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Research Article

Moderate Exercise Improves Cognitive Performance and Decreases Cortical Activation in Go/No-Go Task

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Abstract

Background: A lot of studies have reported that physical activity has a beneficial influence not only on physical and mental disorders but also on cognitive and brain function. Performance of a go/no-go task improves after exercise. However, few studies have compared neural activity in a go/no-go task performed before and after exercise to identify brain regions that may respond to exercise and underlie this result. Therefore, the purpose of this study was to examine the brain blood flow and compare the cortical activation pattern during a go/no-go task performed before and after exercise.

Method: Fifteen healthy subjects performed a go/no-go task before and after exercise. Functional near-infrared spectroscopy (fNIRS) was used to measure oxygenated hemoglobin concentration at 44 locations over both hemispheres. The exercise was of moderate intensity, defined as 50% of peak oxygen uptake.

Result: The reaction time on the go/no-go task was significantly faster after exercise than before. The oxygenated hemoglobin concentration quantified across the whole brain was lower after exercise, and this was the case for go trials and no-go trials. In go trials, the oxygenated hemoglobin concentration in dorsolateral prefrontal cortex and supplementary motor area were significantly lower after exercise.

Conclusion: These results suggest that the dorsolateral prefrontal cortex and supplementary motor area had lower activity in go trials in the go/no-go task performed after exercise than in go trials in the go/no-go task performed before exercise.

Keywords: Near-infrared spectroscopy; oxygenated hemoglobin concentration; brain; cognitive task.

Introduction

Physical activity has been associated with a reduction in the severity of symptoms of a number of physical and mental disorders. Some studies have reported a beneficial influence not only on physical and mental disorders, but also on cognitive and brain function. For example, aerobic and resistance exercise training over several months improved cognitive function and altered brain function [1,2,3].

To examine whether exercise is beneficial for the brain, it is necessary to perform a cognitive task before and after performing exercise. Recent studies provide evidence that an acute bout of moderate exercise improves cognitive performance in a choice reaction task [4], a simple reaction time task [5], and conflict tasks such as the Eriksen flanker task and the Stroop task [6].

Neuroimaging techniques have been used to examine which brain regions exhibit a change in activation in response to exercise. Functional magnetic resonance imaging (fMRI) performed during the performance of a cognitive task that involved behavioral conflict showed that the increase in the cardiorespiratory fitness level after a 6-month aerobic training program was associated with greater activation of the prefrontal and parietal cortices and significantly lower activity in the anterior cingulate cortex [7]. Previous studies have used the blood-oxygen-level-dependent signal obtained with fMRI to measure regional cerebral blood flow or local concentration changes in paramagnetic deoxy-hemoglobin, and this has rapidly become the gold standard for in vivo imaging of human brain activity, due in large part to the relatively high spatial resolution afforded by this technique. However, fMRI also presents several challenges such as high sensitivity to participant motion, a loud, restrictive environment, low temporal resolution, and relatively high cost [8]. Functional near-infrared spectroscopy (fNIRS) is a

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functional brain imaging technique that measures cerebral blood volume changes through oxygenated hemoglobin (oxy-Hb), deoxygenated hemoglobin (deoxy-Hb) , and total hemoglobin concentrations. The basic principle of fNIRS lies in the different wavelength of near infrared light being translated to changes in oxy-Hb and deoxy-Hb concentration. The principles of fNIRS have been extensively described and appear suitable to assess the relation between cortical activation and hemodynamic response with a high sampling rate [9, 10,11]. In contrast to other neuroimaging methods, fNIRS requires only compact experimental systems, and can be easily installed in a small room. This is advantageous for our study as it allows for an environment in which exercise intensity can be strictly controlled. In addition, on-site neuroimaging allows precise control over the interval between exercise and brain measurement. fNIRS is noninvasive, and can be conducted in a natural setting, with the subject in a sitting position, with eyes open and speaking. As such, fNIRS is well suited to functional neuroimaging studies. fNIRS, therefore, allows the measurement of distinct regional cerebral responses and typical hemodynamic responses during functional tasks.

