page, the words RED, GREEN, and BLUE were printed in black ink. On the second page, the words RED, GREEN, and BLUE were printed in red, green, or blue ink, with the limitation that the word meaning and ink color could not match. The items on both pages were randomly distributed, with the exception that no item could appear directly after the same item within a column.

Before the task, the examiners instructed the participants as follows: "This is to test how quickly you can read the words on the first page, and say the colors of the words on the second page. After we say 'begin,' please read the words in the columns, starting at the top left, and say the words/colors as quickly as you can. After you finish reading the words in the first column, go on to the next column, and so on. After you have read the words on the first page for 45 s, we will turn the page. Please repeat this procedure for the second page."

The entire Stroop color-word task sequence consisted of three cycles of 45-s spent reading the first page, followed by 45-s spent reading the second page (the color-word task). The task ended with 45-s spent reading the first page, which we designated as the baseline task (Fig. 1 (C)). We recorded the number of correct answers in each cycle. Examiners who were blind to the diagnoses of the participants administered the Stroop color-word task.

The Stroop task used in this study was different to the traditional Stroop task. We

excluded the color naming task (part of the traditional Stroop task) because we needed only two tasks (baseline task and activation task) for our NIRS study. At the NIRS study, it has been shown previously that suitable brain activation in healthy adults is elicited by using the word reading task and incongruent color naming task [29, 40], suggesting that this was an appropriate approach for the present study.

NIRS Measurements

Increased oxy-Hb and decreased deoxy-Hb, as measured by NIRS, have been shown to reflect cortical activation. In animal studies, because the direction of change in deoxy-Hb is determined by the degree of changes in venous blood oxygenation and volume, oxy-Hb is the most sensitive indicator of regional cerebral blood flow [41]. Thus, we determined to focus on changes in oxy-Hb. We measured oxy-Hb using a 24-channel NIRS machine (Hitachi ETG-4000, Hitachi Medical Corporation, Tokyo, Japan). We measured the absorption of two wavelengths of near-infrared light (760 and 840 nm). We analyzed the optical data based on the modified Beer-Lambelt Law [42] as previously described [17]. This method enabled us to calculate signals reflecting the oxy-Hb, deoxy-Hb, and total-Hb signal changes. The scale of the hemoglobin quantity is $mmol \times mm$, which means that all concentration changes depend on the path length of the near-infrared light. The recording channels resided in the optical path in the brain between neighbouring pairs of emitters and detectors (Fig. 1 (A)). The inter-probe

intervals of the machine were 3.0 cm, and previous reports have established that the machine measures at a point 2–3 cm beneath the scalp, ie the surface of the cerebral cortex [31, 43].

The participants were asked to adopt a natural sitting position for the NIRS measurements. The distance between the eyes of each participant and the paper on which the items were listed was between 30 cm to 40 cm. The NIRS probes were placed on the scalp over the prefrontal brain regions, and arranged to measure the relative changes in Hb concentration at 24 measurement points that made up an 8 × 8 cm square. The lowest probes were positioned along the Fp1-Fp2 line according to the international 10/20 system commonly used in electroencephalography. The probe positions and measurement points on the cerebral cortex were confirmed by overlaying the probe positions on a three-dimensionally reconstructed MRI scan of the cerebral cortex of a representative participant from the control group (Fig. 1 (B)). The absorption of near-infrared light was measured with a time resolution of 0.1 s. The data were analyzed using the "integral mode": the pre-task line was determined as the mean across the 10 s just before the task period, the post-task line was determined as the mean across the 25 s immediately after the task period, and using two line the baseline was drawn by least-squares method, and then the oxy-Hb changes for three times of activation task was averaged. Moving average methods were used to exclude short-term motion artifacts in the analyzed data (moving average window, 5 s).

We attempted to exclude motion artifacts by closely monitoring artifact-evoking body movements, such as neck movements, biting, and blinking (identified as being the most influential in a preliminary artifact-evoking study), and by instructing the participants to avoid these movements during the NIRS measurements. Examiners were blind to diagnoses of the participants.

