Chapter 36
Cortical Oxyhemoglobin Elevation Persists After Moderate-Intensity Cycling Exercise: A Near-Infrared Spectroscopy Study

Atsuhiro Tsubaki, Nana Takehara, Daisuke Sato, Shinichiro Morishita, Yuta Tokunaga, Kazuhiro Sugawara, Sho Kojima, Hiroyuki Tamaki, Yudai Yamazaki, and Hideaki Onishi

Abstract Near-infrared spectroscopy (NIRS) can measure cortical activity during gross motor tasks based on the cerebral hemodynamic response. Although some reports suggest that cycling exercise improves cortical oxygenation, its after-effects are unknown. We examined the after-effects of low- and moderate-intensity cycling exercise on cortical oxygenation. Ten healthy volunteers (mean age 21.3 ± 0.7 years; 4 women) underwent cycle ergometer exercise at 30% or 50% of VO_2peak for 20 min, followed by an 8-min post-exercise rest (PER). O_2Hb levels of the supplementary motor area (SMA) and sensorimotor cortex (SMC) were recorded using a near-infrared spectroscopy system. Skin blood flow (SBF) and mean arterial pressure (MAP) were continuously measured. The peak values of O_2Hb between exercise and PER were compared. The O_2Hb, SBF, and MAP increased in the exercise phase. SBF degraded over time, and MAP decreased immediately after exercise. The O_2Hb decreased immediately and increased again in the PER. There were no significant differences between exercise and PER in the SMC in the 30% VO_2peak experiment or in the SMA and SMC in the 50% VO_2peak experiment. The O_2Hb in the motor-related area was elevated during both exercise and PER especially in the 50% VO_2peak experiment.

Keywords Cortical oxyhemoglobin • Cycling exercise • Moderate-intensity • Motor-related area • After-effects

A. Tsubaki (✉) • N. Takehara • D. Sato • S. Morishita • K. Sugawara • S. Kojima • H. Tamaki
Y. Yamazaki • H. Onishi
Institute for Human Movement and Medical Sciences, Niigata University of Health and Welfare, 1398 Shimami-cho, Kita-ku, Niigata-city, Niigata 950-3198, Japan
e-mail: tsubaki@nuhw.ac.jp

Y. Tokunaga
Niigata Rehabilitation Hospital, 761, Kizaki, Kita-ku, Niigata-shi, Niigata 950-3304, Japan

H.J. Halpern et al. (eds.), *Oxygen Transport to Tissue XXXIX*, Advances in Experimental Medicine and Biology 977, DOI 10.1007/978-3-319-55231-6_36

1 Introduction

Near-infrared spectroscopy (NIRS) measures the concentration of oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) in tissues, using the modified Beer-Lambert law [1], and is suitable for investigating cortical oxygenation during human gait [2] and cycling exercise [3, 4] based on its non-invasiveness. It is well known that aerobic training leads to an increase in grey matter volume in motor-related areas [5]. Additionally, the effect of a single bout of aerobic exercise on cortical oxygenation has been measured during exercise [4, 6]. However, the after-effects of a single bout of aerobic exercise and the effect of exercise intensity are currently unknown.

Our study determined the after-effects of constant-load cycle ergometer exercise performed at low- and moderate-intensity in terms of O_2Hb changes in motor-related cortical areas.

2 Methods

2.1 Participants

Ten healthy volunteers (mean age 21.3 years, SD 0.7 years; 4 women) participated in this study. The subjects did not exhibit symptoms of neurological, medical, or cardiovascular disease and were not taking any medications. Each subject provided written consent after receiving information regarding the potential risks, study objectives, measurement techniques, and benefits associated with the study. This study was approved by the Ethics Committee of Niigata University of Health and Welfare and conformed to the standards of the Declaration of Helsinki.

2.2 Experimental Procedure

To determine individual exercise workload, peak oxygen consumption (VO_2peak) was obtained by an automated metabolic analyzer (AE-310, Minato Medical Science, Osaka, Japan) using an incremental protocol on a cycle ergometer (Aerobike 75XLII; Combi, Tokyo, Japan) before the main experiments. Exhaustion was defined as described previously [4].

In the main experiment, subjects performed constant work-rate exercise corresponding to 30% or 50% of VO_2peak on a cycle ergometer for 20 min, following a 4-min rest and a 4-min warm-up period. An 8-min post-exercise rest (PER) followed the main exercise. During this experiment, the NIRS signals, skin blood flow (SBF), and mean arterial pressure (MAP) were measured continuously.

