

Dynamic exercise improves cognitive function in association with increased prefrontal oxygenation

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Abstract The Stroop test was performed before and after ergometer exercise for 15 min at 20, 40, and 60 % of maximum voluntary exercise (EX_{max}), in order to examine whether dynamic exercise is capable of improving cognitive function and whether the changes in regional cerebral blood flow of the prefrontal cortex are associated with the cognitive improvement. Subjects were asked to answer the displayed color of incongruent color words as quickly as possible. The total time period and the number of errors for the Stroop test were measured as an index of cognitive function. The concentrations of oxygenated-hemoglobin (Oxy-Hb) and deoxygenated-hemoglobin (Deoxy-Hb) in the cerebral prefrontal area were measured with near-infrared spectroscopy to determine the changes in regional cerebral blood flow. Ergometer exercise at 40 % of EX_{max} , but not 20 and 60 % of EX_{max} , shortened ($P < 0.05$) the total time period for the Stroop test by 6.6 ± 1.5 % as compared to the time control. In contrast, the number of errors was not altered by exercise at any intensity. The Oxy-Hb in bilateral prefrontal cortices increased during the Stroop test, while the Deoxy-Hb in those areas was

unchanged. Ergometer exercise at 40 % of EX_{max} , but not at 20 and 60 % of EX_{max} , significantly augmented the response in the prefrontal Oxy-Hb during the Stroop test. The magnitude of the increased prefrontal Oxy-Hb response tended to correlate with the reduction in total time period for the Stroop test. Thus, it is likely that ergometer exercise at moderate intensity for 15 min may improve cognitive function through the increased neural activity in the prefrontal cortex.

Keywords Stroop test · Near-infrared spectroscopy · Prefrontal cortex · Dynamic exercise · Cognitive function

Introduction

Physical exercise such as walking and running may lead to definite benefits, not only for physical function but also for cognitive function. It has been demonstrated that the reaction time for the Stroop test and a mental arithmetic test can be improved following ergometer and treadmill exercise at an intensity of 50–75 % of maximum voluntary exercise (EX_{max}) [1–3]. However, Ferris et al. [4] reported no improvement of the reaction time for the Stroop test after ergometer exercise at 55 % of EX_{max} , suggesting that improvement of cognitive function is not always observed following exercise. These controversial results may be attributed to differences in experimental interventions such as exercise duration, the type of cognitive task, and the time interval between the cessation of exercise and the cognitive task. On the other hand, the response time to a simple reaction task has never shown substantial changes following dynamic exercise at any intensity ranging from 50 to 75 % of EX_{max} [1, 3, 4]. Although the previous findings suggested that the

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incongruent complex cognitive response, but not the simple reaction response, may be improved through a bout of dynamic exercise, the effect of exercise on incongruent cognitive function remained to be solved under a well-controlled condition.

The prefrontal cerebral cortex is essentially important for human cognitive function such as visual discrimination, attention, selection, and decision making, etc. [5–7]. When performing a cognitive task, increased neuronal activity of the prefrontal cortex has been detected by using near-infrared spectroscopy (NIRS) [8–10], functional magnetic resonance imaging (fMRI) [11–13], and positron emission tomography [14, 15]. The NIRS studies [9, 10] provided evidence that the concentration of oxygenated-hemoglobin (Oxy-Hb), which reflects regional cerebral blood flow, increased in the prefrontal area during the Stroop test, probably depending on the neuronal activity in the prefrontal area. MacDonald et al. [11], using fMRI, reported that the dorsolateral prefrontal cortex (DLPFC; Brodmann's areas 9 and 46) was more active for naming color words than for reading words in black, whereas the anterior cingulate cortex (ACC; Brodmann's areas 24 and 32) was more active when responding to incongruent stimuli. Milham et al. [16] reported that the DLPFC and ACC were more active for incongruent-eligible trials than those for incongruent-ineligible trials of the Stroop test and for neutral trials.

Both the Stroop test and dynamic exercise lead to increments of the Oxy-Hb in the prefrontal cortex [17–20]. Since the increase in the prefrontal Oxy-Hb lasted for several minutes during the postexercise period [17, 18], it is expected that sustained neural activity in the brain area may lead to improvement of cognitive function. To date, no study has been systematically conducted regarding this issue. We hypothesized that dynamic exercise influences cognitive function examined with the Stroop test, depending on the exercise settings (intensity and duration), and that the improvement of cognitive function by a bout of dynamic exercise is associated with increased neural activity in the prefrontal area. To test this hypothesis, the present study was undertaken: (1) to determine the changes in the performance of Stroop test immediately after ergometer exercise with different intensities and durations; and (2) to examine the relationship between the simultaneous changes in the cognitive score and prefrontal Oxy-Hb. Since the placement of the NIRS probes on the forehead surface between Fp1 and F3 and between Fp2 and F4 corresponds to underlying cortical areas including the DLPFC [21, 22], the Oxy-Hb signal may detect regional cortical oxygenation in the DLPFC and its vicinity.

Methods

Subjects

Thirteen volunteers (8 females and 5 males; age, 23 ± 1 years; height, 162 ± 3 cm; body weight, 54 ± 2 kg) participated in the present study. They did not suffer from any known cardiovascular or psychiatric disease. All subjects gave their informed written consent prior to the experiments. Each subject was instructed not to ingest caffeine and alcohol at least 12 h prior to the experiments. The experimental protocols and procedures were performed in accordance with the Declaration of Helsinki and approved by an Institutional Ethical Committee.

Determination of EX_{\max}

To determine the intensity of EX_{\max} in a given subject, an incremental exercise test was conducted on a separate day prior to the main experiments. Dynamic exercise was performed on a cycling ergometer (Aero bike 2100R; Combi Wellness, Tokyo, Japan) at 60 revolutions/min (rpm), starting at an intensity of 50 W and increasing the workload by 10 W every minute. The incremental bout was continued until the subjects could no longer perform the cycling or maintain the required revolutionary speed. The intensity of EX_{\max} was defined as the maximal workload (171 ± 11 W), at which each subject could maintain the exercise at 60 rpm for 1 min.

