

ความสัมพันธ์ของคลื่นสมองความถี่สูงกับปริมาณเลือดที่มาเลี้ยงสมองขณะออกกำลังกาย: การศึกษาโดยใช้เนียร์อินฟราเรดสเปกโทรสโกปีและเครื่องมือวัดคลื่นสมอง

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บทคัดย่อ

เป็นที่ทราบกันดีว่าการออกกำลังกายมีผลในการเพิ่มการไหลเวียนของเลือดในสมอง ในการออกกำลังกายด้วยการปั่นจักรยานแบบเพิ่มความหนักของการออกกำลังกายพบว่าการเพิ่มปริมาณเลือดที่มาเลี้ยงสมองบริเวณสมองส่วนหน้าขณะออกกำลังกายขึ้นกับความหนักของการออกกำลังกายโดยเริ่มเพิ่มจากความหนักประมาณร้อยละ 40 ของความสามารถในการใช้ออกซิเจนสูงสุด (มล./กก./นาที) แต่อย่างไรก็ตามการเพิ่มขึ้นของปริมาณเลือดที่สมองกับการทำงานของสมองยังเป็นที่ถกเถียงกันว่ามีความสัมพันธ์กันหรือไม่อย่างไร งานวิจัยครั้งนี้ได้ทำการศึกษาความสัมพันธ์ระหว่างการเปลี่ยนแปลงของปริมาณเลือดและคลื่นสมองขณะออกกำลังกายที่ระดับความหนักของการออกกำลังกายระดับต่ำไปจนถึงปานกลาง ทำการวัดโดยใช้เนียร์อินฟราเรดสเปกโทรสโกปีวัดการเปลี่ยนแปลงของปริมาณเลือดและเครื่องมือวัดคลื่นสมองวัดคลื่นสมองก่อน ขณะ และหลังออกกำลังกายของอาสาสมัคร 9 คน ซึ่งปั่นจักรยานวัดงานเป็นเวลา 10 นาทีที่ความหนักร้อยละ 20, 40 และ 60 ของความสามารถในการใช้ออกซิเจนสูงสุด พบการเพิ่มขึ้นของคลื่นสมองอัลฟาหลังการออกกำลังกายที่ร้อยละ 20 และ 40 ของความสามารถในการใช้ออกซิเจนสูงสุด ในขณะที่คลื่นสมองเบต้าเพิ่มขึ้นหลังการออกกำลังกายที่ร้อยละ 40 และ 60 ของความสามารถในการใช้ออกซิเจนสูงสุด นอกจากนี้ยังพบความสัมพันธ์ระหว่างการเพิ่มขึ้นอย่างมีนัยสำคัญของคลื่นสมองเบต้ากับปริมาณเลือดที่มาเลี้ยงสมอง ($r = 0.53$, $P < 0.01$) ผลการทดลองนี้เสนอแนะว่าการออกกำลังกายที่มีผลในการเพิ่มปริมาณเลือดที่มาเลี้ยงสมองมีความสัมพันธ์กับคลื่นสมองที่อาจจะเกี่ยวข้องกับการตื่นตัวของสมอง

คำสำคัญ: คลื่นสมอง, เนียร์อินฟราเรดสเปกโทรสโกปี, สมองส่วนหน้า, ปริมาณเลือดในสมองเฉพาะส่วน, การตื่นตัวของสมอง

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High frequency brain waves increase depending upon exercise intensity and associated with cerebral blood volume: A simultaneous NIRS-EEG study