2.3 NIRS Measurements

A multichannel NIRS imaging system (OMM-3000; Shimadzu Co., Kyoto, Japan) with continuous multiple wavelengths (780, 805, and 830 nm) was used to detect changes in oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) using the modified Beer-Lambert law [4] at a sampling rate of 190 ms. NIRS optodes, consisting of 12 light-source fibers and 12 detectors providing 34-channel simultaneous recording, were set in a 3 × 8 multichannel probe holder. A 30-mm interoptode distance was used to measure cortical tissue oxygenation. We used a double-density probe holder, consisting of 2 sets, one of which was shifted to half the optode distance from the origin. The Cz position of the international 10–20 system was used to ensure consistent optode placement among all subjects [6]. The NIRS array map covered the right central, left central, and parietal areas of the scalp to measure cortical tissue-oxygenation in motor-related areas. Regions of interest (ROI) were the supplementary motor area (SMA) and sensorimotor cortex (SMC) (Fig. 36.1).

2.4 Blood Pressure and Skin Blood-Flow Measurements

Beat-to-beat MAP was recorded by volume clamping the finger pulse with a finger photoplethysmograph (Finometer; Finapres Medical Systems, Amsterdam, the Netherlands) on the left middle finger. Changes in SBF were measured at the forehead using a laser Doppler blood flow meter (Omegaflow FLO-CI; Omegawave Inc., Osaka, Japan). Analogue data were converted to digital data using an A/D converter (PowerLab; AD Instruments, Australia) at a 1000-Hz sampling rate.

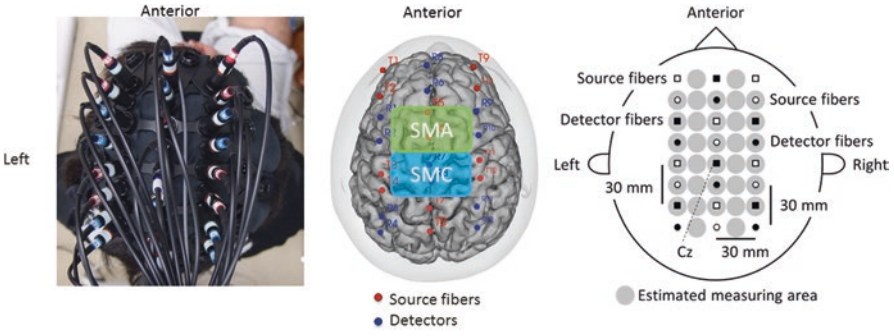

Fig. 36.1 Location of the 12 light-source fibers and 12 detectors, and regions of interest (ROI). White squares and white circles are light-source fibers and black squares and black circles are detector fibers. Each set (squares and circles) consisted of six light-source fibers and six detector fibers, with an interoptode distance of 30 mm, and were spaced evenly

Table 36.1 Comparison of oxyhemoglobin (O_2Hb) between exercise and post-exercise rest (PER) for each region of interest (ROI) (mM.cm)

	ROI	Exercise	PER	*p*-value
30% VO_2peak	SMA	0.038 ± 0.013	0.024 ± 0.009	< 0.05
	SMC	0.044 ± 0.016	0.032 ± 0.011	0.09
50% VO_2peak	SMA	0.084 ± 0.015	0.072 ± 0.009	0.23
	SMC	0.099 ± 0.042	0.097 ± 0.036	0.83

Values are presented as mean ± standard error of the mean (SEM). Paired *t*-test was used to obtain *p*-values

2.5 Statistical Analysis

SBF and MAP were down-sampled by adopting the sampling rate for NIRS monitoring. To obtain temporal changes, the averages of the O_2Hb and HHb for each ROI, SBF, and MAP were expressed as the change from the average rest phase value and were calculated every 1 min. The peak values of O_2Hb during exercise and PER were compared by a paired t-test with the significance level set at $p < 0.05$. The relationship between O_2Hb and SBF was assessed using Pearson's correlation coefficients, with significance set at $p < 0.05$ during the main exercise period and PER period.

3 Results

O_2Hb moderately elevated through the main experiment in SMA and SMC at 30% of VO_2peak. HHb drifted below the rest phase in both ROI. During 50% VO_2peak exercise, O_2Hb increased during the initial 7 min of the 20-min main exercise, and then maintained its value in both regions until the end of exercise. The SBF and MAP increased in the exercise phase.