Using these neuroimaging techniques, the brain regions that are activated during a cognitive task are measured and the activation level can be compared before and after exercise. The go/no-go task is a cognitive task that can be used to examine the prefrontal cortex and is frequently used to investigate response inhibition. Response inhibition is an essential executive function implemented by the prefrontal cortex [12,13,14]. However, performance of go/no-go tasks requires a variety of cognitive components in addition to response inhibition. Previous studies have reported that performance of a go/no-go task improved after exercise [15]. However, few studies have used fMRI or fNIRS to identify the brain regions that exhibited a change in activation to bring about these results.

The purpose of this study was to use fNIRS to examine brain blood flow and compare the cortical activation pattern during a go/no-go task performed before and after exercise. These results will allow us to investigate in detail the influence that exercise has on the brain.

Method

Subject

Fifteen healthy right-handed participants (age 21.7 ± 2.4 years, nine men age 21.8 ± 2.2 years and six women age 21.6 ± 3.0 years) were recruited as volunteer subjects. No subjects had a history of neurological, major medical, or physical disorders, and none were taking medication at the time of the study. Prior to participating in the experiment, all subjects gave their written informed consent. This study was approved by the Ethics Committee of the School of Medicine, Shinshu University, Japan.

Go/No-Go Task

In the go/no-go task subjects were instructed to squeeze a rubber ball in response to a red light (go task) but not in response to a yellow light (no-go task). In this paper, the term "number of errors" indicates an incorrect response whereby the subjects did not squeeze the rubber ball when it should have been squeezed and the subjects did squeeze the rubber ball when it was should not have been squeezed.

Study Protocol

First, we measured oxy-Hb while subjects performed the go task and no-go task using fNIRS. In go/no-go task, the experiment time was 7 min 30 s including rest periods. It consists of eleven rest periods and five go task and five no-go task in the following sequence: 40 s rest, then followed by 10 series of 1 s task plus 40 rest. The time between consecutive stimuli was 40 s to allow brain blood flow return to baseline. The sequence of the lights red or yellow was randomly generated by the program, but always consists of five red and five yellow lights.

After subjects performed the go/no-go task, they exercised on a bicycle ergometer for 20 min at 50% of peak oxygen intake (VO_{2peak}). We assessed the VO_{2peak} for each subject and defined moderate exercise intensity as 50% of VO_{2peak}, which was calculated using the Karvonen formula [16]. Exercise intensity was a critical factor to control in this study. Behavioral studies have shown that the effects of acute exercise on cognitive performance and brain response differ depending on the exercise intensity. Exercise intensity was a critical factor to control in this study. The best improvements are generally achieved with moderate-intensity exercise [17]. However, exercise of the same absolute intensity will have a different impact on each subject depending on their fitness level. Therefore, we defined exercise intensity as 50% of VO_{2peak} for each subjects.

After subjects exercised on the bicycle ergometer they performed go/no-go task again while fNIRS was performed to measure oxy-Hb. Reaction time on the go/no-go task and the number of errors were also measured.

fNIRS Data Acquisition

fNIRS was performed throughout the go/no-go task using a multi-channel near-infrared spectroscope (OMM-3006, Shimadzu, Kyoto, Japan). Subjects wore a head cap that covered the whole head. The head cap contained 15 optodes (corresponding to 22 channels) over each hemisphere, including C3/C4 of the international 10/20 system in the caudal portion (9 × 9-cm square area). Each channel consisted of one emitter optode (red) and one detector optode (white), located 3 cm apart. The locations of the channels are shown in Fig 1. The sampling rate for each channel was approximately 8 Hz. We focused on oxy-Hb concentration, as this is reported to be sensitive to neuro-hemodynamic relations [18,19]. Changes in oxy-Hb concentration were detected using three wavelengths (780, 805, and 830 nm) of near-infrared light with a pulse width of 5 ms. The mean total irradiation power was less 1 mW. The change in oxy-Hb concentration from the control baseline was estimated using a modified Lambert-Beer law [20]. The depth of light penetration from the surface of the brain in adult humans has been reported to range from 0.5 to 2 cm [21].

