

<研究報告>

The effect of mode of ventilation on cerebral oxygenation during static exercise

Kohei SATO, Ai HIRASAWA and Tomoko SADAMOTO

Abstract

The purpose of the present study was to determine the effect of the mode of ventilation on the cerebral oxygenation during heavy static exercise. Eight subjects performed static arm flexion exercise (70~80% of the maximal voluntary contraction force) with the following three different ventilation mode ; exercise with continued ventilation (CONT), exercise with concomitant breath holding (EX + BH), and exercise with pre-exercise hyperventilation (HV + EX). The levels of oxy-hemoglobin (HbO₂), deoxy-hemoglobin (HHb), and total hemoglobin (THb) in the left prefrontal cortex were continuously monitored by the Near-infrared spectorscopy (NIRS). The main findings in the present study are as follows : 1) In EX + BH, prefrontal cortex O₂Hb and THb during exercise show sharper and more marked increase than in CONT ; and 2) In HV + EX, prefrontal cortex O₂Hb and THb responses during exercise were significantly smaller than those in CONT. These results show that the respiration mode before and during exercise affects prefrontal cortex oxygenation and blood volume during heavy static exercise.

Key words: Valsalva breathing, hyperventilation, cerebral blood flow

Introduction

Change in the middle cerebral artery mean blood flow velocity ($MCA V_{mean}$) during heavy static and resistance exercise could be associated with the mode of ventilation, including the potential for expiratory strain with heavy exercise (Valsalva-like maneuver) (Pott *et al.* 2003), and hypocapnia induced by hyperventilation before exercise (Edwards *et al.* 2002 ; Romero and Cook 2007). A previous study reported marked increase in $MCA V_{mean}$ at the on-

set of maximal two-legged extension with concomitant Valsalva-like maneuver (Pott *et al.* 2003). More recently, Romero and Cooke (2007) demonstrated that hypocapnia induced by hyperventilation before exercise exacerbates the reduction in $MCA V_{mean}$ during and after leg-press resistance exercise. However, these investigations mainly focus on the blood flow responses in the large vessel of the brain and there is no information regarding the effect of the mode of ventilation on the cerebral tissue oxygenation and blood volume at the level of arteriolar, capillary, and venule during heavy

exercise.

Cerebral oxygenation reflected cerebral functional activity, and can be measured with several techniques (Obrig *et al.* 1996 ; Colier *et al.* 1999). Near-infrared spectroscopy (NIRS) allows for non-invasive monitoring of regional changes in cortical tissue oxygenation in response to various stimuli (Obrig *et al.* 1996 ; Colier *et al.* 1999 ; Obrig *et al.* 2000). NIRS permits monitoring of change in oxy-hemoglobin (HbO₂) and deoxy-hemoglobin (HHb) with a high temporal resolution. The sum of these parameters provides an index of the relative change in total Hb (THb), which is considered to reflect the blood volume change of the cerebral tissue.

The purpose of the present study was to determine the effect of the mode of ventilation on the cerebral oxygenation during heavy static exercise by using NIRS. In order to clarify this effect, the subjects performed heavy static exercise with the following three different ventilation mode ; 1) exercise with continued ventilation, 2) exercise with concomitant breath holding, and 3) exercise with pre-exercise hyperventilation.

Methods

Subjects

Eight male field athletes (6 shot putters and 2 hammer throwers ; mean age \pm SD : 21.5 \pm 1.3 years) volunteered to participate in this study after providing informed consent to the protocol, as approved by the ethics committee of Japan Women's College of Physical Education.

Exercise protocol and mode of ventilation

In this study, right elbow flexion was performed with the use of a multifunctional dynamometer (VINE, Japan). The subjects were seated in a custom-made chair in which a con-

stant body position could be maintained throughout the exercise. The right upper arm was kept on a padded rest, and the wrist was attached to an arm lever by a Velcro strap. The exercise load selected was 70-80% of the maximal voluntary contraction (MVC) force.