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Abstract

Exercise is proved to have impacts on cerebral hemodynamic changes. Cerebral hemodynamic changes with exercise have been shown in an intensity-dependent from the mild intensity (about 40 % $\text{VO}_{2\text{max}}$) during a graded cycling exercise. However, its association with brain activation is still unknown. In this paper, the relationship between hemodynamic and EEG-changes with exercise was examined at different intensities from low to moderate. The regional cerebral blood volume (rCBV) and the brain waves were monitored by using NIRO 300 and EEG simultaneously with exercise. Nine healthy volunteers performed a 10-minute of cycling with 30-minute rest intervals at the intensity of 20 %, 40 % and 60 % $\text{VO}_{2\text{max}}$. The EEG resulted in a significant increase in their percentage changes of alpha at 20 % and 40 % $\text{VO}_{2\text{max}}$ and beta at 40 % and 60 % $\text{VO}_{2\text{max}}$. A significant positive correlation between rCBV and beta wave was also reported ($r=0.53$, $P < 0.01$). These results show that changes in rCBV with exercise have a significant correlation with high frequency brain wave and implicate that exercise-enhanced rCBV in the prefrontal cortex might be associated with brain arousal.

Keywords: Electroencephalography (EEG), Near-infrared spectroscopy (NIRS), Prefrontal cortex, Regional cerebral blood volume (rCBV), Brain arousal

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Introduction

Impacts of mental and physical tasks on regional cerebral blood volume (rCBV) have been well stated in both human and animals ⁽¹⁻³⁾. An increase of CBV, which exceeds a smaller increase in oxygen consumption, occurs accompanying the cerebral activation ⁽⁴⁾. There have been attempts to investigate the impacts of exercise on brain function using various existing methods. Previous studies reported that hemodynamic increases varied with the exercise intensity ^(5,6). Incremental cycling exercise was also found to enhance the rCBV in the frontal cortex as monitored by near-infrared spectroscopy (NIRS). The pattern of rCBV has been shown in a threshold-like manner. An exercise at about 40 % VO_2max , which is lower than of lactate threshold level, has been designated to be the cerebral blood volume threshold (CBVT) ⁽⁶⁾, suggesting a possible role of mild exercise in enhancing CBV.

One of the widely used methods on monitoring the human brain function is the electroencephalography (EEG). The EEG used in studies on physical exercise has been able to detect the changes in each brain wave depending on the condition of exercise ⁽⁷⁻⁸⁾. Kubitz & Mott (1996) found an increase in beta wave but decrease in alpha wave at moderate intensity of cycling exercise. In addition, Oda et al. (1999) reported that after an intermediate exercise in water, the percentage change of alpha wave increased. The results suggested that high frequency or fast waves increased with intensity. The arousal level, estimated from the analysis of change in contingent negative variation (CNV) during S1-S2 reaction time task, also altered as a function of exercise intensity in an inverted-U relationship (i.e., arousal level increased from low to moderate intensity whereas decreased from moderate to high intensities)⁽⁹⁾. Although the EEG has been widely used as a physiological indicator of brain activation with a high temporal resolution, its spatial resolution

is very poor. NIRS, on the other hand, is a useful noninvasive real-time monitoring tool for the tissue oxygenation. It has a high temporal resolution in less than one second ⁽¹⁰⁾. Combination the merits of each instruments might explain clearer about the physiological change phenomena, thus the synchronous multi-modal imaging has been an increase in interest since the mid 1990s ⁽¹¹⁾. Recently, The simultaneous NIRS-EEG recording has been studied and suggested the usefulness for correlating hemodynamic responses to neural activity during right median nerve electrical stimulation and in a simple functional activation in motor cortex ^(12,13). It is of interesting to use NIRS-EEG recording during the exercise session. We hypothesized that hemodynamic changes would increase in parallel with the high frequency brain waves. The purpose of this study was to assess the association between hemodynamic change and EEG activity (i.e., brain waves) during low to moderate exercise intensity. The hemodynamic change and EEG were simultaneously monitored.

Materials and methods

Subjects

Nine students (8 male and 1 female, with the average age of 25.7 ± 3.6 yrs, average weight 63.6 ± 7.8 kg, and average VO_2max 48.6 ± 5.6 ml/kg/min: mean $\pm$ SD) were recruited from the University of Tsukuba. All participants were in good physical and mental health conditions with no history of any major psychiatric or neurological disorders. None of them has a history of substance abuse, head injury, or major physical illness and were not on any psychotropic medications at the time of the study. The study was approved by the Ethics Committee for Research on Human Subjects of the University of Tsukuba, according to standards established in the Declaration of Helsinki.