Statistical Analyses

Oxy-Hb changes were compared between each of the two groups with Student's t-tests using the grand average waveforms every 0.1 s in each channel. This analysis enabled more detailed comparison of oxy-Hb changes along the time course of the task. Data analyses were conducted using MATLAB 6.5.2 (Mathworks, Natick, MA, USA) and Topo Signal Processing type-G version 2.05 (Hitachi Medical Corporation, Tokyo, Japan). OT-A4 version 1.63 K (Hitachi Medical Corporation, Tokyo, Japan) was used for the overlap display of the grand average waveforms in both groups in Fig. 2 and was also used to calculate mean oxy-Hb measurements in Table 2. Since we performed 24 paired t-tests, a Bonferroni correction for multiple comparisons was applied. PASW Statistics 18.0 J for Windows (SPSS, Tokyo, Japan) was used for statistical analysis.

Results

Demographic data

Demographic and clinical data are shown in Table 1. Age, sex and FIQ did not differ significantly across patients with adult ADHD and healthy controls (t=0.11, df=22, P=0.92; chi-square=0.00, df=1, P=1.00; t=0.23, df=22, P=0.82). The mean CAARS-Inv total score of adult ADHD subjects was 28.42 (SD, 8.11; range, 16 to 48). There were no significant differences in the SCWC-1, SCWC-2, and SCWC-3 scores between the two groups (t=-0.12, df=22, P=0.90; t=-0.57, df=22, P=0.58; t=-0.52, df=22, P=0.61).

NIRS data of the subjects during the Stroop color word task

The grand average waveforms of oxy-Hb concentration changes during the Stroop color-word task in both groups can be seen in Fig. 2. The grand average waveforms of oxy-Hb concentration change in the control group increased during the task period, while those of the ADHD group did not change well. The difference of mean oxy-Hb measurements between task and post-task periods in the 24 channels can be seen in Table 2. Group differences were tested with Bonferroni correction. Between task and post-task periods, the mean oxy-Hb difference of the control group was significantly larger than that of the ADHD group in channels 11, 16, 18, 21, 22, 23 and 24. A topographic representation of the t-values of oxy-Hb comparison between the ADHD group and the control group during the Stroop color-word task is shown in Fig. 3. The oxy-Hb changes in the control group were significantly increased greater compared to those seen in the ADHD group during the task period in the prefrontal cortex. Correlation between the severity of ADHD symptoms and NIRS data

Spearman's ρ correlations between the CAARS-Inv total score and the oxy-Hb changes at 7 channels (Ch 11, Ch 16, Ch 18, Ch 21, Ch 22, Ch 23 and Ch 24) are shown in Table 3. At Ch 16, Ch 21, Ch 23 and Ch 24 of the ADHD group, there were negative correlations between the CAARS-Inv total score and the oxy-Hb changes. At Ch 11, Ch 18 and Ch 22 of the ADHD group, there were no correlations between the CAARS-Inv total score and the oxy-Hb changes.

Discussion

To the best of our knowledge, there are no other studies using the Stroop task to examine prefrontal hemodynamic responses in adult ADHD. We found that oxy-Hb changes in the prefrontal cortices of 12 treatment-naïve adult ADHD participants during the Stroop color-word task were significantly smaller than those in 12 healthy control subjects. These results were in line with our hypotheses, providing support for the proposed prefrontal dysfunction in adults with ADHD identified by other imaging modalities, such as SPECT, PET and fMRI. Amen and Carmichael reported that children and adolescents with ADHD showed decreased perfusion in the prefrontal cortex as measured by SPECT [12]. In another SPECT study, Amen et al [13] reported that patients over the age of 50 with ADHD had significantly lower cortical activity, particularly in the frontal pole cortex, orbitofrontal cortex, and parietal cortex. Studies of adult ADHD patients using PET have suggested glucose metabolism reduction in the premotor cortex and the superior prefrontal cortex [15], and relative lack of task-related frontal activations during performance of a working memory task [44]. Evidence from fMRI studies suggests that there are frontal dysfunctions localized to ventrolateral and dorsolateral prefrontal cortex, as well as in the dorsal anterior cingulate cortex, during performance of a Stroop task by adult patients with ADHD [45, 46]. A meta-analysis of fMRI studies of adult ADHD revealed that almost all (97%) hypoactivated voxels were located in a frontoparietal network [47]. In adult ADHD, reduced prefrontal hemodynamic responses have been measured by NIRS [48, 49]. Schecklmann et al [49] found reduced bilateral activation of the inferior frontal cortex in adults with ADHD compared with healthy adults as measured by NIRS during a working memory and response inhibition task. In this study, additionally, there were negative correlations between the CAARS-Inv total score and the oxy-Hb changes at channels 16, 21, 23, and 24 of the ADHD group, ie lower brain activity was associated with severity of ADHD symptoms. Multi-channel NIRS systems may therefore be very useful tools to assess the symptoms of ADHD, as well as frontal function.