After a 3-min resting period, the subjects performed 15-s static exercises at 70-80% MVC with the following 3 different modes of ventilation (in random order) : 1) exercise with continued ventilation (control ; CONT), 2) exercise with concomitant breath holding (EX + BH), and 3) pre-exercise hyperventilation with exercise (HV + EX) .

In CONT, all subjects were instructed to breathe normally and avoid holding their breath at rest and recovery, and during exercise. In EX + BH, all subjects performed 15-s static exercises with concomitant breath holding. In HV + EX, after a 2-min rest, the subjects were instructed to perform voluntary hyperventilation for 1-min in order to achieve a P_{ET}CO₂ of \sim 3.5% (Cooke and Romero 2007). After the 1-min hyperventilation, the subjects performed 15-s static exercises with continued ventilation. Subjects were positioned so that they could see their P_{ET}CO₂ level.

Measurement

Cerebral oxygenation

The detection and emission probes of an NIRS (NIRO-300 ; Hamamatsu Photonics, Japan) were separated by 4 cm. The probe was fixed in place by using a dense rubber vinyl holder that also eliminated any incidental room light. It was placed over the left frontal lobe (Bhambhani *et al.*, 2007). The prefrontal lobe was chosen as it has been previously studied during exercise (Bhambhani *et al.*, 2007). The NIRO-300 uses laser light at four wavelengths (775, 810, 850, 905 nm) to calculate relative concentration changes in oxy-haemoglobin (HbO₂), deoxy-

haemoglobin (HHb) and total hemoglobin (THb = HbO₂ + HHb) using the modified Beer-Lambert Law (Ferrari *et al.*, 2004). A differential pathlength factor (DPF) was not used in this study, and thus values for HbO₂, HHb and tHb are reported as relative quantitative changes in concentration from the baseline (mM*cm). The levels of HbO₂, Hb, and THb were continuously sampled by the NIRS unit at a rate of 2 Hz. These parameters are expressed as a change from 0.

MCA V_{mean} and cardiorespiratory responses

MCA V_{mean} measurement was performed with an ultrasound system (Vivid 7; GE Yokogawa Medical Systems, Japan) equipped with a 2.0 MHz sector transducer. We first used B-mode imaging to visualize the ipsilateral MCA, and subsequently, real-time Doppler velocity spectrum was identified in PW-mode. Blood flow velocity measurements were obtained with the sample volume set at 7~8 mm and with the vector of the cursor positioned in the center of the blood stream, parallel to the vessel axis. The MCA V_{mean} was defined as the time-averaged mean velocity obtained in automatic calculation mode.

MAP was measured non-invasively by photoelectric plethysmography with Finometer (Finapres Medical Systems, Netherlands). Furthermore, we determined the heart rate (HR), stroke volume (SV), and thus cardiac output (CO), from the blood pressure wave form by using the Model flow software program, which incorporated gender, age, height, and weight (Beat Scope 1.1, Finapres Medical Systems, Netherlands). The CO was calculated as SV × HR.

Respiratory parameters were determined with an online system for the breath-by-breath method. Respiratory gas was sampled continuously from a face mask. The gas fractions were

analyzed by a mass spectrometer (ARCO-2000, Arco System, Japan) that was calibrated and confirmed before each test. The expired gas volume was measured by a Fleisch pneumotachometer (WLSU-5201, Westron, Japan). Breath-by-breath data were analyzed with customized software on a computer (PC-9821, Toshiba, Japan), and expiratory minute ventilation (\dot{V}_E) and $P_{\text{ET}} \text{CO}_2$ were calculated.

Data processing and statistics

The beat-to-beat values of HbO₂, Hb, THb, MAP, and CO were averaged over 1-s intervals. Breath-by-breath values for respiration and $P_{\text{ET}} \text{CO}_2$ were averaged over 5-s intervals. Moreover, the MCA V_{mean} for each subject was averaged over 2-s intervals immediately before, during, and immediately after exercise.