Stroop test

We used a modified Japanese version of the Stroop test [23], which requires attention, response inhibition, interference, and behavioral conflict resolution. The test consisted of four words ('red', 'blue', 'green', and 'yellow'), which were randomly displayed in a color different from the word's meaning. A series of the color words were presented consecutively during the Stroop test. The subjects were instructed to answer the color of the displayed word as quickly as possible, instead of the word's meaning, whenever an incongruent color word appeared on a screen. The presenting rate was dependent on the subject's response speed, because the color word was changed into new one by the subjects clicking a mouse button. We measured the total time period required for processing the Stroop test consisting of 100 questions and the number of trials in which the subjects exhibited a wrong answer. To become accustomed to the cognitive test, all subjects performed a practice session before starting the experiments.

Cardiovascular responses to exercise

A blood-pressure cuff was wrapped around the left upper arm to record mean arterial blood pressure (MAP) with a non-invasive automatic blood pressure monitor (BP-103N; Colin Medical Instruments, Tokyo, Japan). MAP and heart rate (HR) were measured at intervals of 1–5 min throughout the experiments. The subjects were asked for a rating of perceived exertion, with the Borg scale grade from 6 to 20 [24], immediately after ergometer exercise.

Changes in the concentrations of Oxy-Hb and Deoxy-Hb in the prefrontal cortex

The relative concentrations of the Oxy-Hb and deoxygenated-hemoglobin (Deoxy-Hb) in the left prefrontal area were measured using NIRS (NIRO 200; Hamamatsu Photonics, Hamamatsu, Japan) in 7 subjects; in 4 of the subjects, a NIRS probe was also placed on the right forehead. The NIRS probes were placed on the forehead surface between Fp1 and F3 (left side) and between Fp2 and F4 (right side) (referring to the international EEG 10–20 system) and were covered with a black cloth. Since the NIRS probe placement corresponds to underlying cortical areas including the DLPFC [21, 22], the Oxy-Hb signal may detect regional cortical oxygenation in the DLPFC and its vicinity. With NIRS, the reflected near-infrared light (wavelengths 775, 810, and 850 nm) through cerebral tissue was sampled at a rate of 1 Hz and converted to optical densities. NIRS measured the changes in concentrations of the Oxy-Hb and Deoxy-Hb in regional arterial and venous blood vessels and capillaries, which reflect alterations in the oxygen supply–oxygen demand relationship of the illuminated tissue.

To clarify the possible contribution of skin blood flow to the Oxy- and Deoxy-Hb signals of the NIRS during dynamic exercise at 40 % of EX_{max} , a laser-Doppler flow probe was placed on the left forehead surface adjacent to the NIRS probe and skin blood flow was monitored with a laser-Doppler instrument (ALF21; ADVANCE, Tokyo, Japan) in 4 of the 7 subjects with the NIRS measurements. Furthermore, skin blood flow was monitored during Stroop test in newly recruited 5 subjects. Skin flow signal was integrated with a time constant of 0.1 s.

Protocols

The subjects took a rest for 5 min on a seat of the ergometer and performed the first Stroop test (Stroop 1). Then, they took another 5-min rest and started performing ergometer exercise (pedaling rate, 60 rpm) with a constant load for 15 min and with no load for 1 min (cooling down). The intensity of exercise was set at 20, 40, or 60 % of

EX_{max} (34 ± 2 , 68 ± 5 , and 103 ± 7 W, respectively). The second Stroop test (Stroop 2) was performed 5 min after the cessation of exercise. As time control, the subjects took a 15-min rest on the ergometer, instead of performing dynamic exercise (without exercise). Each exercise session with a different intensity (without exercise, 20, 40, or 60 % of EX_{max}) was conducted on a separate day. The order of exercise intensity was randomized in individual subjects.

To examine whether dynamic exercise with a shorter duration can improve cognitive function, the Stroop test score was compared before and after performing ergometer exercise at 40 % of EX_{max} for 5 min in 9 subjects. Next, to examine how long improvement of the cognitive function can last following exercise, the Stroop test was performed at 5 and 20 min following exercise at 40 % of EX_{max} for 15 min in 7 subjects.

Data and statistical analyses

The changes in HR and MAP in response to exercise were measured at 14 min from the onset of exercise. The prefrontal Oxy-Hb and Deoxy-Hb signals were preset to zero before exercise and their average changes over the whole 15-min period of exercise were calculated. These cardiovascular and NIRS signal changes were compared statistically with the preexercise baseline values by a paired *t* test. The effects of exercise intensity on the above variables were analyzed by a one-way analysis of variance with repeated measures. If a significant *F* value in the main effect of intensity was present, a Dunnett post hoc test was performed to detect a significant difference from the mean value in the time control (without exercise).

With respect to the Stroop 1 test before exercise, the changes in HR and MAP were measured at the end of the Stroop test, and the average changes in the NIRS signals over the whole period of the Stroop test were calculated. These cardiovascular and NIRS signal changes were statistically compared with the baseline values prior to the Stroop test by a paired *t* test. Similarly, the cardiovascular and NIRS signal changes in response to the Stroop 2 test following exercise were analyzed. The cardiovascular and NIRS signal responses, the total time period required for the Stroop test, and the number of errors were compared before and after exercise by a paired *t* test (Stroop 1 vs. Stroop 2). The effects of exercise intensity on the above variables were analyzed by a one-way analysis of variance with repeated measures and the Dunnett or Bonferroni/Dunn post hoc test. The relationship between the simultaneous differences in the Stroop time score and the prefrontal Oxy-Hb response to the Stroop test before and after dynamic exercise was analyzed with a linear regression and Pearson's correlation coefficient. The level of statistical significance was defined at $P < 0.05$. All data are expressed as mean \pm SE.

Results

The changes in HR, MAP, and Borg Scale during dynamic exercise

HR increased ($P < 0.05$) by 25–74 beats/min during exercise and the Borg scale increased to 10–14 grade, depending on the exercise intensity (Table 1). MAP increased ($P < 0.05$) by 11–22 mmHg during ergometer exercise at 40 and 60 % of EX_{max} , although MAP unchanged during exercise at 20 % of EX_{max} .