At channels 11, 16, 18, 21, 22, 23, and 24, adults with ADHD showed significantly smaller oxy-Hb changes than those seen in the healthy controls in the present study. Negoro et al [35] used NIRS to examine reduced prefrontal hemodynamic responses in

pediatric ADHD during the Stroop color-word task, which is the same task used in this study. They reported a lower increase of the oxy-Hb changes at channels 8, 18, 19, 21, and 22 in pediatric ADHD compared to control subjects. These findings are in line with our own: the oxy-Hb changes in the ADHD group were significantly smaller than those in the control group in the inferior prefrontal cortex, which has been described as one of the regions that is most strongly related to Stroop interference [37].

Potential limitations of the present study should be taken into consideration. First, NIRS has disadvantages compared to other modalities [18]: for instance, it enables measurement of Hb concentration changes only as relative values, not as absolute values. We used the Stroop color-word task that had a clear baseline task to overcome these potential problems. Additionally, we measured Hb concentration changes from the activation task to the baseline task and performed the task three times to average potential accidental changes and prevent the participants from becoming tired. The grand average waveforms of oxy-Hb concentration changes in the ADHD group do not show a regional cerebral blood flow decrease during the activation task or a difference between the blood flows during the baseline and activation tasks. Second, spatial resolution for detecting hemodynamic responses from the scalp surface using NIRS is lower than those for fMRI, SPECT and PET. However, abnormal prefrontal hemodynamic responses in individuals with ADHD are certainly detectible by NIRS. Third, several studies have shown that superficial hemodynamic changes such as skin

blood flow can affect the prefrontal NIRS hemoglobin signals [50, 51]. The present findings could be skin blood flow. However, Sato et al [52] conducted simultaneous NIRS, fMRI, and laser Doppler flowmeter measurements to determine whether prefrontal NIRS hemoglobin signals reflect cortical activity rather than superficial effects. They concluded that NIRS can be used to measure hemodynamic signals originating from prefrontal cortex activation. Fourth, the sample size was small, although the 12 adults with ADHD were treatment-naïve and none of them had comorbid psychiatric, neurodevelopmental or neurological disorder. Future research is needed, with larger sample sizes. Fifth, the range of their age was wide. However, it was thought that the influence was small because there were no correlations between the age and the oxy-Hb changes, and between the age and the performance of the Stroop color-word task. Sixth, adults with ADHD, who were confirmed the presence of ADHD symptoms prior to age 12 years, participated in the present study, although there is the late-onset adult ADHD that do not have ADHD symptoms prior to age 12 years. In the future study, it is needed to compare the prefrontal hemodynamic response between the present adult ADHD and the late-onset adult ADHD.

Conclusion

To the best of our knowledge, this is the first NIRS study using the Stroop task to examine prefrontal hemodynamic response in adult ADHD. We found that the oxy-Hb

changes in the ADHD group were significantly smaller than those in the control group in the inferior prefrontal cortex. We also found that smaller oxy-Hb changes were associated with severer ADHD symptom. Multi-channel NIRS system appears to be a very useful tools for assessing the symptom of ADHD as well as frontal function, as it enables non-invasive functional mapping of the cerebral cortex and has much shorter measurement times (about 5 min) compared with other functional brain imaging methodologies.

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Disclosure Statement

All the authors declare that they have no conflicts of interest.

Author Contributions

SU was involved in the collection of the data and wrote the first draft of the manuscript. TO, JI, KY, HY, NK and TK supervised the entire project, were critically involved in the

design, and contributed to the editing of the final manuscript. All authors have read and approved the final manuscript.