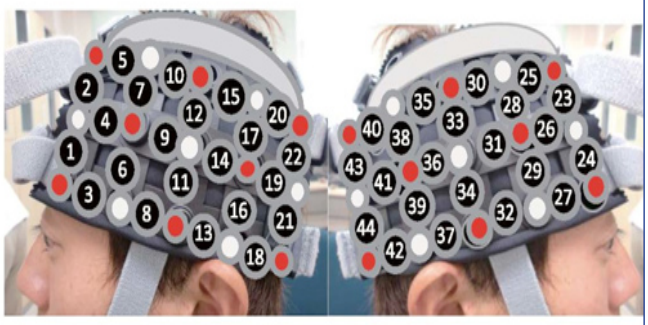

Fig1. Location of near-infrared spectroscopy probes on the scalp. Near-infrared spectroscopy data were obtained using a 44-channel spectrometer. Subjects wore a head cap such that channels 1–22 were located over the left hemisphere (A) and channels 23–44 were located over the right hemisphere (B).

fNIRS Data Analysis

Analyses of the fNIRS data were performed with a least-squares estimation using a general linear model [22, 23]. The time course of oxy-Hb in the go/no-go task was correlated with the design matrix using a boxcar function with two possible values: 1 and -1. The model equation, including the observed data, the design matrix and the error term, was convoluted with a Gaussian kernel [24]. The design matrix employed a 6-s delayed boxcar function convolved with a Gaussian kernel of dispersion of 6-s full-width at half-maximum, which modeled the temporal correlation in the fNIRS time series. The task periods were contrasted against the sedentary periods for each go/no-go task using a two-tailed t test. Oxy-Hb in each channel during the go/no-go task was calculated using a two tailed-t test.

Statistical Analysis

Oxy-Hb was compared across the pre and post exercise go/no-go tasks using a paired-t test. Reaction time and the number of errors were also compared across the pre and post exercise tasks using a paired-t test. The level of significance was set at $p < 0.05$. Statistical analyses were performed using the SPSS statistical package (SPSS Inc., Chicago, USA).

Results

fNIRS was performed while subjects performed a go/no-go task before and after exercise. Oxy-Hb concentration was measured at 44 locations over the two hemispheres during the go/no-go task and compared across the tasks performed before and after exercise.

Reaction Time and the Number of Errors

We first examined whether performance of the go/no-go task improved after exercise. Reaction times were significantly faster after exercise (310.2 ± 85.7 ms) than before exercise (351.9 ± 94.7 ms ; $p < 0.01$). The number of errors was similar before (0.7 ± 0.8) and after (0.2 ± 0.6) exercise ($p = 0.06$, Table 1).

	Before exercise (mean ± SD)	After exercise (mean ± SD)	p-value
Reaction time (ms)	351.9 ± 94.7	310.2 ± 85.7	0.003
Number of errors	0.7 ± 0.8	0.2 ± 0.6	0.055

Table 1. Reaction time and the number of errors in the go/no-go task performed before and after exercise.

Oxy-Hb measured by fNIRS

In each of the 15 subjects, oxy-Hb in the cerebral cortex was measured by fNIRS during the go/no-go task. Measurement points were 22 channels in the left hemisphere and 22 channels in the right hemisphere. Oxy-Hb was compared across the pre and post exercise go/no-go tasks using a paired- t test. In go trials, oxy-Hb was significantly lower after exercise (0.000620 ± 0.001085 mmol/L·cm) than before exercise (0.001155 ± 0.000859 mmol/L·cm; $p < 0.001$; Fig. 2).

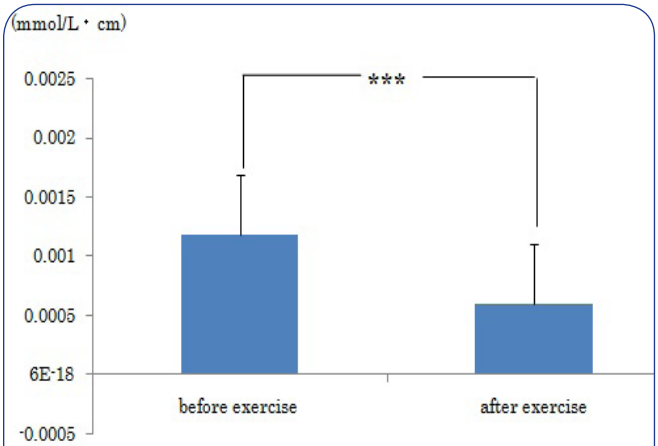

Fig2. The change in oxy-Hb in go trials of the go/no-go task performed before and after exercise. *** p<0.001.

