Different blood flow responses to dynamic exercise between internal carotid and vertebral arteries in women

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Sato K, Sadamoto T. Different blood flow responses to dynamic exercise between internal carotid and vertebral arteries in women. J Appl Physiol 109: 864–869, 2010. First published July 1, 2010; doi:10.1152/japplphysiol.01359.2009.—The blood flow regulation in vertebral system during dynamic exercise in humans remains unclear. We examined the blood flow responses in both the internal carotid artery (QICA) and vertebral artery (QVA) simultaneously during graded dynamic exercise by Doppler ultrasound to evaluate whether cerebrovascular responses to exercise were similar. In the semisupine position, 10 young women performed a graded cycling exercise at three loads of 30, 50, and 70% of peak oxygen uptake (V02peak) for 5 min for each workload. Mean arterial pressure, heart rate, and cardiac output increased progressively with three workloads (P < 0.01). The end-tidal partial pressure of CO2 (PetCO2) in the expired gas increased from the resting level (P < 0.01) at 30 and 50% V02peak. The PetCO2 at 70% V02peak (43.2 ± 1.6 Torr) was significantly lower than that at 50% V02peak (45.3 ± 1.4 Torr). In parallel with the changes in PetCO2, QICA increased from the resting level by 11.6 ± 1.5 and 18.4 ± 2.7% at 30 and 50% V02peak (P < 0.01), respectively, and leveled off at 70% V02peak. In contrast, QVA did not show a leveling off and increased proportionally with workload: 16.8 ± 3.1, 32.8 ± 3.6, and 39.5 ± 3.4% elevations at the three exercise loads, respectively (P < 0.01). With increasing exercise load, the cerebrovascular resistance in internal carotid artery increased (P < 0.01), while cerebrovascular resistance in vertebral artery remained stable during exercise. The different responses between QICA and QVA in the present study indicate a heterogenous blood flow and cerebrovascular control in the internal carotid and vertebral systems during dynamic exercise in humans.

METHODS

Ten healthy young women [22 ± 2 yr (mean ± SD), 164 ± 6 cm, 58 ± 4 kg, and peak oxygen uptake (V02peak): 38.3 ± 5.1 ml·kg⁻¹·min⁻¹] participated in this study. All procedures and protocols confirmed to Declaration of Helsinki and were approved by the Institutional Review Board at the Japan Women’s College of Physical Education. Following a detail verbal explanation of the intended experimental measures and procedures, each subject gave informed, written consent before participation. The subjects were not performing endurance training on a regular basis. In addition, they were free of any known cardiovascular and pulmonary disorders and were not using prescribed or over-the-counter medications. Before the experiment, each subjects visited the laboratory for familiarization with the CBF measurement by Doppler ultrasound and dynamic exercise protocol.

Aerobic power. The V02peak was determined by an incremental protocol on a cycle ergometer (Aerobike 800, Combi) 2 wk before the experiments. Subjects were exposed to an initial work rate of 30 W at a pace of 60 cycles/min. The subjects were told to maintain the frequency of pedaling, and work rate was increased 10–15 W every minute until volitional exhaustion. Respiratory variables were determined breath by breath, and gas fractions were analyzed by a mass spectrometer (ARCO-1000, Arco System), while expired gas volume was measured by a Fleisch pneumotachometer (WLCU-5201, We-
The highest value obtained for oxygen uptake (\(\dot{V}O_2\)) over 30 s was taken as \(\dot{V}O_2\)peak.

**Exercise and experimental protocol.** The subjects were seated on a semisupine cycle ergometer (Cateye-Ergociser EC-3700, Cateye) with a backrest inclination of \(\sim 40-50^\circ\). The upper body of the subject was held by shoulder straps and a waist belt to the cycle frame, and head and neck were also held in a stable position by a padded head rest (Fig. 1). The procedure included a 5-min baseline period, followed by exercise with loads of 30, 50, and 70% of \(\dot{V}O_2\)peak, with each stage lasting 5 min. This graded dynamic exercise was followed by a further 3 min of recovery period in a constant position.

**Cerebral blood flow.** The measurements of CBF in this study were carried out during the rest (for 2 min between the 2nd and 4th min), the exercise stage (for 1 min between the 4th and 5th min) and the recovery (for 1 min between the 2nd and 3rd min). The representative values of CBF at each period were the average of three recordings taken.