Experimental protocol

A few days prior to the exercise, maximal oxygen consumption (VO_2max) was determined during a continuous graded exercise test on a cycle ergometer (StrengthErgo 240, Mitsubishi, Japan). Subjects pedaled without load for the first minute, and then the load was increased by 15 watts per minute until they could not keep the pedaling rate of 60 rpm longer than few minutes, or they reached volitional exhaustion. Expired gas was analyzed through an AE300S Aero Monitor (Minato Medical Science Co., Ltd., Osaka, Japan)

The exercise protocol consisted of 7 minutes of pre-exercise session, 10 minutes of exercise session, and 2 minutes of post-exercise session. Before the exercise session, the participants sat on the cycle ergometer (StrengthErgo 240, Mitsubishi, Japan) for 15 minutes while EEG electrodes, NIRO 300 optode, and a chest belt POLAR[®] heart rate monitor were attached. The subjects were instructed to close their eyes in pre-, during-, and post-exercise session. Before and after the exercise, the subjects were asked to sit quietly on the cycle ergometer for adaptation. The subjects performed 3 sets of the exercise at 20 %, 40 %, and 60 % of the VO_2max with 30-minute rest between intensity consecutively in the same day. A metronome was used to keep the pedaling rate at 60 rpm. Chest belt POLAR[®] heart rate monitor was administered to monitor heart rate every minute throughout the session. The expired gas was analyzed through the AE300S Aero Monitor (Minato Medical Science Co., Ltd., Osaka, Japan).

Outcome measures

Cerebral oxygenation

The NIRO 300 (Hamamatsu Photonics, Hamamatsu city, Japan) was used in this study. It uses four wavelengths of near-infrared light at 775, 825,

850, and 904 nm, and the sensor contains a laser diode and three detectors placed 4 or 5 cm from the source of emitting light⁽¹⁴⁾. The cerebral oxygenation was defined as the changes in concentration of oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb).

The position on the forehead, Fp1 according to the international 10-20 system, was chosen from the previous data which showed the highest tissue oxygenation during graded cycling exercise with the NIRS probe held in place with bandages and light shielding tapes. The distance between the emitter and the detector was 4-5 cm. Most of the cases we used 5 cm, however, 4 cm of distance has been chosen to obtain the good initialization in some subjects. The O_2Hb and HHb were monitored and obtained at a sample rate of 6 Hz and recorded on-line using custom-designed software (N300OL, Hamamatsu Photonics, Japan) from pre- to post-exercise sessions in all intensities. The changes in concentration of O_2Hb and HHb were calculated with respect to an arbitrary zero baseline at the start of measurement. The O_2Hb change was calculated by compare the average of O_2Hb during 2 minutes before the exercise and 2 minutes immediately after the exercise.

EEG

The EEG was recorded using surface Ag-AgCl electrode (Electroencephalograph Model EEG 4314: Nihon Kohden, Tokyo) at Fp1 according to the international 10-20 system. The skin was cleaned with alcohol and scrub gently with skinpure[®] to keep the impedance below 5 kOhms. The recording electrode was attached just next to the NIRO 300 optode, whereas, the reference and the earth electrodes were attached at the left ear lobe and the area between eyebrows (frontal bone), respectively. NIRS recording was synchronized with EEG by external trigger.

Data reduction / processing

Both EEG and NIRS signals were stored on a magnetic tape and then converted into digital data through an A/D converter installed in a personal computer. The EEG signals were amplified and filtered (0.24-29.7 Hz), then digitized at a sampling rate of 128 Hz, and then recorded using data acquisition program Sleepsign version 2.0 (Kissei Comtec, Nagano). The mean power spectrum of delta (0.24-3.91 Hz), theta (3.91-7.08 Hz), alpha (7.08-12.94 Hz), and beta (12.94-29.79 Hz) bands in every 10 second were analyzed by using Fast Fourier transforms (FFT, Sleepsign). Six 10-s epochs were taken at the sixth minute of pre-exercise and the first minute of post-exercise to calculate the percent change in each of exercise intensities.