The cardiovascular responses during the Stroop test

HR and MAP increased ($P < 0.05$) by 12–15 beats/min and by 7–11 mmHg during the Stroop 1 test prior to dynamic exercise (Table 2). The increments of HR and

Table 1 The changes in Oxy-Hb, Deoxy-Hb, HR, MAP, and Borg scale during ergometer exercise ($n = 7$ subjects)

	Baseline	During
Without exercise (time control)		
Oxy-Hb (μmol)	0	-0.62 ± 0.17
Deoxy-Hb (μmol)	0	0.32 ± 0.23
HR (beats/min)	65 ± 2	66 ± 4
MAP (mmHg)	78 ± 2	78 ± 3
Borg scale	–	–
20 %- EX_{max}		
Oxy-Hb (μmol)	0	-0.49 ± 0.30
Deoxy-Hb (μmol)	0	0.11 ± 0.21
HR (beats/min)	65 ± 4	$90 \pm 8^{*,\#}$
MAP (mmHg)	80 ± 2	84 ± 3
Borg scale	–	10 ± 1
40 %- EX_{max}		
Oxy-Hb (μmol)	0	0.63 ± 0.44
Deoxy-Hb (μmol)	0	0.17 ± 0.16
HR (beats/min)	65 ± 5	$109 \pm 5^{*,\#}$
MAP (mmHg)	79 ± 2	$90 \pm 1^{*,\#}$
Borg scale	–	12 ± 0
60 %- EX_{max}		
Oxy-Hb (μmol)	0	$3.24 \pm 1.29^{*,\#}$
Deoxy-Hb (μmol)	0	0.28 ± 0.25
HR (beats/min)	66 ± 4	$140 \pm 6^{*,\#}$
MAP (mmHg)	79 ± 3	$101 \pm 3^{*,\#}$
Borg scale	–	14 ± 1

Oxy-Hb oxygenated hemoglobin, Deoxy-Hb deoxygenated hemoglobin, HR heart rate, MAP mean arterial blood pressure, EX_{max} maximal voluntary exercise

* Significant difference (paired t test, $P < 0.05$) from the baseline before exercise

Significant difference (Dunnett's test, $P < 0.05$) from the change during time control (without exercise)

MAP during the Stroop test were not affected ($P > 0.05$) by dynamic exercise at any intensity, although the baseline HR increased slightly following dynamic exercise at 60 % of EX_{max} (Table 2).

Effect of dynamic exercise on the Stroop score

The total time period required for execution of the Stroop test before and after dynamic exercise are shown in Fig. 1 and Table 2. The total time period for the Stroop test was shortened ($P < 0.05$) after 15 min of dynamic exercise at 40 and 60 % of EX_{max} , whereas dynamic exercise at 20 % of EX_{max} did not alter the time period (Table 2). The reduction in total time period between Stroop 1 and 2 tests had no significant correlation with the total time period for the Stroop 1 in any exercise session (Fig. 1a). When comparing the difference in total time period among different intensities of exercise, the reduction in total time period was the greatest ($P < 0.05$) following exercise at 40 % of EX_{max} (Fig. 1b). In contrast, the number of errors for the Stroop test, ranging approximately 2–4, was not significantly ($P > 0.05$) affected by preceding dynamic exercise at any intensity.

When exercise duration was shortened to 5 min, the short-lasting exercise at 40 % of EX_{max} failed to affect the Stroop time score (62.7 ± 2.7 s before vs. 62.5 ± 2.7 s after exercise, $P > 0.05$). Furthermore, with respect to the time interval between the cessation of exercise and the onset of the Stroop test, a longer time interval of 20 min also failed to affect the total time period for the Stroop test (70.2 ± 2.3 s before vs. 67.2 ± 3.0 s at 20 min after exercise, $P > 0.05$), as compared to the time interval of 5 min (65.8 ± 3.3 s at 5 min after exercise, $P < 0.05$). The number of errors for the Stroop test was not altered by the dynamic exercise in either case.

The Oxy-Hb and Deoxy-Hb responses to ergometer exercise

Both prefrontal Oxy- and Deoxy-Hb did not significantly change during the time control period when the subjects kept the resting state (without exercise) in Fig. 2. During ergometer exercise, the prefrontal Oxy-Hb initially decreased until 5 min from the onset of exercise and increased during the later period of exercise. The initial decrease and later increase in the Oxy-Hb were dependent on the exercise intensity (Fig. 2). The average values of the Oxy-Hb over the whole 15 min exercise period at intensities of 20 and 40 % EX_{max} were not significantly different from the preexercise control, whereas the average Oxy-Hb increased ($P < 0.05$) during exercise at the intensity of 60 % EX_{max} (Table 1). On the other hand, the peak Oxy-Hb during the later period of exercise increased

Table 2 The changes in Oxy-Hb, Deoxy-Hb, HR, and MAP during Stroop test ($n = 7$ subjects)

	Stroop 1 (before exercise)		Stroop 2 (after exercise)	
	Baseline	During	Baseline	During
Without exercise (time control)				
Oxy-Hb (μmol)	0	2.17 \pm 0.36*	0.31 \pm 0.31	1.68 \pm 0.55
Deoxy-Hb (μmol)	0	0.49 \pm 0.13	-0.02 \pm 0.03	-0.13 \pm 0.28
HR (beats/min)	71 \pm 3	85 \pm 8*	70 \pm 3	77 \pm 5*
MAP (mmHg)	78 \pm 3	89 \pm 4*	79 \pm 3	85 \pm 3
Total time period (s)	-	68.9 \pm 4.8	-	68.1 \pm 3.7
20 %-EX _{max}				
Oxy-Hb (μmol)	0	2.03 \pm 0.76*	0.64 \pm 0.63	2.85 \pm 1.32
Deoxy-Hb (μmol)	0	-0.43 \pm 0.15	0.05 \pm 0.02	-0.53 \pm 0.19
HR (beats/min)	68 \pm 4	80 \pm 7*	69 \pm 4	82 \pm 5*
MAP (mmHg)	81 \pm 3	85 \pm 2	83 \pm 3	87 \pm 3
Total time period (s)	-	58.0 \pm 2.5	-	58.1 \pm 2.7
40 %-EX _{max}				
Oxy-Hb (μmol)	0	1.75 \pm 0.37*	1.29 \pm 0.85	4.09 \pm 1.09* [†]
Deoxy-Hb (μmol)	0	-0.54 \pm 0.08	-0.05 \pm 0.05	-0.51 \pm 0.20
HR (beats/min)	68 \pm 4	80 \pm 6*	71 \pm 5	86 \pm 7* [†] ,#
MAP (mmHg)	80 \pm 3	90 \pm 3*	84 \pm 3	93 \pm 3*
Total time period (s)	-	63.4 \pm 3.4	-	59.1 \pm 2.9 [†]
60 %-EX _{max}				
Oxy-Hb (μmol)	0	2.58 \pm 0.77*	7.39 \pm 1.48 [†] ,#	9.27 \pm 1.22 [†] ,#
Deoxy-Hb (μmol)	0	-0.36 \pm 0.23	-0.04 \pm 0.06	-0.50 \pm 0.12
HR (beats/min)	70 \pm 5	82 \pm 6*	81 \pm 5 [†] ,#	93 \pm 6* [†] ,#
MAP (mmHg)	80 \pm 3	89 \pm 3*	82 \pm 4	91 \pm 4*
Total time period (s)	-	60.8 \pm 2.1	-	57.9 \pm 2.8 [†]