The \(Q_{ICA}\) was measured with a high-resolution ultrasound system (Vivid 7 Pro, GE Yokogawa Medical Systems) equipped with a 10-MHz linear transducer. Measurements were performed \(\sim 1.0-1.5\) cm distal to the carotid bifurcation on the right ICA, while the subject’s chin was slightly elevated (Fig. 2). We first used brightness mode to measure the mean vessel diameter of ICA (\(D_{ICA}\)) in the longitudinal section, and, thereafter, the Doppler velocity spectrum was identified by pulsed wave Doppler mode. The systolic and diastolic diameters of the ICA were measured, and the \(D_{ICA}\) was calculated in relation to the blood pressure curve: \(D_{ICA} = (\text{systolic diameter} \times 1/3) + (\text{diastolic diameter} \times 2/3)\). Moreover, the time-averaged mean flow velocity obtained by the pulsed wave Doppler mode was defined as the mean blood flow velocity (\(V_{ICA};\) m/s). The recordings of the \(V_{ICA}\) were taken from the average of \(\sim 10\) cardiac cycles to eliminate the effects caused by the breathing cycle. In \(V_{ICA}\) measurement, care was taken to ensure that the probe position was stable, that the insonation angle did not vary (in most cases, \(60^\circ\)), and that the sample volume was positioned in the center of the vessel and adjusted to cover the width of the vessel diameter. Three data of \(D_{ICA}\) and \(V_{ICA}\) were obtained for rest and for the last 1 min of exercise with each workload and for the last 1 min of the recovery period, and then the average of three data was defined as the representative value of \(D_{ICA}\) and \(V_{ICA}\) in the individual period. \(Q_{ICA}\) was calculated by multiplying the cross-sectional area \(\pi \times (D_{ICA}/2)^2\) with \(V_{ICA}\): \(Q_{ICA} = V_{ICA} \times \text{area} \times 60\) (ml/min).

The \(Q_{VA}\) was measured with a similar Doppler ultrasound systems (Vivid e, GE Yokogawa Medical Systems) equipped with a 10-MHz linear transducer. Measurements were mainly performed between the transverse processes of the C4 and C5 vertebrae on the left side, and the \(Q_{VA}\) was calculated as described for \(Q_{ICA}\). To avoid the ultrasound interference, we chose the right ICA and left VA for CBF measurement. In a pilot study, we confirmed no significant differences in blood flow volume in the left and right side of ICA, whereas the left VA tended to have a larger blood flow than the right VA (31). All of CBF measurements were performed by the same two experienced operators (28, 29).

The coefficients of variation (CV) in \(Q_{ICA}\) and \(Q_{VA}\) were 5.3 ± 1.2 and 5.8 ± 1.0% at rest, 6.1 ± 0.9 and 6.3 ± 1.2% at 30% \(\dot{V}O_2\)peak, 5.9 ± 0.7 and 5.8 ± 1.0% at 50% \(\dot{V}O_2\)peak, and 5.3 ± 0.7 and 6.3 ± 0.6% at 70% \(\dot{V}O_2\)peak, respectively. Moreover, we carried out a test-retest experiment to confirm the reproducibility of \(Q_{ICA}\) and \(Q_{VA}\) measurement at rest and during dynamic exercise.

**Fig. 1.** Position of the subject while semisupine cycle exercising (A), and the head position for cerebral blood flow measurement (B).

**Fig. 2.** Ultrasound Doppler screen while the internal carotid (ICA; A) and vertebral artery (VA; C) blood flow are measured. B: probe and head placement.
exercise in the pilot study (n = 6). Such determinations of Q˙ICA and Q˙VA are made with an average CV of 4.6 ± 1.0% for Q˙ICA and 5.3 ± 1.3% for Q˙VA at rest, 6.3 ± 0.9 and 6.2 ± 1.3% at 30% V˙O2peak, 5.0 ± 0.9 and 4.9 ± 1.2% at 50% V˙O2peak, and 6.4 ± 0.8 and 6.5 ± 1.1% at 70% V˙O2peak, respectively. The intraclass correlation coefficient of the repeated measurements of Q˙ICA was 0.94, and that in Q˙VA was 0.96, respectively. The CVs in Q˙ICA and Q˙VA at rest and during dynamic exercise were within the range of reported values at rest and all workloads (11, 13, 14, 31).