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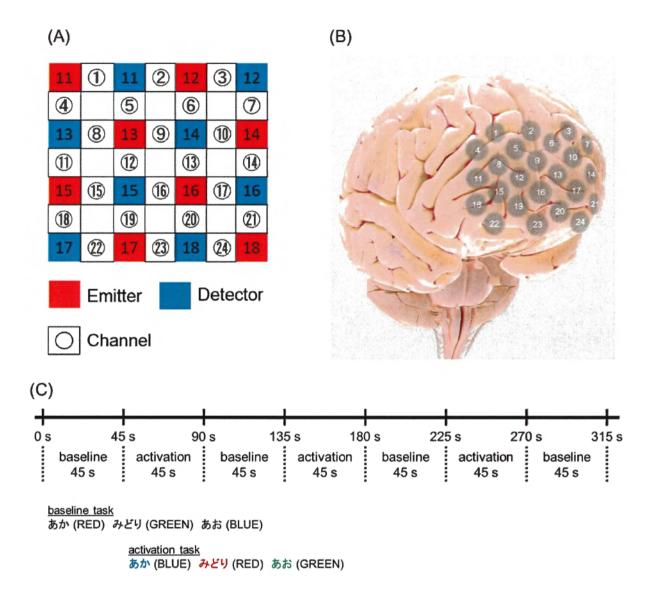


Fig. 1. Location of the 24 channels in the near-infrared spectroscopy instrument. (A) Arrangement of emitters and detectors according to the definition of each channel. (B) Corresponding anatomical site of each channel. (C) Timeline of stimulus presentations. The baseline task is the word reading task. The activation is the incongruent color naming task.

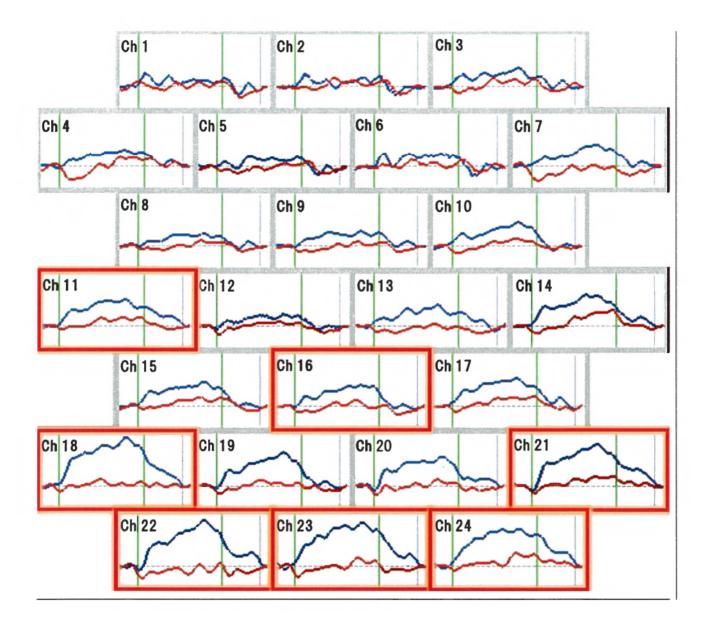


Fig. 2. Grand average waveforms showing changes in oxyhemoglobin (oxy-Hb) during the Stroop color-word task in both groups (red lines denote the ADHD group and blue lines denote the control group). The task occurred in the interval represented by the green lines (the first line indicates the beginning of the task; the second line indicates the end of the task).

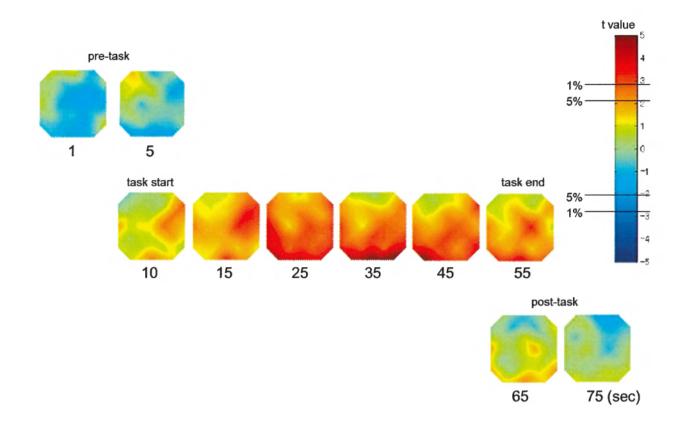


Fig. 3. Topographic representation of t values corresponding to the difference in oxyhemoglobin (oxy-Hb) between the control group and the attention-deficit/hyperactivity disorder (ADHD) group during the Stroop color-word task. The t values of oxy-Hb for the control and ADHD groups are presented as a topographic map along the time course of the task (from top to bottom). The red, green, and blue areas in the maps indicate positive, zero, and negative t values, with ±2.8 and ±2.1 for 1% and 5% statistical significance levels, respectively.