* Significant difference (paired t test, $P < 0.05$) from the baseline before Stroop 1 or before Stroop 2

[†] Significant difference (paired t test, $P < 0.05$) between Stroop 1 and Stroop 2

Significant difference (Dunnett’s test, $P < 0.05$) from the values during time control (without exercise)

($P < 0.05$) to $4.4 \pm 0.8 \mu\text{mol}$ at 40 % EX_{max} and $9.1 \pm 1.6 \mu\text{mol}$ at 60 % EX_{max}, respectively. Subsequently, when the Stroop 2 was started, the Oxy-Hb level did not change ($P > 0.05$) from the preexercise control in the case of 20 and 40 % EX_{max} exercise but it remained elevated following 60 % EX_{max} exercise (Table 2). In contrast, the Deoxy-Hb remained near the baseline level throughout exercise at any intensity, except the initial period (Fig. 2; Table 1). The time courses and magnitudes of the changes in the Oxy-Hb and Deoxy-Hb of the right prefrontal cortex during exercise were almost similar to those of the left prefrontal cortex (Fig. 2).

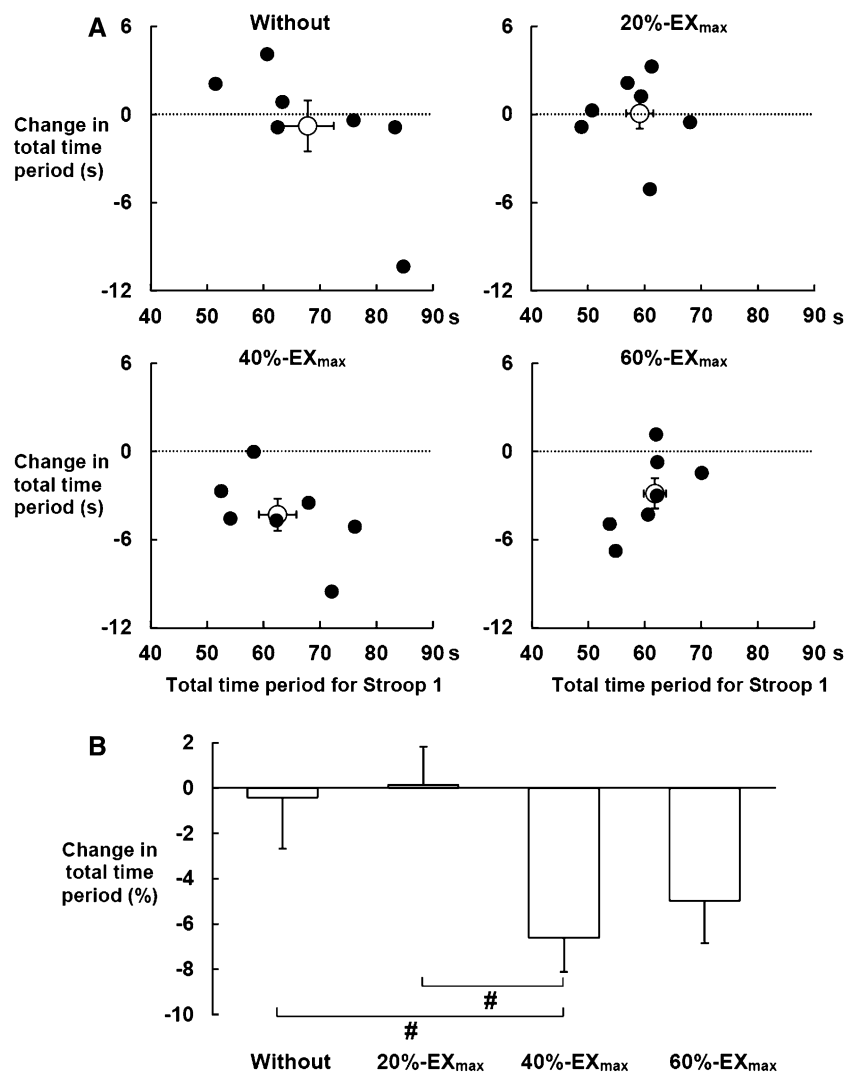
Effect of dynamic exercise on the Oxy-Hb response during the Stroop test

The time courses of the changes in the left prefrontal Oxy-Hb in response to the Stroop test were compared before and after exercise at different intensities in Figs. 3 and 4. The

average changes in the prefrontal Oxy-Hb and Deoxy-Hb over the whole period of the Stroop test are summarized in Table 2. The left prefrontal Oxy-Hb abruptly increased as soon as the Stroop 1 test was started (Figs. 3 and 4). The increase in the left prefrontal Oxy-Hb reached the peak at 21–54 s from the onset of the Stroop test. On the other hand, the Deoxy-Hb did not change significantly ($P > 0.05$) during the Stroop 1 test (Table 2). When the Stroop test was completed, the Oxy-Hb gradually decayed to the baseline level in approximately 120 s (Fig. 4).