Values were expressed as the mean ± SE. To confirm whether the parameters had actually changed as a result of exercise as compared with the resting values, two-way analysis of variance (ANOVA) with repeated measurements and Dunnett's t-test were conducted. Differences between the three trials were further analyzed with Scheffe's post-hoc analysis. These statistical analyses were computed by SPSS 12.0 software (SPSS, Tokyo, Japan) and $P < 0.05$ was considered to indicate a significant difference.

Results

Cerebral oxygenation and MCA V_{mean}

The cerebral oxygenation and MCA V_{mean} responses at rest, during, and after exercise are illustrated in **Fig. 1**. **Fig. 2** also shows the cerebral oxygenation responses immediately before, during, and immediately after exercise over an expanded time scale.

In EX + BH, O₂Hb increased sharply after the start of exercise and reached the maximum

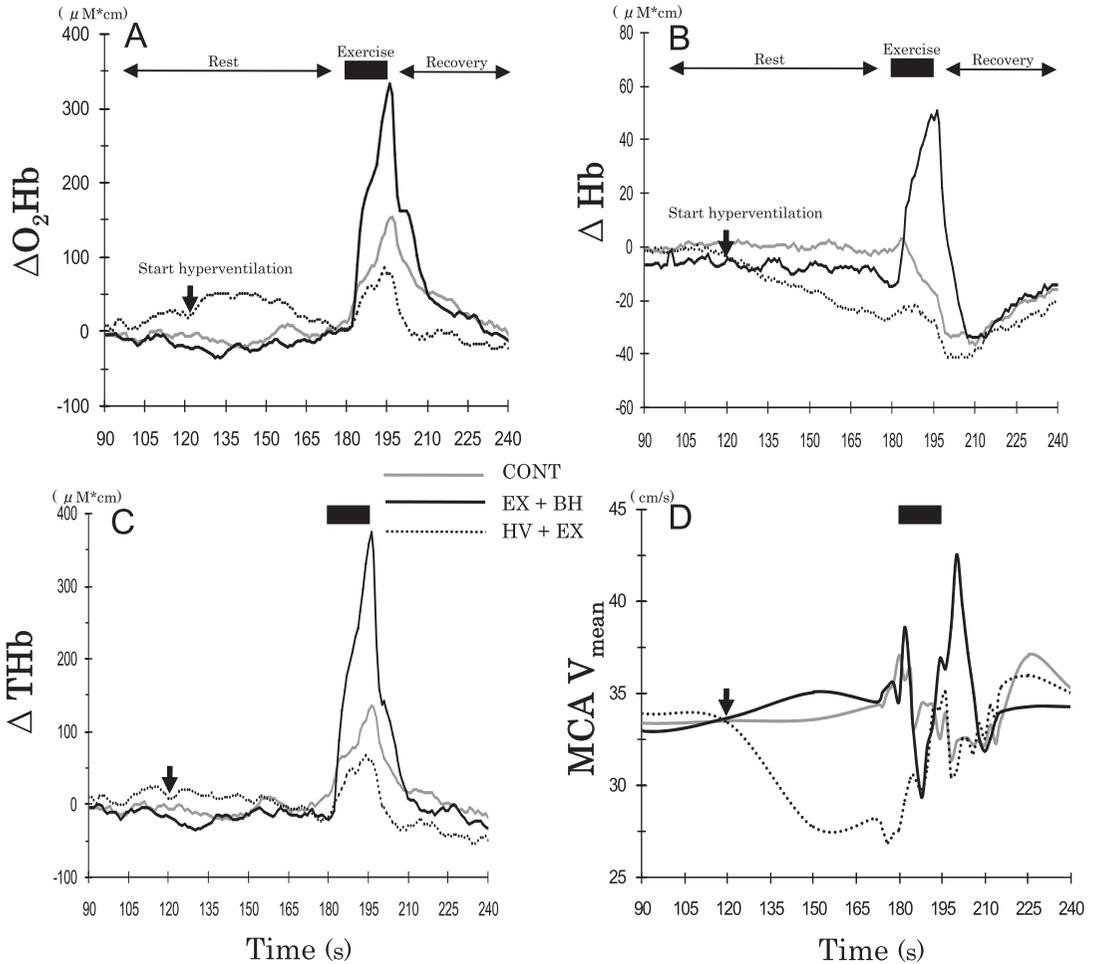


Fig. 1 Cerebral oxygenation and middle cerebral artery mean blood flow velocity at rest, during, and after static exercise. (A) ΔO_2Hb ; oxy-hemoglobin concentration, (B) ΔHHb ; deoxy-hemoglobin concentration, (C) ΔTHb ; total hemoglobin, (D) $MCA V_{mean}$; middle cerebral artery mean blood flow velocity.