Cardiorespiratory responses. Heart rate was continuously monitored using a three-lead electrocardiogram (OEC-6401, Nihon Koden). Beat-to-beat blood pressure was measured using finger photoplethysmography obtained from the middle or index finger of the nondominant hand (Finometer, Finapres Medical Systems). These methods of blood pressure measurement have been validated for use both at rest and during low to moderate level of exercise (15). Furthermore, stroke volume and CO were determined from the blood pressure wave form by the Modelflow software program that incorporates sex, age, height, and weight (Beat Scope 1.1, Finapres Medical Systems). This method provides a reliable estimate of change in stroke volume and CO in healthy humans at rest and during moderate exercise (15, 16, 36). Respiratory variables were determined as described for V˙O2peak, and end-tidal partial pressure of CO2 (PETCO2) was measured. The cardiorespiratory responses at rest were analyzed over 2 min that ended 1 min before the onset of exercise. During exercise, these parameters were analyzed within the last 1 min of each workload. In addition, the data of the last 1 min of the recovery period were analyzed.

Data processing and statistics. The ratio of mean arterial pressure (MAP) at ICA level to Q˙ICA and the ratio of MAP at VA level to Q˙VA were, respectively, taken as indices of cerebrovascular resistance (CVRICA and CVRVA). The MAP at ICA level or VA level took into consideration the vertical distance from the fourth intercostal space in the midclavicular line (heart level) to the Doppler probe (i.e., hydrostatic pressure = the vertical distance × 0.77 mmHg/cm) (25). The gCBF was calculated as the sum of volume flow in ICA and VA [Q˙ICA + Q˙VA] × 2 (ml/min)] (7). The distribution of CO to brain was expressed as gCBF/CO × 100 (%). The relative contribution of Q˙ICA and Q˙VA to gCBF was estimated as Q˙ICA/gCBF × 100 (%) and Q˙VA/gCBF × 100 (%), respectively.

The cerebrovascular and cardiorespiratory responses at rest were analyzed over 2 min that ended 1 min before the onset of exercise. During exercise, these parameters were analyzed from the last 1 min of each workload and also expressed relative to rest. In addition, the data of the last 1 min of recovery period were analyzed.

Values are expressed as means ± SE, and differences between values at rest, exercise, and recovery were evaluated by ANOVA with repeated measures and Dunnett post hoc test. To compare differences between in the cerebrovascular responses in the ICA and VA, two-way repeated-measures ANOVA were used. If the data were normally distributed, a two sample t-test was performed. Otherwise, Wilcoxon signed-rank test was used (SPSS12.0, SPSS), and P < 0.05 was considered to indicate a significant difference.

RESULTS

The resting values, the change in the cardio-respiratory and cerebrovascular responses to graded exercise, and the recovery are shown in Table 1. V˙O2, MAP, heart rate, and CO increased with workload (P < 0.01) and also PetCO2 was higher than at rest (P < 0.01). Yet, at the 70% V˙O2peak workload, PetCO2 was lower than at 50% V˙O2peak (from 45.3 ± 1.4 to 43.2 ± 1.6 Torr; P < 0.05). All cardio-respiratory variables in the recovery were lower than during exercise, but they remained higher than at rest.

We confirmed whether metabolism had reached steady state at each workload by difference in V˙O2 between the 4th or 5th min of each exercise stage. According to this results, there were no significant differences in V˙O2 between the 4th or 5th min of exercise during 30 and 50% V˙O2peak, suggesting that a steady-state V˙O2 was achieved during 30 and 50% V˙O2peak. However, 70% V˙O2peak did not show a steady-state V˙O2.

With exercise, Q˙ICA increased (P < 0.01: Table 1 and Fig. 3A). At 30% V˙O2peak, the increase was by 11.6 ± 5.9%, and it then
increased further to 18.4 ± 2.7% above rest at 50% VO_2peak. However, at 70% VO_2peak, Q_{ICA} leveled off (17.2 ± 2.0%). There were no significant changes in the DICA during exercise or in the recovery, and, therefore, the increase in Q_{ICA} during exercise was by an increase in VICA.

During exercise, Q_{VA} showed a different pattern. With increasing exercise load, a continuous increase was seen: 16.8 ± 3.1, 32.8 ± 3.6, and 39.5 ± 3.4% at 30, 50, and 70% of VO_2peak, respectively (P < 0.01: Table I and Fig. 3A). The increase in Q_{VA} during exercise was by both an increase in the VA mean blood flow velocity (P < 0.01) and VA mean diameter (P < 0.05). Accordingly, the change in Q_{VA} at 50 and 70% VO_2peak was larger than that in Q_{ICA} (P < 0.01). In the recovery period, Q_{VA} was still higher than at rest (15.8 ± 4.8%, P < 0.01).