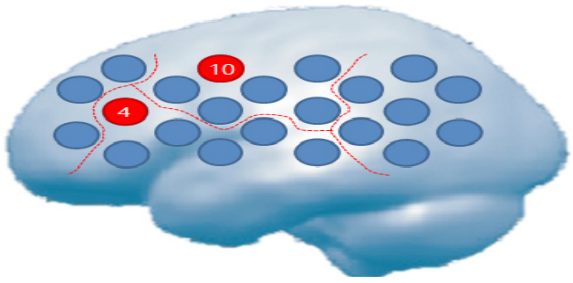

Fig4. Schematic showing the channels in which there was a main effect of setting on oxy-Hb during the go/no-go task. This is Left hemisphere. Channel 4 was located dorsolateral prefrontal cortex and 10 was located supplementary motor area.

In no-go trials, oxy-Hb was significantly lower after exercise (-0.000026 ± 0.000782 mmol/L·cm) than before exercise (0.000563 ± 0.001138 mmol/L·cm, $p < 0.05$; Fig. 3, Table 2).

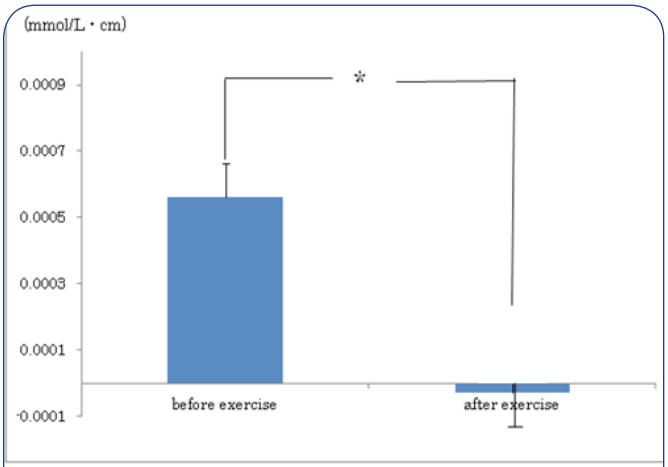

Fig3. The change in oxy-Hb in no-go trials of the go/no-go task performed before and after exercise. * p<0.05.

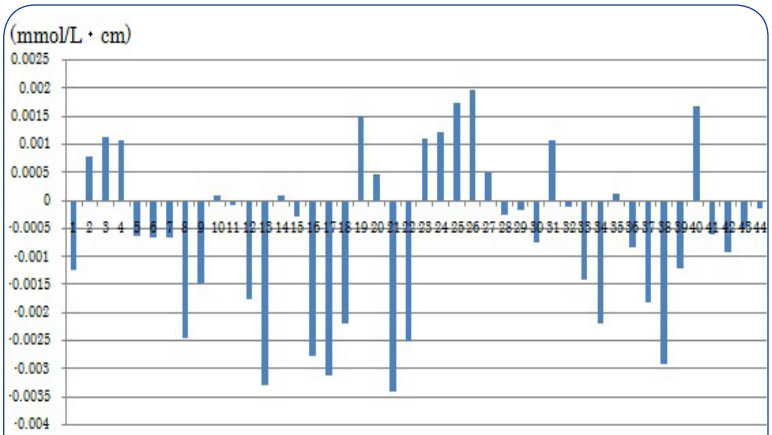

Fig6. The difference in the change in oxy-Hb in no-go trials from pre to post exercise. Oxy-Hb was not significantly different from pre to post exercise in any channel.

	Before exercise (mean ± SD)	After exercise (mean ± SD)	p-value
Go trials (mmol/L 'cm)	0.001155 ± 0.000859	0.000620 ± 0.001085	0.0008
No-go trials (mmol/L 'cm)	0.000563 ± 0.001138	-0.000026 ± 0.000782	0.0111

Table 2. The change in oxy-Hb in go and no-go trials performed before and after exercise.

To examine the location of the changes in oxy-Hb, we analyzed each channel individually of oxy-Hb. In go trials, oxy-Hb was significantly lower after exercise than before exercise in two channels in the left hemisphere: channel 4 (-0.00075 ± 0.002138 mmol/L·cm vs. 0.001224 ± 0.002577 mmol/L·cm, $p < 0.05$) and channel 10 (0.000538 ± 0.002358 mmol/L·cm vs. 0.00293 ± 0.003487 mmol/L·cm, $p < 0.05$). These channels were located over dorsolateral prefrontal cortex (DLPFC) and supplementary motor area (SMA) (Fig. 4). In no-go trials, oxy-Hb was not significantly lower after exercise than before exercise in any channel (Figs. 5 and 6).