Data analysis

The paired sample t-test was used to compare the percentage change of EEG and O_2Hb concentration change at the post-exercise compared to the baseline. The relationship between the O_2Hb concentration change and spectrum density power of each band of the brain wave were analyzed using Pearson correlation coefficients. The significance level was set at $P < 0.05$.

Results

The rCBV at Fp1, as represented by the level of O_2Hb ; 1.66 ± 2.25 , 5.08 ± 2.96 , and 8.73 ± 3.41 a.u. in the exercise intensity at 20 %, 40 %, and 60 % VO_{2max} , respectively, showed a non-linear increase with increasing intensity. The O_2Hb was not increased at the 20% VO_{2max} intensity but increased significantly at 40 % and 60 % VO_{2max} ($P < 0.01$) (**Figure 1**).

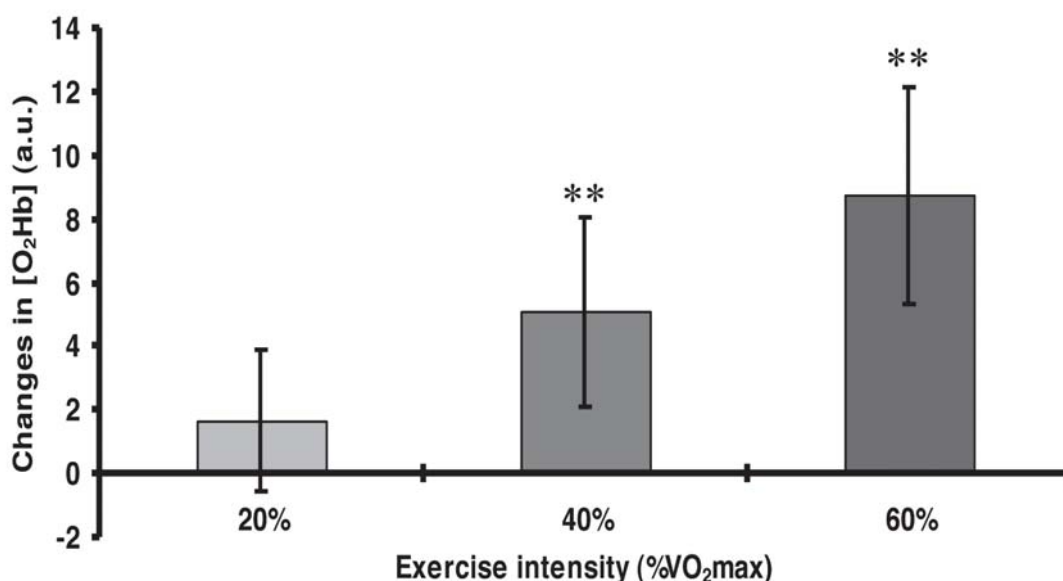


Figure 1 The hemodynamic changes after exercise at 20 %, 40 %, and 60 % VO_{2max} (1.66 ± 2.25 , 5.08 ± 2.96 , and 8.73 ± 3.41 a.u., respectively). Significant difference from pre-exercise, ** P -value < 0.01 .

Figure 2 illustrated the power spectrum density of EEG waves for the representative case (beta wave at 60 % VO_{2max}). The power spectrum as a percentage change in all four EEG waves compared

to baseline as shown in **Table 1**, increased significantly in alpha wave at 20 % and 40 % VO_2max whereas increased in beta wave at 40 % and 60 % VO_2max . There was no significant change in delta and theta waves. In addition, there was a significant positive correlation between beta wave and rCBV at Fp1 area

(correlation coefficient, $r = 0.53$, $P < 0.01$) (**Figure 3**). A positive correlation between alpha band and rCBV at Fp1 also presented ($r = 0.33$, $P = 0.05$). The results of hemodynamic change and EEG especially high frequency brain waves showed similar way by increase with the higher intensity of exercise.