Without exercise, there were no significant changes in the baseline Oxy-Hb of the left prefrontal cortex and its response to the Stroop test before and after the time control period, although the Oxy-Hb response appeared to be blunted in the Stroop 2 test (Figs. 3, 4; Table 2). Correspondingly, the baseline and Stroop response in the Oxy-Hb were not significantly altered by ergometer exercise at 20 % of EX_{max}. In contrast, following exercise at 40 % of EX_{max}, the baseline Oxy-Hb did not change ($P > 0.05$) but

Fig. 1 a The change in total time period between the two Stroop tests (Stroop 1 and Stroop 2) were plotted against the absolute time period for the Stroop 1 in individual trials. *Open circles and small bars* indicate their mean values \pm SE. Dynamic exercise at 40 and 60 % of maximal voluntary exercise (EX_{max}) shortened the total time period for the Stroop test, whereas dynamic exercise at 20 % EX_{max} did not alter the time period (Table 2). The reduction in total time period between Stroop 1 and 2 tests, however, had no significant correlation with the total time period for the Stroop 1 in any exercise session. **b** Relative percent changes in total time period between the two Stroop tests before and after exercise at different intensities of 20, 40, and 60 % EX_{max} are compared. #Significant difference ($P < 0.05$) in the percent changes of total time period between different intensities of exercise



the response to the Stroop 2 test was significantly augmented (Figs. 3, 4; Table 2). On the other hand, following exercise at 60 % of EX_{max} , the baseline Oxy-Hb elevated ($P < 0.05$) but the response magnitude of the Oxy-Hb increase appeared to be blunted (Figs. 3, 4; Table 2). When the differences in the left prefrontal Oxy-Hb responses between Stroop 1 and Stroop 2 were plotted against the exercise intensity (Fig. 5a), the enhanced Oxy-Hb response following exercise at 40 % of EX_{max} was solely significant ($P < 0.05$). The differences in the right prefrontal Oxy-Hb responses between Stroop 1 and Stroop 2 showed the similar tendency (Fig. 5a). Taken together with the simultaneous changes in the Stroop time scores, the differences in the left and right prefrontal Oxy-Hb responses tended to show a negative linear correlation (correlation coefficient = 0.702, $P = 0.052$) with the differences in total time period in Fig. 5b.

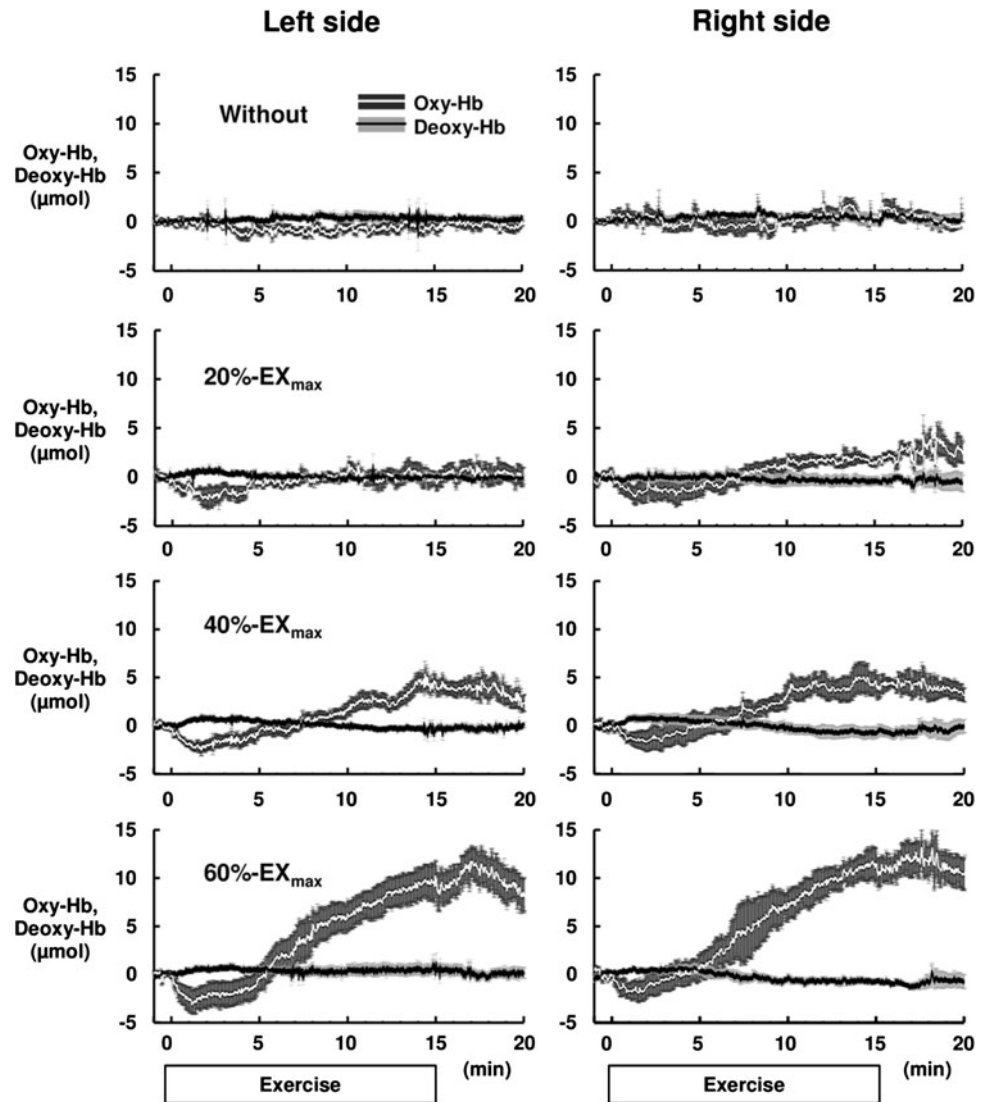
With respect to the prefrontal Deoxy-Hb signal, the baseline Deoxy-Hb was not affected ($P > 0.05$) by

dynamic exercise at any intensity and the Deoxy-Hb remained unchanged throughout the Stroop test before and after exercise at any intensity (Table 2). Similarly, the baseline values and the Stroop responses in HR and MAP were not significantly ($P > 0.05$) affected by dynamic exercise at any intensity, although the baseline HR was elevated (Table 2).

Change in skin blood flow during dynamic exercise and during Stroop test

Although skin blood flow gradually increased from the baseline of 4.3 ± 1.4 to 8.6 ± 2.7 ml/min/100 g until the end of exercise at 40 % of EX_{max} , skin blood flow returned to the baseline more quickly immediately after exercise, as compared to the Oxy-Hb signal. On the other hand, skin blood flow remained unchanged throughout the Stroop test in 3 of the 5 subjects examined; otherwise, it increased from the baseline level of 6.9 ± 3.0 to 14.2 ± 6.1 ml/min/

Fig. 2 The time courses of the average changes in the prefrontal Oxy-Hb and Deoxy-Hb during ergometer exercise at different intensities (*left side*, $n = 7$ subjects; *right side*, $n = 4$ subjects). The data were taken every 1 s



100 g only at the initial brief phase of the Stroop test in the remaining subjects. As a result, the time courses of the changes in skin blood flow were different from those of the changes in the prefrontal Oxy-Hb.