value ($330 \pm 17 \text{ mM}^*cm$) at 1 s after the completion of exercise. The amount of increase in O_2Hb in EX + BH was approximately 2 times that in CONT. In HV + EX, on the other hand, O_2Hb started to increase slightly beginning from the start of hyperventilation following a 2 minute rest but returned to the resting value at the start of exercise. The amount of increase in O_2Hb during exercise in HV + EX was about one-half that in CONT ($77 \pm 22 \text{ mM}^*cm$ at the completion of exercise). O_2Hb values at the

completion of exercise in EX + BH and HV + EX were significantly different from the value in CONT.

In CONT, HHb gradually decreased after the start of exercise and reached the minimum value ($-37 \pm 5 \text{ mM}^*cm$) at 15 s after the completion of exercise. Then, HHb gradually returned to the resting value; however, the value at 45 s after the completion of exercise was still significantly higher than the resting value. Contrary to CONT, in EX + BH, HHb started to

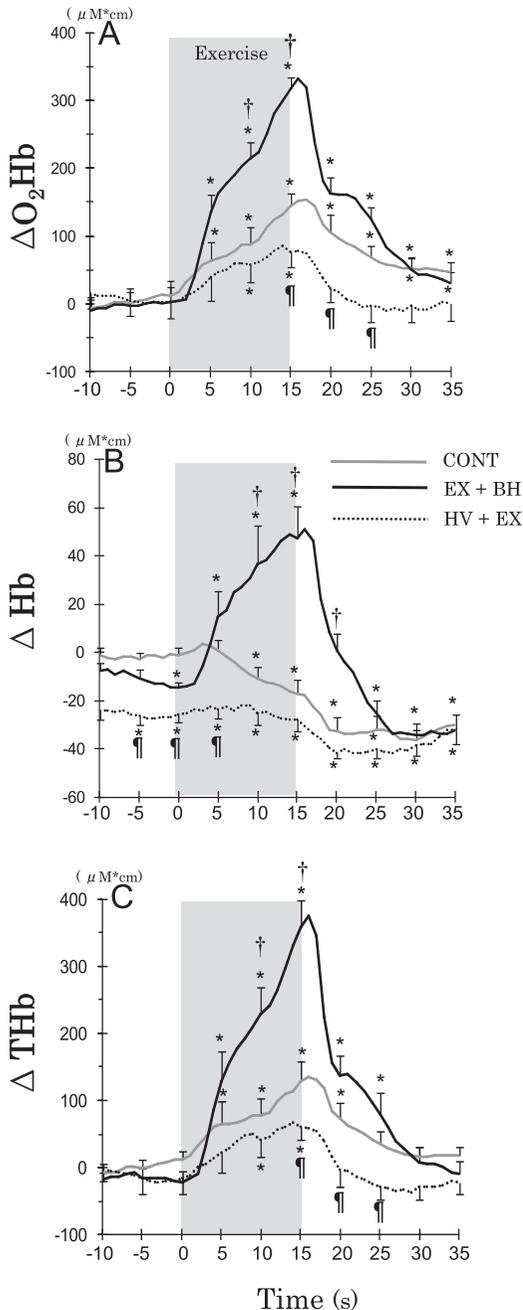


Fig. 2 (A) ΔO_2Hb , (B) ΔHb , (C) ΔTHb at rest, during, and after static exercise over an expanded time scale. * different from rest ($P < 0.05$). † ‡ different from CONT ($P < 0.05$).