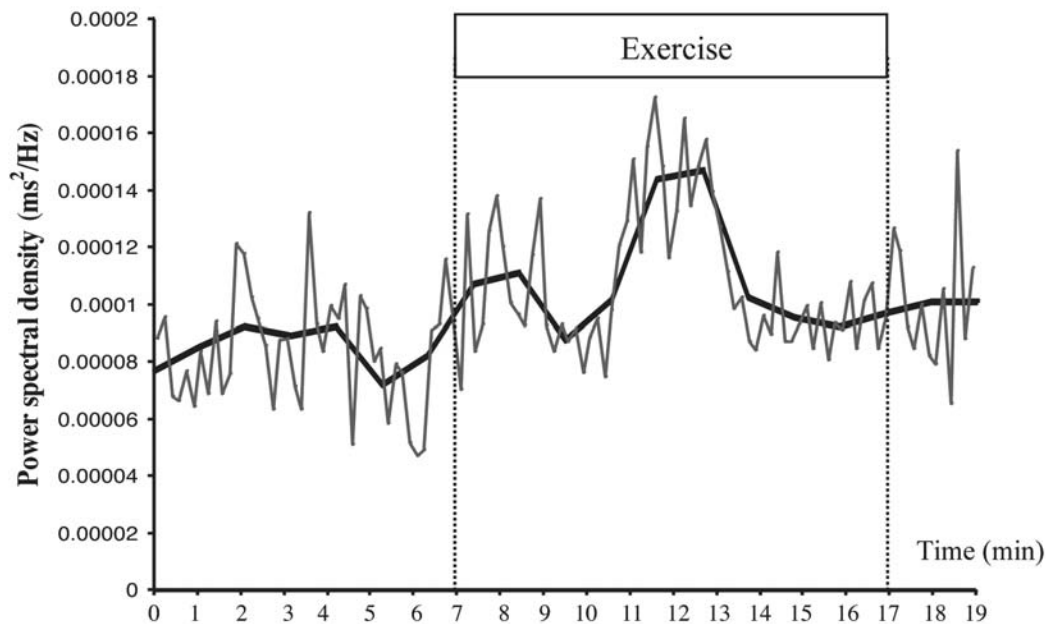


Figure 2 The representative EEG power spectrum density of beta wave at 60 % VO_2max of exercise intensity. Grey line represents data in every second. Black line represents average data.

Table 1 The mean power spectrum of delta (0.24-3.91 Hz), theta (3.91-7.08 Hz), alpha (7.08-12.94 Hz), and beta (12.94-29.79 Hz) obtained from at various intensities of cycling exercise as a percentage compared to 100 % of baseline. Data were presented in mean $\pm$ SD. * P -value < 0.05 .

	20 % VO_2max		40 % VO_2max		60 % VO_2max	
	% change	P -value	% change	P -value	% change	P -value
Delta	116.05 ± 32.95	0.08	104.86 ± 27.40	0.50	135.98 ± 74.05	0.50
Theta	109.18 ± 28.08	0.23	104.35 ± 16.63	0.33	118.87 ± 60.59	0.33
Alpha	107.17 ± 11.86	0.03 *	109.48 ± 16.67	0.04 *	116.29 ± 37.28	0.11
Beta	103.02 ± 11.02	0.31	107.74 ± 12.08	0.03 *	127.44 ± 44.64	0.03 *