Discussion

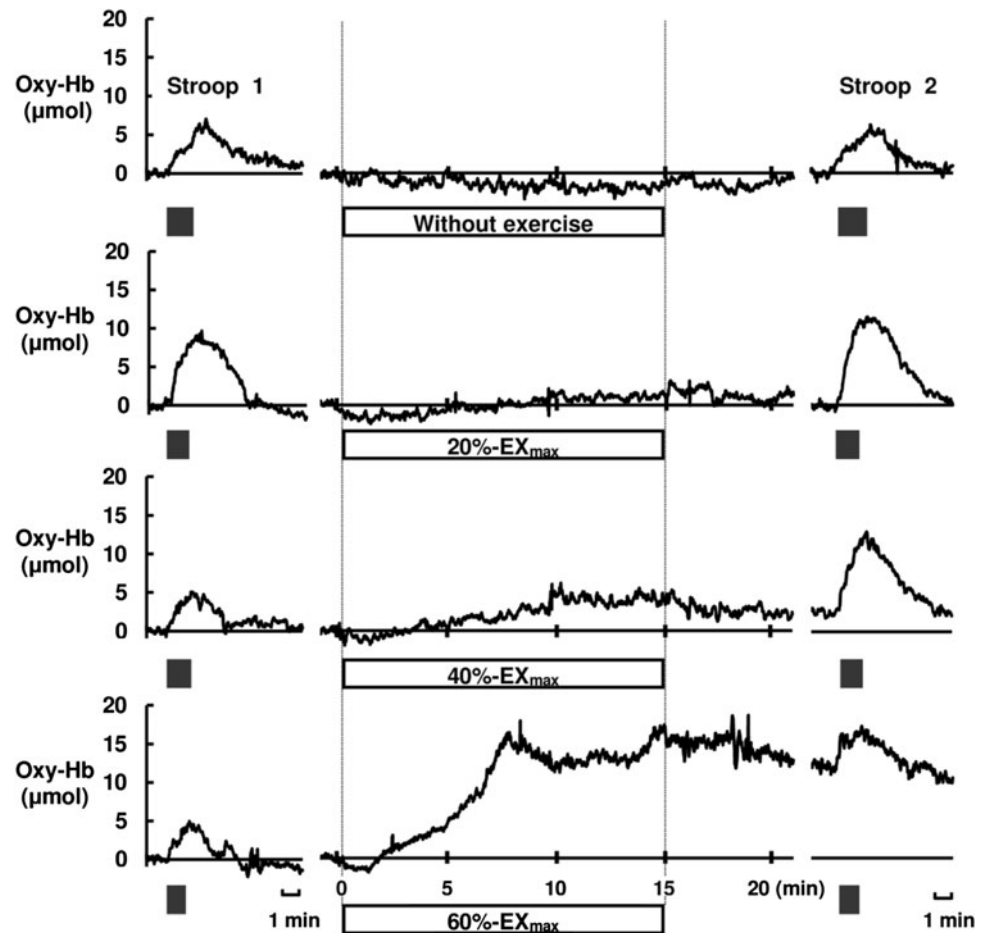
We have examined the question of whether acute dynamic exercise leads to increased neural activity in the prefrontal cerebral cortex, which in turn may cause improvement of the cognitive performance with the Stroop test. To this end, the relationship between the cognitive function and the changes in the cerebral oxygenation of the prefrontal cortex was compared before and after dynamic exercise for a period of 15 min. The major findings of this study are that: (1) ergometer exercise at an intensity of 40 % EX_{max} was able to significantly decrease the time score for the Stroop

test, whereas dynamic exercise at a lower or higher intensity unchanged or improved cognitive function with a less amount; (2) the Stroop test increased the Oxy-Hb of the bilateral prefrontal cortices without altering the Deoxy-Hb, suggesting increased regional cerebral blood flow; and (3) the enhanced Oxy-Hb response to the Stroop test tended to correlate with improvement of the cognitive function. Taken together, it is likely that ergometer exercise at the moderate intensity for 15 min may improve mental cognitive function through augmented neural activity in the prefrontal cortex.

Effects of dynamic exercise on cognitive function

It is important for quantifying the effect of exercise on cognitive function to maintain a level of intentional effort constant. HR and MAP increased during the Stroop test [25], suggesting that the cognitive process during the

Fig. 3 An example of the time courses of the consecutive changes in the left prefrontal Oxy-Hb during the first Stroop test (Stroop 1) and during dynamic exercise at a different intensity, which was followed by the second Stroop test (Stroop 2). Dynamic exercise started 5 min after completing the Stroop 1. The Stroop 2 started 5 min after the end of dynamic exercise. *Filled columns* indicate the total time period for the Stroop tests



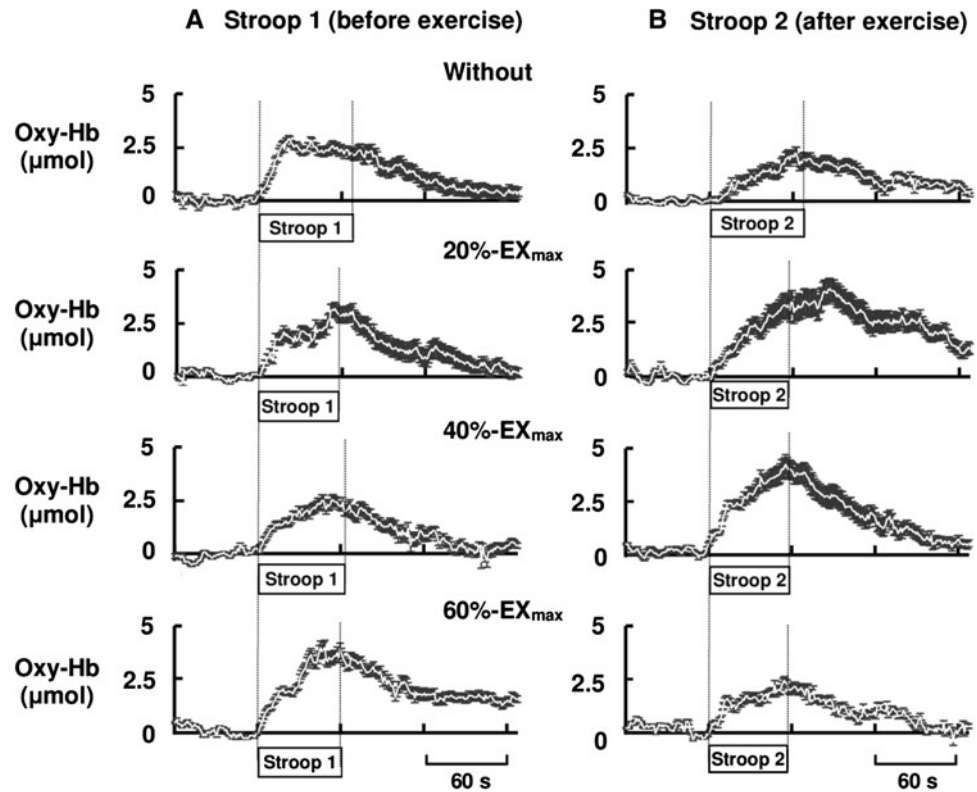
Stroop test causes on the cardiovascular responses. Assuming that these changes in HR and MAP are taken as an index of the subjective effort for the Stroop test, the changes in HR and MAP during the Stroop test were not influenced by dynamic exercise (Table 2), suggesting that the intentional effort during the Stroop test equaled in all cases. Nevertheless, the total time period for the Stroop test was significantly shortened by ergometer exercise at 40 % EX_{max} as compared to the time control, indicating that dynamic exercise at the moderate intensity is able to improve cognitive function. Since the Stroop time score was not altered in the time control (without exercise), habituation and/or learning for the Stroop test, if any, are unlikely to affect the Stroop time score in this study. Furthermore, the fundamental characteristics of the effects of dynamic exercise on the total time period and the number of errors were identical irrespective of imposing 50 or 100 questions in the Stroop test (unpublished observation), demonstrating the reproducibility and reliability of the cognitive response to the Stroop test in this study.