increase sharply after the start of exercise and reached the maximum value ($50 \pm 13 \text{ mM}^* \text{cm}$) immediately after the completion of exercise. Hb decreased sharply after the completion of exercise and reached the minimum value ($-34 \pm 4 \text{ mM}^* \text{cm}$) at about 15 s after the completion of exercise and then gradually returned to the previous value. In HV + EX, Hb gradually decreased after the start of hyperventilation and reached $-22 \pm 5 \text{ mM}^* \text{cm}$ at the start of exercise. Hb remained almost unchanged during exercise and showed the minimum value ($40 \pm 3 \text{ mM}^* \text{cm}$) at about 10 s after the completion of exercise. Hb during exercise in EX + BH was significantly higher than that in CONT, and Hb immediately before and immediately after exercise in EX + BH was significantly lower than that in CONT.

In all respiration modes, THb responses during exercise were similar to HbO₂ responses. THb at 10 to 15 s after the start of exercise in EX + BH was significantly higher than that in CONT, and THb responses at the completion of exercise and until 10 s after the completion of exercise in HV + EX were significantly lower than those in CONT.

MCA V_{mean} responses were completely different among the 3 respiration modes. In CONT, MCA V_{mean} slightly increased immediately before the start of exercise and gradually decreased during exercise. MCA V_{mean} was lower than the resting value until at 15 s after the completion of exercise and then returned to the previous value. In EX + BH, on the other hand, MCA V_{mean} increased sharply for several seconds immediately after the start of exercise, then decreased sharply until 8 s after the start of exercise and reached the minimum value ($29 \pm 8 \text{ cm/s}$). Then, MCA V_{mean} continued to increase toward the completion of exercise and reached the maximum value ($42 \pm 6 \text{ cm/s}$) at 5 s

after the completion of exercise. That is, $MCA V_{\text{mean}}$ showed 3-phase responses during exercise and an overshoot after exercise. In HV + EX, beginning from the start of hyperventilation, $MCA V_{\text{mean}}$ showed a significant decrease than the resting value and decreased to 27 ± 4 cm/s at the start of exercise. $MCA V_{\text{mean}}$ during exercise gradually increased toward the completion of exercise. $MCA V_{\text{mean}}$ decreased temporarily and then returned to the resting value.

Cardiorespiratory responses

The $P_{\text{ET}} \text{CO}_2$, MAP, and CO responses at rest, during, and after exercise are also displayed in Fig. 3. In CONT, $P_{\text{ET}} \text{CO}_2$ decreased from about 38.5 mmHg at rest to about 35.5 mmHg at 5 s after the start of exercise. $P_{\text{ET}} \text{CO}_2$ gradually increased after the completion of exercise and reached about 42 mmHg at 20 seconds after the completion of exercise. The subjects in EX + BH performed breath holding during exercise, and no $P_{\text{ET}} \text{CO}_2$ data during exercise are available ; $P_{\text{ET}} \text{CO}_2$ at about 15 s after the completion of exercise was higher (about 41 mmHg) than the resting value. In HV + EX, $P_{\text{ET}} \text{CO}_2$ decreased sharply from the start of hyperventilation and reached the steady state at about 28 mmHg. $P_{\text{ET}} \text{CO}_2$ increased during exercise and then gradually returned to the resting value after the completion of exercise.

MAP in CONT started to increase immediately before the start of exercise. MAP in CONT then showed 3-phase responses consisting of the following : 1) a sharp increase after the start of exercise ; 2) a temporary decrease during exercise ; and 3) an increase toward the completion of exercise. MAP responses in EX + BH were 3-phase responses as in CONT, but the amount of increase in EX + BH was significantly larger than that in CONT. However, MAP responses in HV + EX were different from those in other ventilation modes. MAP in HV +