Discussion

In this study, we used fNIRS to examine the difference in oxy-Hb concentration during a go/no-go task performed before and after exercise. First, we assessed the effect of an acute bout of moderate exercise on go/no-go task. After the subjects exercised on a bicycle ergometer for 20 min at 50% VO_{2peak} the reaction time on the go/no-go task significantly improved with no change in the number of errors.

One study of a two-year health program reported that go/no-go task reaction time increased significantly and the number of errors decreased significantly after the first year of continuous exercise in which participants performed an average of 6,552 steps a day. The reaction time and number of errors improved again after the second year of the study, in which participants performed walking exercise (an average of 7,170 steps per day) and 2 h of weight training per week [15]. Another study examined whether an aquatic exercise intervention that involved aerobic exercise and was performed twice a week for 90 min per session influenced restraint inhibition

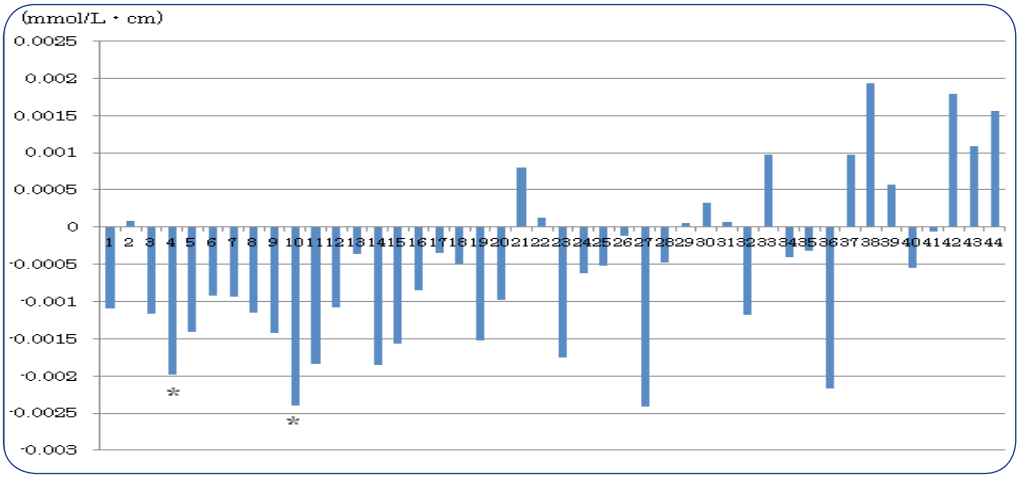

Fig5. The difference in the change in oxy-Hb in go trials from pre to post exercise. Oxy-Hb was significantly lower after exercise than before exercise in channels 4 and 10. *p<0.05.

in children with attention deficit hyperactivity disorder (ADHD). Thirty participants performed a go/no-go task before and after the 8-week exercise intervention or a control intervention. This intervention caused significant improvements in reaction time and number of errors in case of both go and no-go task in the exercise group [25]. These results are consistent with our finding that exercise enhanced performed of the go/no-go task.

A major finding this study was that oxy-Hb concentration quantified over the whole brain was significantly lower after exercise for both go trials and no-go trials. When channels were analyzed individually, oxy-Hb concentration for no-go trials was not significantly lower after exercise. On the other hand, in go trials, oxy-Hb was significantly lower after exercise in DLPFC and SMA (channels 4 and 10). An important function of the DLPFC is the executive functions, such as working memory, cognitive flexibility, planning, inhibition, and abstract reasoning. Possible functions attributed to the SMA include the postural stabilization of the body, the coordination of both sides of the body such as during bimanual action, the control of movements that are internally generated rather than triggered by sensory events, and the control of sequences of movements. These results suggest that, in go trials, activation of the cortical areas associated with the working memory, cognitive flexibility, planning, inhibition, abstract reasoning and the control of movements were lower after exercise than before exercise.