The effect of dynamic exercise on cognitive function may depend on both intensity and duration of the exercise. Dynamic exercise at 75 % $\dot{V}O_{2max}$ for 20–60 min [1, 2]

and at 50 % $\dot{V}O_{2max}$ for 10 min [3] improved the reaction time score for the Stroop test or mental arithmetic test. Dynamic exercise at 60 % $\dot{V}O_{2max}$ for 3.5 min also improved the reaction time for the Erikson flanker task [26]. In this study, the Stroop time score was significantly improved by 15 min ergometer exercise at 40 % of EX_{max} . Since the most effective intensity of exercise for the cognitive improvement was lower than those in the previous studies, it is likely that the effect of exercise on cognitive function depends on not only the intensity but also the duration of exercise and/or the time interval between the cessation of exercise and a cognitive task. In fact, short-lasting exercise for 5 min failed to improve cognitive function despite the same exercise intensity. Furthermore, the time interval between the cessation of exercise and the onset of the Stroop test is important for cognitive improvement, because the Stroop test performed at 20 min following 15 min dynamic exercise failed to show cognitive improvement.

In contrast to the time score for the Stroop test, the number of errors was not influenced by dynamic exercise at any intensity in agreement with the previous studies [1, 3, 4]. The effect of dynamic exercise on cognitive function is

Fig. 4 The time courses of the average responses in the left prefrontal Oxy-Hb during the Stroop 1 (before exercise) and the Stroop 2 (after exercise) in 7 subjects. The baseline levels before the Stroop 1 or before Stroop 2 were set to zero. The data were taken every 1 s



expected to improve cognitive process so as to accelerate the response speed without sacrificing the response accuracy.

Increase in Oxy-Hb of the prefrontal cortex during dynamic exercise

The Oxy- and Deoxy-Hb signals of the NIRS reflect the relative concentrations of oxygenated and deoxygenated hemoglobin in red blood cells in arterioles, capillaries, and venules within the illuminated area. The Oxy-Hb concentration is dependent on a balance between oxygen supply and demand in the regional area. Oxygen supply predominantly depends on regional blood flow. If oxygen supply is increased without changing oxygen demand, the Oxy-Hb signal is increased. If oxygen demand is increased without increasing oxygen supply, the Oxy-Hb signal is decreased. Fox and Raichle [27] reported that increased regional blood flow in association with brain neural activity exceeded oxygen metabolic demand. Hoshi et al. [28] demonstrated using a perfused rat brain model that increasing total cerebral blood flow causes an increase in regional Oxy-Hb and a decrease in Deoxy-Hb, while neural activity augmented by pentylentetrazole accompanies an increase in regional Oxy-Hb and small changes in Deoxy-Hb. Taken together, the changes in Oxy-Hb are considered to be a more sensitive indicator of the changes in regional cerebral blood flow than the changes in Deoxy-Hb, while the

changes in Deoxy-Hb are determined more by venous oxygenation and blood volume than blood flow [28].

In this study, the prefrontal Oxy-Hb decreased or unchanged until 5 min from the onset of exercise and gradually increased in proportion to the exercise intensity until the end of dynamic exercise (Fig. 2), in agreement with the previous results [17, 18]. Since the Deoxy-Hb was unchanged throughout exercise except in the initial period, the signal of Oxy-Hb is considered to reflect regional cerebral blood flow in the prefrontal cortex [28–30]. It is known that changes in the Oxy-Hb are positively correlated with the changes in blood flow velocity of the middle cerebral artery [17, 18, 31]. MAP increased by 8–16 mmHg during dynamic exercise (Table 1). The small rises in perfusion pressure may have little influence on the prefrontal cerebral blood flow, because the increased MAP during exercise was within the range of cerebral autoregulation [32]. Instead, it is conceivable that the change in regional cerebral blood flow follows an increase in neural activity of the prefrontal cortex, which may in turn cause improvement of cognitive function.