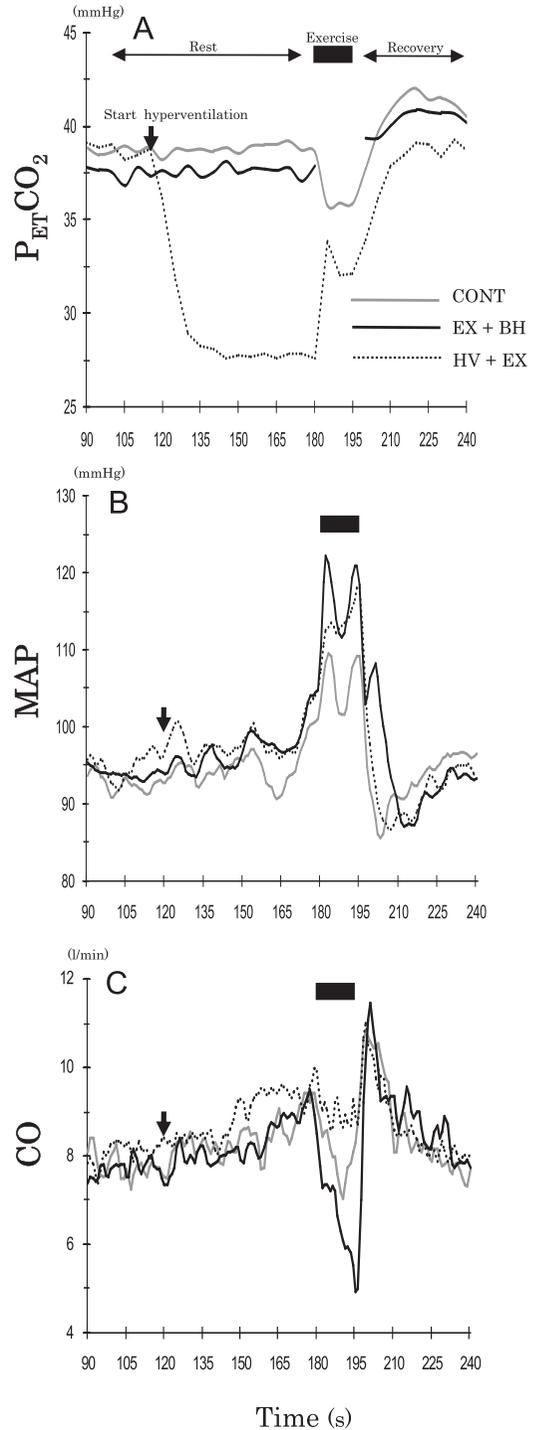


Fig. 3 Cardiorespiratory responses at rest, during, and after static exercise. (A) $P_{\text{ET}} \text{CO}_2$; end-tidal CO_2 pressure, (B) MAP; mean arterial pressure, (C) O; cardiac output.

EX increased sharply after the start of exercise and continued to increase toward the completion of exercise. In all respiration modes, the blood pressure temporarily became lower than the resting value after the completion of exercise; this temporary decrease in blood pressure was slightly delayed only in EX + BH.

In CONT, CO increased slightly before the start of exercise, but decreased from the start toward the middle of exercise. CO reached the minimum value (7.0 ± 0.8 l/min) at 10 s after the start of exercise, and then increased and reached the maximum value (10.7 ± 0.6 l/min) at 10 s after the completion of exercise. In EX + BH, the reduction in CO during exercise was more marked; CO decreased to 4.9 ± 0.8 l/min at the completion of exercise. Then, CO showed a sharp overshoot for 5 s after the completion of exercise and reached the maximum value (11.4 ± 0.7 l/min) and then returned to the resting value. In HV + EX, CO started to increase slightly at about 40 s before the start of exercise. CO during exercising did not change significantly from the resting value and, as in other respiration modes, increased after exercise, showing the maximum value (11.0 ± 0.5 l/min).

Discussion

The main findings in the present study are as follows: 1) When the subjects underwent breath holding during heavy static exercise, prefrontal tissue O_2Hb and THb during exercise show sharper and more marked increase than in CONT without breath holding; and 2) When the subjects underwent hyperventilation followed by heavy static exercise, prefrontal tissue O_2Hb and THb responses during exercise were significantly smaller than those in respiration modes without hyperventilation. These re-

sults show that the respiration mode before and during exercise affects cerebral oxygenation and blood volume in prefrontal cortex during heavy static exercise.