After the exercise, O_2Hb decreased immediately and subsequently increased again in the PER for 30% VO_2peak and 50% VO_2peak conditions. The elevated O_2Hb persisted throughout the PER in both ROIs. SBF degraded over time, and MAP decreased immediately after the exercise. For the 30% VO_2peak experiment, O_2Hb during exercise was significantly larger than during PER in the SMA. There were no significant differences between exercise and PER in the SMC in the 30% VO_2peak experiment or in the SMA and SMC in the 50% VO_2peak experiment (Table 36.1) (Figs. 36.2 and 36.3).

The correlation coefficients between SBF and O_2Hb differed between the exercise phase and PER (Table 36.2). There were significant positive correlations between O_2Hb and SBF in both ROIs and for both intensities during the exercise phase. However, in the PER there were no significant correlations between O_2Hb and SBF for either ROI or intensity level.

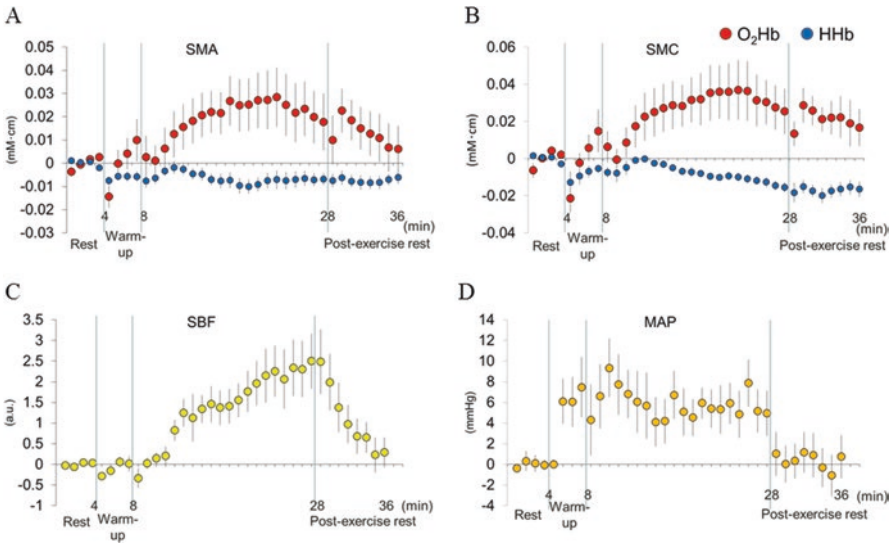

Fig. 36.2 Temporal changes in oxyhemoglobin (O_2Hb, red circle) and deoxyhemoglobin (HHb, blue circle) values in the supplemental motor area (SMA, A), in the sensorimotor cortex (SMC, B), and skin blood flow (SBF, C) and mean arterial pressure (MAP, D) for exercise at 30% of VO_2peak. Values are presented as mean ± standard error of the mean (SEM)