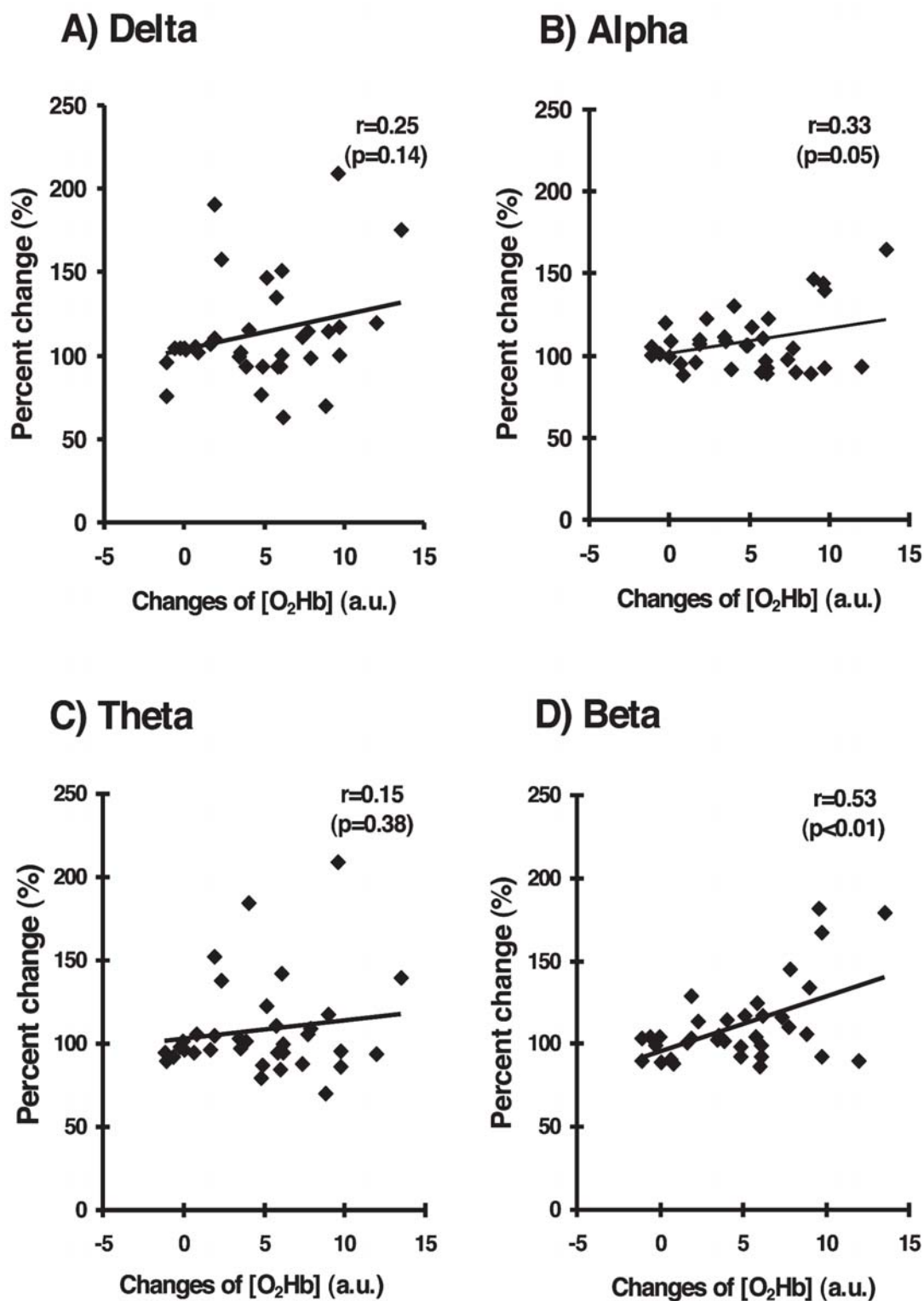


Figure 3 Scatter plot of percent change in O_2Hb concentration vs percent change of EEG power spectrum density immediately after 20 %, 40 %, and 60 % VO_2 max of exercise intensity. (A) Delta wave, (B) Alpha wave, (C) Theta wave, and (D) Beta wave. Note; at left prefrontal area, beta wave showed positive significant correlation with rCBV (as represented by O_2Hb concentration), whereas alpha wave showed mild to moderate positive correlation with rCBV.