In the present study, the amount of increase in MAP in EX + BH was nearly two times that in CONT; moreover, CO decreased during exercise by as much as 35%. This excessive increase in MAP and the sharp decrease in CO are considered to be caused by Valsalva-like maneuver due to breath holding during heavy exercise (Meyer *et al.* 1966). That is, the vena cava is compressed by an increase in intrathoraco-abdominal pressure due to breath holding during heavy exercise. Then, venous drainage decreases, finally resulting in reductions in stroke volume and thus CO (Pott *et al.* 2003). The time course of MAP and $MCA V_{mean}$ during exercise was similar to the responses observed in previous studies in which the subjects concurrently underwent heavy exercise on lower limbs with Valsalva-like maneuver (Pott *et al.* 2003). Based on these results, it can be speculated that the respiratory state of the subjects during exercise in EX + BH was like Valsalva breathing.

O_2Hb during exercise in EX + BH showed a sharper and more marked increase than that in CONT; the increase in EX + BH was more than two times that in CONT. Moreover, because THb showed marked increases, the increase in O_2Hb is considered to be due to the sharp increase in blood volume in the prefrontal cortex. Based on the fact that $MCA V_{mean}$ temporarily decreased after the increase at the start of exercise, it is speculated that the blood supply to the brain during exercise is considered to be lower than that at rest. That is, it is suggested that the sharp increase in blood volume in EX + BH was not due to the increase in arterial blood flow. Within the sample volume of the

NIRS, hemoglobin is contained in arterioles, capillaries, and venules, but the relative position of the pigment determined by NIRS remains unknown. From the anatomic studies of the brain, the venule to total vessel volume ratio ranges from 2/3 to 4/5. Because $\sim 5\%$ of the blood is within the capillaries and $\sim 20\%$ in the arterioles, it may be argued that NIRS is dominated by the local venous O_2 saturation rather than a tissue O_2 content (Ferrari *et al.* 2004). Therefore, it is likely that the increase in blood volume in the prefrontal area observed in the present study was mainly due to pooling of blood in the venules of the brain.

The subjects in HV + EX performed spontaneous hyperventilation starting at 1 minute before the start of exercise ; a decrease in CO_2 concentration in arterial blood can be speculated from the decrease in $P_{ET} CO_2$ as well. After the start of hyperventilation, $MCA V_{mean}$ started to decrease gradually and reached a constant value in 30 s. The reduction in $MCA V_{mean}$ was caused by the cerebral vasoconstriction due to hypocapnia (Ainslie *et al.* 2005). On the other hand, hyperventilation led to a slight increase in O_2Hb and a decrease in HHb ; as a result, no change was observed in THb . Although it is not clear why O_2Hb and THb did not reflect the decrease in $MCA V_{mean}$ during hyperventilation, it is likely that cerebral nerve activity associ-

ated with respiratory muscle activity due to spontaneous hyperventilation affected O_2Hb . The amount of increase in O_2Hb during exercise in HV + EX was less than that in CONT. Our result suggested that hyperventilation before exercise suppresses an increase in cerebral oxygenation at the onset of heavy exercise and it may be caused by cerebral vasoconstriction due to hypocapnia (Edwards *et al.* 2002 ; Ainslie *et al.* 2005 ; Romero and Cook 2007) .

The present study demonstrates that although respiration modes affect $MCA V_{mean}$ responses before and during exercise, cerebral oxygenation does not necessarily reflect changes of $MCA V_{mean}$. This disparity between cerebral oxygenation and $MCA V_{mean}$ was not in conformance with the results of previous studies (Pott *et al.* 2003). Further research is required clarify this point.

The present study has shown that hyperventilation before exercise and breath holding during heavy exercise affect cerebral oxygenation and blood volume. It has been demonstrated that breath holding during heavy exercise induces an excessive increase in blood volume (pooling of blood) in the prefrontal cortex and that hyperventilation before exercise suppresses an increase in oxy-haemoglobin response during exercise.

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