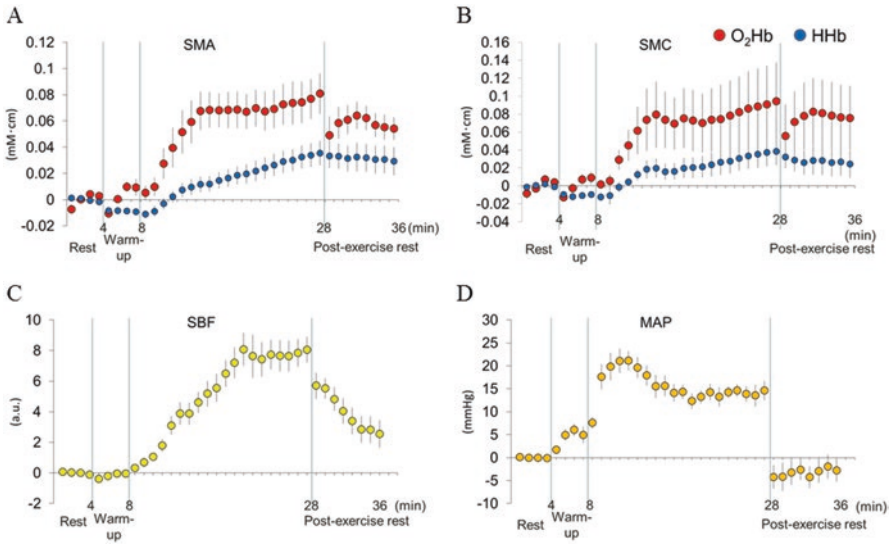

Fig. 36.3 Temporal changes in oxyhemoglobin (O_2Hb, red circle) and deoxyhemoglobin (HHb, blue circle) values in the supplemental motor area (SMA, A), in the sensorimotor cortex (SMC, B), and skin blood flow (SBF, C) and mean arterial pressure (MAP, D) for exercise at 50% of VO_2peak. Values are presented as mean ± standard error of the mean (SEM)

Table 36.2 Relationship between oxyhemoglobin (O_2Hb) and skin blood flow (SBF) during exercise and post-exercise rest (PER) for each intensity and each region of interest (ROI)

	ROI	Exercise	*p*-value	PER	*p*-value
30% VO_2peak	SMA	0.807	< 0.01	0.546	0.162
	SMC	0.831	< 0.01	0.070	0.870
50% VO_2peak	SMA	0.896	< 0.01	– 0.100	0.813
	SMC	0.869	< 0.01	– 0.620	0.101

Pearson's correlation coefficients

4 Discussion

In the present study, we measured cerebral oxygenation in motor-related areas during and after low- and moderate-intensity cycling exercise. O_2Hb increased during exercise, and then increased again after participants stopped the exercise; O_2Hb values following exercise did not differ from the values obtained during exercise, most notably for moderate-intensity exercise.

NIRS can be used to measure changes in the cerebral hemodynamic response and metabolism, thus allowing for the use of multichannel NIRS recording for functional optical imaging of human brain activity [7]. Although many studies have reported cerebral oxygenation levels during incremental [3, 4, 8] or constant work-rate [6, 9] exercise, the after-effects of the exercise were unknown. Our study clarifies the after-effects of a gross motor task, and thus provides fundamental data regarding neural plasticity induced by exercise.

It is necessary to consider the effect of systemic changes on initial O_2Hb levels. In this study, SBF, MAP, and O_2Hb all increased during 20-min of exercise at 30% of VO_2peak and 50% of VO_2peak. In contrast, we observed that O_2Hb, SBF, and MAP exhibited different changes in the PER in this study. The correlation coefficients between SBF and O_2Hb were 0.807 to 0.896 during exercise. Meanwhile, the correlation coefficients between SBF and O_2Hb were −0.620 to 0.546 in the PER. These results indicate that, although O_2Hb might be affected by SBF and/or MAP during 20-min cycling exercise, the effects of systemic changes on O_2Hb were very weak in the PER. Several studies have indicated that SBF influences O_2Hb changes as measured by NIRS [10, 11]. In addition, MAP influences O_2Hb [12]. We have previously described that, although SBF, MAP, and O_2Hb were moderately to strongly correlated during 5-min of exercise at 30% of VO_2peak or 50% of VO_2peak [13], correlation coefficients between SBF, MAP, and O_2Hb fluctuated during 20-min of exercise at 30% of VO_2peak [6]. Our previous study showed correlation coefficients between SBF, MAP, and O_2Hb that were negative or very weak after the exercise (r = −0.798 in SBF; r = 0.253 in MAP) [13].

The O_2Hb values increased again in SMA and SMC in the PER following both exercise intensities. In particular, O_2Hb values in the PER after 50%VO_2peak exercise did not differ significantly from the values obtained during the exercise. These results suggest that cerebral oxygenation in the PER in motor-related areas was similar to that during the exercise, even though the participants had stopped their

movements. We consider that the exercise-induced blood flow increase might be based on vasodilation of the capillaries in the motor-related area. Moderate intensity aerobic exercise increases cerebral blood flow [14]. Increased blood flow produces nitric oxide (NO), which is a vasodilator in neurovascular coupling [15, 16]. NO-induced vasodilation may cause elevated O_2Hb to persist after moderate-intensitycycling exercise. In contrast, O_2Hb reflects changes in cortical neural activation [2, 17, 18]. Based on this phenomenon, neural activation in motor-related areas may remain after exercise. We need to ascertain that neural activation persists after exercise using other modalities.