Discussion

The goal of this present study was to assess the cortical activation as hemodynamic pattern change at low to moderate exercise intensity. This was accomplished by simultaneously using a noninvasive hemodynamic imaging (oxygenation change) monitor, NIRO 300, and electrophysiology monitor, the EEG. The results showed that the hemodynamic response increased with the increasing in exercise intensity. To our knowledge, the present study is the first attempt to correlate the hemodynamic response with brain wave in a time-course pattern on various exercise intensities.

Regarding the influence of skin blood flow which may contaminate the NIRS signals, previous studies^(15,16) have been reported the minor effects of skin blood flow on the NIRS-derived measurements. In addition, we used a laser Doppler tissue flowmeter (FLO-C1, Omegawave, Japan) to monitor the skin blood flow at Fp2 during exercise. The data suggested no significant influence of skin blood flow signal on the NIR-derived signals (data not shown here). These skin blood flow results provided supportive data to shed light on the NIRO 300 signals that measure the rCBV in the cerebral cortex. In addition, the increase of O_2Hb after exercise at about 40 % and 60 % VO_{2max} in this study, verified our previous study⁽⁶⁾ about the possible role of mild exercise in enhancing CBV in the prefrontal cortex.

The EEG results showed that the exercise intensity of 20 %, 40 % and 60 % VO_{2max} , induced changes of the high frequency brain waves (alpha and beta) with the greater proportion of high frequency waves reflects increased brain activation. Our results were consistent with previous studies of Kubitz and Mott (1996) whose reported alpha and beta activity increased during and after cycle ergometer⁽⁷⁾, and Oda et al. (1999) reported the increase of percent power of alpha after the underwater exercise⁽⁸⁾.

The positive correlation between the rCBV and the high frequency wave activity (beta and alpha) observed in this study corresponded with the previous studies in patients with cerebral infarction (18-20). In addition, not just in the increase direction, Nagata et al. (1994) reported decrease of beta-percentage power fraction was associated with reduction of rCBF and $rCMRO_2$ in frontal, central and parietal areas. Low frequency wave, theta and delta negatively correlated with the reduction of CBF and/or in patients with cerebral infarction especially in chronic stage. The correlation between hemodynamic response and EEG has been analyzed by Kilner et al.⁽²¹⁾ who proposed that brain activation caused an acceleration of temporal dynamics leading to (i) increased energy dissipation; (ii) decreased effective membrane time constants; (iii) increased effective coupling among neuronal ensembles; and (iv) a shift in the EEG spectral profile to higher frequencies.

There are some limitations of our study. First, we monitored EEG and CBV only 2 minutes immediately after exercise which limited us to describe the recovery pattern of rCBV. However, based on observation in each participant, the rCBV reached the maximum value within 2 minutes immediately after exercise. Second, regarding the protocol, we could not exclude the carry over effect if it has occurred. Last, due to technical limitations, although EEG has been monitored through the exercise session, the EEG data during exercise showed high noise to signal ratio in most cases which hampered us to relate the NIRS and EEG data during exercise session.

In the present study, we found an increase of rCBV at the prefrontal cortex had significant correlation with the increased beta-wave just after exercise, which has been increased with exercise above 40 % VO_{2max} , suggesting that certain extent of increased hemodynamic changes might be associated with brain arousal just after exercise.