Previous study performed fNIRS while subjects learnt a multi-joint discrete motor task. The task involved tossing a ball connected by a string to a kendama stick (a picking-up movement) and catching the ball in the cup attached to the stick (a catching movement). Participants performed a trial every once every 20 s for 90 trials, and oxy-Hb concentration was measured around the predicted location of the sensorimotor cortices on both hemispheres. The magnitude of the event-related oxy-Hb response to a trial in the left sensorimotor cortex decreased significantly as learning progressed [26]. This is a similar tendency to that observed in our study. An fMRI study also reported a learning-related decrease in activation in the primary motor cortex for a visuomotor coordination task [27]. These results suggest that as subjects learn a motor or visuomotor coordination task, cortical activation decreases, indicating that the subjects perform the task more efficiently therefore need less oxy-Hb.

In the current study, cortical activation in DLPFC and SMA during the go/no-go task decreased after exercise. This change in oxy-Hb might suggest that subjects experienced a similar effect to that reported in these previous studies of motor and visuomotor coordination tasks. The performance of the go/no-go task significantly improved after the moderate exercise. Therefore, we suggest oxy-Hb changed because, after the exercise, the subject became more expert at the task and was able to perform the task more efficiently, therefore requiring less oxy-Hb in DLPFC and SMA than before exercise.

In this study, we chose young participants; however, our previous study showed that health education for the elderly results in similar tendencies towards improved reaction time and number of errors in go/no-go tasks after exercise [15]. These results may be attributable to elderly participants becoming more expert at the task and able to perform the task more efficiently thanks to the exercise regime included in the study's health education program. Therefore, while our current experiment targeted only young participants, the results may also apply to the elderly.

The current study supports the idea that fNIRS and go/no-go tasks may have the potential to be applied for disease prediction or diagnosis. As an example of this for the go/no-go task, one study, which compared the go/no-go results of a control group with those of a dementia group, showed that the number of errors, where the subjects did not squeeze the rubber ball when they should have, was significantly higher in the dementia group than in the control group [28]. A go/no-go task does not take more time than a conventional screening test to diagnose dementia, and task performance could be expected to serve as a screening test to distinguish dementia patients from healthy individuals.

As an example of this for fNIRS, several fNIRS studies have compared findings for patients with Alzheimer's disease (AD) with those for healthy controls. AD studies have reported a reduction of prefrontal oxygenation in both the frontal and parietal lobes in AD groups during verbal fluency tasks [29, 30]. In addition, another AD study found activation deficits in the parietal cortex during a visuospatial task in an AD group [31]. Similarly, fNIRS studies of late-life depression reported significantly less activation in the prefrontal cortex in AD patients [32], and several other studies have reported hypofrontality [33,34,35]. Further, there is a study that made a comparison between oxy-Hb in the frontal and parietal cortices in late-life depression and that in AD during two tasks: a verbal fluency task and a visuospatial task. The results of this study showed that oxy-Hb was significantly lower in the depressed group than in the AD group, and significant differences were observed in the parietal cortex [36]. Therefore, fNIRS can detect differences in brain activation between patients with late-life depression and those with AD, making fNIRS is a promising tool for a differential diagnosis of late-life depression and AD.

In the present study, cortical activation was significantly lower after exercise; this result reveals the potential of fNIRS measurements to be applied as part of a screening test in the future.

Conclusion

The purpose of this study was to examine the brain blood flow and compare the cortical activation pattern during a go/no-go task performed before and after exercise. The exercise was cycling on a bicycle ergometer for 20 min at 50% VO_{2peak}. The results showed that the acute bout of moderate-intensity exercise significantly improved performance of the go/no-go task and decreased oxy-Hb in DLPFC and SMA during go trials. We suggest that the decrease in activation of DLPFC and SMA reflects the improvement in reaction time on the go/no-go task and oxy-Hb changed because, after the exercise, the subject became more expert at the task and

was able to perform the task more efficiently, therefore requiring less oxy-Hb in DLPFC and SMA than before exercise.

Abbreviation

fNIRS: Functional near-infrared spectroscopy; fMRI: Functional near-infrared spectroscopy; oxy-Hb: oxygenated hemoglobin concentration; ADHD: attention deficit hyperactivity disorder; DLPFC: dorsolateral prefrontal cortex; SMA: supplementary motor area; AD: Alzheimer's disease.

Competing interests

The authors declare that they have no competing interests.

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