This study had some limitations. First, we only measured oxygenation of the motor-related cerebrum, due to methodological limitations. Our study did not consider the distribution of cerebral blood flow within other cortical regions during and after exercise. Second, the measurement locations differed for SBF and O_2Hb. SBF was recorded at the forehead to prevent interference from the near-infrared and laser light emitted from the laser Doppler flow meter.

In conclusion, we found that elevated O_2Hb values in motor-related areas persist after exercise, and indeed remain as high as during exercise. This result suggests that neuroplasticity may be facilitated by aerobic exercise training.

Acknowledgments This study was supported by a Grant-in-Aid for Scientific Research (C) from the Japan Society for the Promotion of Science and a Grant-in-Aid for Exploratory Research from the Niigata University of Health and Welfare.

References

1. Boas DA, Gaudette T, Strangman G et al (2001) The accuracy of near infrared spectroscopy and imaging during focal changes in cerebral hemodynamics. NeuroImage 13:76–90
2. Miyai I, Tanabe HC, Sase I et al (2001) Cortical mapping of gait in humans: A near-infrared spectroscopic topography study. NeuroImage 14:1186–1192
3. Bhambhani Y, Malik R, Mookerjee S (2007) Cerebral oxygenation declines at exercise intensities above the respiratory compensation threshold. Respir Physiol Neurobiol 156:196–202
4. Rupp T, Perrey S (2008) Prefrontal cortex oxygenation and neuromuscular responses to exhaustive exercise. Eur J Appl Physiol 102:153–163
5. Anazodo UC, Shoemaker JK, Suskin N et al (2013) An investigation of changes in regional gray matter volume in cardiovascular disease patients, pre and post cardiovascular rehabilitation. Neuroimage Clin 3:388–395
6. Tsubaki A, Takai H, Kojima S et al (2016) Changes in cortical oxyhaemoglobin signal during low-intensity cycle ergometer activity: a near-infrared spectroscopy study. Adv Exp Med Biol 876:79–85
7. Tamura M, Hoshi Y, Okada F (1997) Localized near-infrared spectroscopy and functional optical imaging of brain activity. Philos Trans R Soc Lond Ser B Biol Sci 352:737–742
8. Peltonen JE, Paterson DH, Shoemaker JK et al (2009) Cerebral and muscle deoxygenation, hypoxic ventilatory chemosensitivity and cerebrovascular responsiveness during incremental exercise. Respir Physiol Neurobiol 169:24–35
9. Higashimoto Y, Honda N, Yamagata T et al (2011) Activation of the prefrontal cortex is associated with exertional dyspnea in chronic obstructive pulmonary disease. Respiration 82:492–500

10. Takahashi T, Takikawa Y, Kawagoe R et al (2011) Influence of skin blood flow on near-infrared spectroscopy signals measured on the forehead during a verbal fluency task. NeuroImage 57:991–1002
11. Kirilina E, Jelzow A, Heine A et al (2012) The physiological origin of task-evoked systemic artefacts in functional near infrared spectroscopy. NeuroImage 61:70–81
12. Minati L, Kress IU, Visani E et al (2011) Intra- and extra-cranial effects of transient blood pressure changes on brain near-infrared spectroscopy (NIRS) measurements. J Neurosci Methods 197:283–288
13. Tsubaki A, Takai H, Oyanagi K et al (2016) Correlation between the cerebral oxyhaemoglobin signal and physiological signals during cycling exercise: A near-infrared spectroscopy study. Adv Exp Med Biol 923:159–166
14. Sato K, Ogoh S, Hirasawa A et al (2011) The distribution of blood flow in the carotid and vertebral arteries during dynamic exercise in humans. J Physiol 589:2847–2856
15. Frangos JA, Eskin SG, Mcintire LV et al (1985) Flow effects on prostacyclin production by cultured human endothelial cells. Science 227:1477–1479
16. Dimmeler S, Fleming I, Fisslthaler B et al (1999) Activation of nitric oxide synthase in endothelial cells by Akt-dependent phosphorylation. Nature 399:601–605
17. Obrig H, Wolf T, Doge C et al (1996) Cerebral oxygenation changes during motor and somatosensory stimulation in humans, as measured by near-infrared spectroscopy. Adv Exp Med Biol 388:219–224
18. Niederhauser BD, Rosenbaum BP, Gore JC et al (2008) A functional near-infrared spectroscopy study to detect activation of somatosensory cortex by peripheral nerve stimulation. Neurocrit Care 9:31–36