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References

1. Roland PE, Meyer E, Shibasaki T, Yamamoto YL, Thompson CJ. Regional cerebral blood flow changes in cortex and basal ganglia during voluntary movements in normal human volunteers. *J Neurophysiol* 1982; 48: 467-80.
2. Obrig H, Hirth C, Junge-Hulsing JG, Doge C, Wolf T, Dirnagl U, et al. Cerebral oxygenation changes in response to motor stimulation. *J Appl Physiol* 1996; 81: 1174-83.
3. Nishijima T, Soya H. Evidence of functional hyperemia in the rat hippocampus during mild treadmill running. *Neurosci Res* 2006; 54: 186-91.
4. Buxton RB, Uludag K, Dubowitz DJ, Liu TT. Modeling the hemodynamic response to brain activation. *Neuroimage* 2004; 23: s220-33.
5. Ide K, Secher NH. Cerebral blood flow and metabolism during exercise. *Prog Neurobiol* 2000; 61: 397-414.
6. Timinkul A, Kato M, Omori T, Deocaris CC, Ito A, Kizuka T, et al. Enhancing effect of cerebral blood volume by mild exercise in healthy young men: a near-infrared spectroscopy study. *Neurosci Res* 2008; 61: 242-8.
7. Kubitz KA, Mott AA. EEG power spectral densities during and after cycle ergometer exercise. *Res Quar Exerc Sport* 1996; 67: 91-6.
8. Oda S, Matsumoto T, Nakagawa K, Moriya K. Relaxation effects in humans of underwater exercise of moderate intensity. *Eur J Appl Physiol* 1999; 80: 253-9.
9. Kamijo K, Nishihira Y, Hatta A, Kaneda T, Kida T, Higashiura T, et al. Changes in arousal level by differential exercise intensity. *Clin Neurophysiol* 2004; 115: 2693-8.
10. Hoshi Y. Near-infrared spectroscopy for studying higher cognition. In: Kraft E, Gulyás B, Pöppel E. eds. *Neural correlates of thinking*. Springer Berlin Heidelberg, 2008: 83-93.
11. Blinowska K, Müller-Putz G, Kaiser V, Astolfi L, Vanderperren K, Van Huffel S, et al. Multimodal imaging of human brain activity: rational, biophysical aspects and modes of integration. *Comput Intell Neurosci* 2009; article ID 813607, 10 pages.
12. Takeuchi M, Hori E, Takamoto K, Tran AH, Satoru K, Ishikawa A, et al. Brain cortical mapping by simultaneous recording of functional near infrared spectroscopy and electroencephalograms from the whole brain during right median nerve stimulation. *Brain Topogr* 2009; 22: 197-214.
13. Cooper RJ, Everdell NL, Enfield LC, Gibson AP, Worley A, Hebden JC. Design and evaluation of a probe for simultaneous EEG and near-infrared imaging of cortical activation. *Phys Med Biol* 2009; 54: 2093-102.
14. Yoshitani K, Kawaguchi M, Tatsumi K, Kitaguchi K, Furuya H. A comparison of the INVOS 4100 and the NIRO 300 near-infrared spectrophotometers. *Anesth Analg* 2002; 94: 586-90.

15. Hampson NB, Piantadosi CA. Near infrared monitoring of human skeletal muscle oxygenation during forearm ischemia. *J Appl Physiol* 1988; 64: 2449-57.
16. Mancini DM, Bolinger L, Li H, Kendrick K, Chance B, Wilson JR. Validation of near-infrared spectroscopy in humans. *J Appl Physiol* 1994; 77: 2740-7.
17. Mechau D, Mücke S, Wei M, Liesen H. Effect of increasing running velocity on electroencephalogram in a field test. *Eur J Appl Physiol* 1998; 78: 340-5.
18. Nagata K. Topographic EEG in brain ischemia-correlation with blood flow and metabolism. *Brain Topogr* 1988; 1: 97-106.
19. Nagata K, Tagawa K, Hiroi S, Shishido F, Uemura K. Electroencephalographic correlates of blood flow and oxygen metabolism provided by positron emission tomography in patients with cerebral infarction. *Electroencephalogr Clin Neurophysiol* 1989; 72: 16-30.
20. Tanaka A, Kimura M, Yoshinaga S, Tomonaga M, Mizoguchi T. Quantitative electroencephalographic correlates of cerebral blood flow in patients with chronic subdural hematomas. *Surg Neurol* 1998; 50: 235-40.
21. Kilner JM, Mattout J, Henson R, Friston KJ. Hemodynamic correlates of EEG: A heuristic. *Neuroimage* 2005; 28: 280-6.