Table 1. Participant characteristics

	ADHD Control		<i>P</i> -value	
	mean(SD)	mean(SD)	<i>F</i> -value	
Number [sex ratio:M:F]	12 [4:8]	12 [4:8]	1.00	
Age(years)	32.50(9.13)	32.08(10.19)	0.92	
FIQ(WAIS-III)	99.75(14.89)	98.58(9.72)	0.82	
CAARS total score	28.42(8.11)			
SCWC-1	42.42(5.98)	42.75(7.15)	0.90	
SCWC-2	44.50(7.35)	46.33(8.50)	0.58	
SCWC-3	42.25(12.69)	44.50(8.12)	0.61	

Group differences tested with Student's t-test

ADHD, attention deficit hyperactivity disorder; M, male; F, female; FIQ (WAIS-III), full-scale IQ score of the Wechsler Intelligence Scale for Children-Third Edition; CAARS, Conners' Adult ADHD Rating Scales; SCWC-1, Stroop color-word task number of correct answers first time; SCWC-2, Stroop color-word task number of correct answers second time; SCWC-3, Stroop color-word task number of correct answers third time

	ADHD (mMmm)		Control (r	Control (mMmm)		Bonferroni
	Mean	SD	Mean	SD	<i>t</i> -test	correction
Ch 1	-0.0028	0.0576	0.0171	0.0451	NS	NS
Ch 2	0.0052	0.0527	0.0179	0.0579	NS	NS
Ch 3	0.0058	0.0445	0.0417	0.0882	NS	NS
Ch 4	0.0027	0.0615	0.0470	0.0479	NS	NS
Ch 5	-0.0088	0.0440	0.0186	0.0601	NS	NS
Ch 6	0.0047	0.0452	0.0289	0.0931	NS	NS
Ch 7	-0.0234	0.0525	0.0533	0.0601	*	NS
Ch 8	-0.0016	0.0426	0.0344	0.0630	NS	NS
Ch 9	-0.0052	0.0373	0.0425	0.0550	*	NS
Ch 10	0.0027	0.0260	0.0540	0.0627	*	NS
Ch 11	0.0128	0.0410	0.0814	0.0398	*	**
Ch 12	-0.0020	0.0372	0.0304	0.0499	NS	NS
Ch 13	-0.0139	0.0476	0.0515	0.0552	*	NS
Ch 14	0.0205	0.0320	0.0901	0.0747	*	NS
Ch 15	0.0123	0.0298	0.0650	0.0496	*	NS
Ch 16	-0.0035	0.0304	0.0575	0.0400	*	**
Ch 17	0.0148	0.0222	0.0828	0.0574	*	NS
Ch 18	0.0084	0.0643	0.1382	0.0997	*	**
Ch 19	-0.0003	0.0556	0.0819	0.0650	*	NS
Ch 20	-0.0019	0.0472	0.0789	0.0951	*	NS
Ch 21	0.0196	0.0557	0.1213	0.0774	*	**
Ch 22	-0.0212	0.0510	0.1228	0.0588	*	**
Ch 23	-0.0046	0.0433	0.1314	0.0751	*	**
Ch 24	0.0228	0.0571	0.1259	0.0653	*	**

Group differences were tested with Student's *t*-tests and Bonferroni correction for multiple comparisons.

*P < 0.05; **P < Bonferroni-corrected P

Table 3. Correlation between the severity of ADHD symptoms and NIRS data

	Ch 11	Ch 16	Ch 18	Ch21	Ch22	Ch23	Ch24
CAARS total score	-0.489	-0.639 *	-0.032	-0.618 *	-0.073	-0.614 *	-0.614 *

Correlations between the severity of ADHD symptoms and NIRS data tested with Spearman's correlation

test

*P < 0.05