Effect of dynamic exercise on the prefrontal Oxy-Hb response during Stroop test

The relationship between the increased neural activity in the prefrontal cerebral cortex and the cognitive performance with the Stroop test was assessed in this study. To

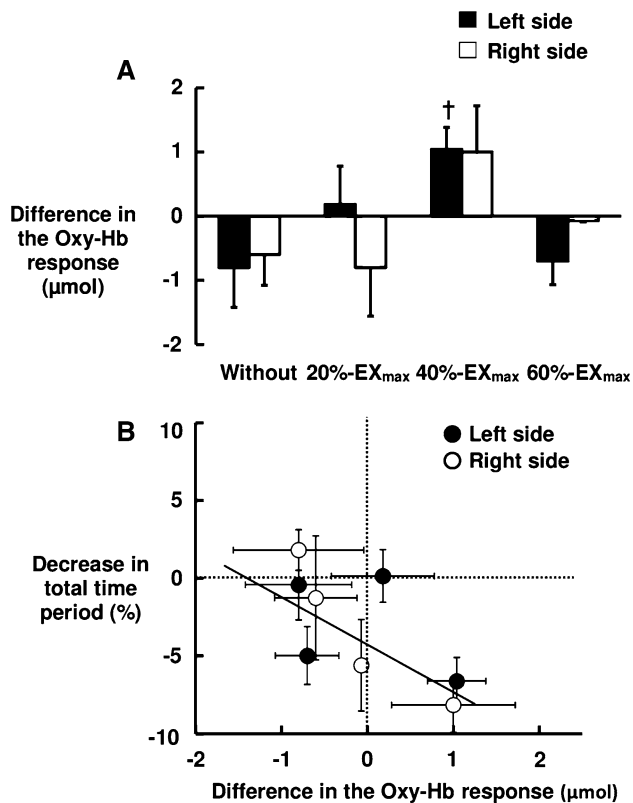


Fig. 5 **a** The differences in the Oxy-Hb response in the left and right prefrontal cortices between the Stroop 1 (before exercise) and Stroop 2 (after exercise) (*left side*, $n = 7$ subjects; *right side*, $n = 4$ subjects). †Significant difference ($P < 0.05$) between Stroop 1 and 2. **b** The overall relationship between the differences in the Oxy-Hb responses and the relative percent decreases in total time period for the Stroop test (correlation coefficient = 0.702, $P = 0.052$)

our knowledge, there are only two research groups investigating this issue. Soya's research group reported using NIRS that the activation of the left prefrontal cortex was related to improvement of the Stroop reaction time following dynamic exercise [3, 33]. On the other hand, Ando et al. [26] reported that the improvement of cognitive function examined with the Erikson flanker task was independent of prefrontal cerebral oxygenation. Both research groups' studies, however, may have substantial limitation in terms of methodology and data explanation. In the studies of Yanagisawa et al. [3] and Hyodo et al. [33], the prefrontal Oxy-Hb was actually unchanged or decreased during an incongruent trial of the Stroop test against 2- or 4-s presentation of a color word and subsequently increased during the intertrial resting period for 9–12 s. They attempted to correlate the increased Oxy-Hb during the intertrial period with the response time to the incongruent Stroop task. However, it is known that the prefrontal Oxy-Hb always increased (but did not decrease) during the Stroop test, and the increase in the Oxy-Hb quickly developed without a time delay at the beginning of an incongruent Stroop trial in this study (Figs. 3, 4) and in

previous studies [9, 10]. In the study of Ando et al. [26], the cognitive test was performed during dynamic exercise, but not following exercise. Thus, it was difficult to distinguish the prefrontal Oxy-Hb responses between dynamic exercise and the cognitive task.

The present study found that there was a corresponding tendency between the changes in the prefrontal Oxy-Hb and cognitive performance with the Stroop test (Fig. 5), suggesting that the more the response of prefrontal Oxy-Hb is enhanced, the more the Stroop time score is shortened. Of course, a possibility that the two phenomena may occur in parallel cannot be neglected, because we have no evidence about the cause–effect relationship between them. Furthermore, the linear regression line between the differences in the prefrontal Oxy-Hb responses and Stroop time score did not cross zero and shifted downward (Fig. 5b). It is likely that there is not a simple relationship between the increase in the prefrontal Oxy-Hb and cognitive performance, and that the prefrontal Oxy-Hb cannot fully explain the improved cognitive function following exercise. Other factors such as an increased arousal level [34] may contribute to the improved cognitive function following exercise. On the other hand, it should be noted that the baseline value of the Oxy-Hb before the Stroop test (as indicated in Table 2) did not correlate with improvement of the cognitive function, suggesting that the basal Oxy-Hb in the prefrontal cortex does not always predict any improvement of cognitive function. In particular, it was surprising that, although the Oxy-Hb response was attenuated following exercise at 60 % of EX_{max}, the exercise improved the Stroop time score to some extent. The reduction in the Oxy-Hb was not due to a ceiling effect, because the prefrontal Oxy-Hb levels during conversation exceeded the peak Oxy-Hb following the 60 %-EX_{max} exercise.

It has been revealed using fMRI that the Stroop test accompanies an increase of neural activity in several cortical areas such as the DLPFC, ACC, parietal, and frontopolar cortex [11, 16, 35]. Milham et al. [16] reported that the DLPFC and ACC were more active for incongruent-eligible trials of the Stroop test. Since the placement of the NIRS probes corresponded to underlying cortical areas including the DLPFC [21, 22], the increase in the prefrontal Oxy-Hb in this study suggested an increase in regional cortical oxygenation in the DLPFC and its vicinity.

Limitations

Several substantial problems are involved in this study. First, we lacked the congruent trials for the Stroop test as control, in which all words were displayed in black.

However, it is known that dynamic exercise does not affect the response to the congruent test [1, 3]. Moreover, the changes in cognitive performance and prefrontal oxygenation following intense ergometer exercise at an intensity of more than 60 % EX_{max} were not examined in this study and remain to be studied. Second, we did not directly assess neural activity in the prefrontal cortex. The measurement of neural activity will be needed in a more direct approach. Third, there is a possibility that the Oxy-Hb is influenced at least partly by skin blood flow. However, we found that the time course of the changes in skin blood flow was completely different from that of the changes in the prefrontal Oxy-Hb during exercise and during the Stroop test. Thus, it is unlikely that skin blood flow influenced the NIRS signals in this study. Finally, the number of the subjects who participated in the NIRS measurements, especially the NIRS from the right prefrontal cortex, was small and may not be sufficient to have an enough statistical power. Moreover, the absolute values of the Stroop time score before exercise varied among the exercise sessions at different intensities probably due to the small sample size.

Conclusions

It is likely that dynamic exercise at 40 % of EX_{max} for 15 min may improve the time score for the Stroop cognitive test without changing response accuracy. The Oxy-Hb of the prefrontal cortex increased during the Stroop test. The dynamic exercise augmented the prefrontal Oxy-Hb response in association with improvement of incongruent cognitive function. Therefore, dynamic exercise at the moderate intensity may improve cognitive function through increased neural activity of the prefrontal cerebral cortex.

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Conflict of interest The authors declare that we have no conflict of interest.

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