The changes in the CVRICA and CVRVA are illustrated in Fig. 3B. With exercise, the CVRICA increased (P < 0.01), while CVRVA remained stable. Thus the increase in CVRICA during exercise at 50 and 70% VO_2peak was higher than those in CVRVA (P < 0.01). The recovery CVRICA returned to the resting value.

The gCBF increased at 30% VO_2peak by 12.9 ± 1.5%. At 50% VO_2peak, gCBF was elevated by 21.9 ± 2.5%, but at 70% VO_2peak, the increase in gCBF leveled off (22.5 ± 2.0%) (Table 1). gCBF in the recovery remained above the resting value by 7.6 ± 1.6% (P < 0.01). At rest, gCBF accounted for 17.7 ± 1.2% of CO, but, during exercise, a progressive decrease was observed: from 10.3 ± 0.7% at 30% VO_2peak to 6.4 ± 0.4% at 70% VO_2peak, and 13.0 ± 0.8% in the recovery. The Q_{VA}/gCBF was 24.8 ± 1.8% at rest, 25.7 ± 2.0% at 30% VO_2peak, 27.0 ± 2.0% at 50% VO_2peak, 28.1 ± 1.8% at 70% VO_2peak, and 26.6 ± 2.0% at recovery, and Q_{VA}/gCBF at 70% VO_2peak was significantly different from that at rest (P < 0.05).

**Differential responses between the Q_{ICA} and Q_{VA} during dynamic exercise.** The increase in Q_{ICA} leveled off over an intensity of 50% VO_2peak, whereas the continuous increase in Q_{VA} occurred until an intensity of 70% VO_2peak, and that the CVRICA increased with increasing exercise load, whereas CVRVA remained stable throughout the graded intensities. These results confirmed our hypothesis that the cerebrovascular responses to dynamic exercise are different between ICA and VA systems. Furthermore, we found that gCBF was elevated ~20% during dynamic exercise, and that the relative contribution of ICA and VA systems to the gCBF varied during dynamic exercise.

**DISCUSSION**

Using Doppler ultrasound, we examined the simultaneous blood flow responses in ICA and VA during graded dynamic exercise. The major findings of the present study were that the increase in Q_{ICA} leveled off over the intensity of 50% VO_2peak, whereas the continuous increase in Q_{VA} occurred until an intensity of 70% VO_2peak, and that the CVRICA increased with increasing exercise load, whereas CVRVA remained stable throughout the graded intensities. These results confirmed our hypothesis that the cerebrovascular responses to dynamic exercise are different between ICA and VA systems. Furthermore, we found that gCBF was elevated ~20% during dynamic exercise, and that the relative contribution of ICA and VA systems to the gCBF varied during dynamic exercise.
during dynamic exercise, despite different contribution of ICA and VA to the increased gCBF during exercise. Our results are consistent with the previous findings that gCBF increased by ~20–25% during moderate intensity of ~50–60% \( \dot{V}O_{2\text{peak}} \), but not during a higher intensity over 70% \( \dot{V}O_{2\text{peak}} \) (11, 17, 22, 26, 33). The increase in gCBF during dynamic exercise reflected \( Q_{ICA} \) leveling off at moderate exercise intensity and is attributed to hyperventilation-induced decreases in \( P_{ET\text{CO}_2} \).

Hence, \( Q_{ICA} \) leveling off at moderate exercise intensity and is not reflected \( Q_{ICA} \) leveling off at moderate exercise intensity and is attributed to hyperventilation-induced decreases in \( P_{ET\text{CO}_2} \). In contrast to our findings, studies using the Kety-Schmidt method to express gCBF as the internal jugular venous flow found no change in dynamic exercise (17, 20, 26, 33, 34). This discrepancy, most likely, reflects that the internal jugular vein is collapsed in the upright position used in human exercise studies (2), and blood is transmitted to an alternative venous pathway (i.e., the spinal veins) (37). In addition, evaluation of CBF by the Kety-Schmidt method is complicated by the asymmetry of the venous drainage from the brain (33).

Although arterial blood supply at rest appears to be balanced between the ICA and VA systems in humans (32), our new finding was that the relative contribution of blood to gCBF via the two systems may vary from rest to dynamic exercise. Furthermore, we observed that the decrease in the distribution of CO to the brain (gCBF/CO) from rest (~18%) to moderate exercise (~6%) and these changes depended on the exercise intensity (27). CO is an important factor that can influence CBF during dynamic exercise (15, 16, 23, 24, 38). However, CO influence on CBF was more pronounced at rest than during dynamic exercise (23), and our results regarding the distribution of CO to brain might be associated with these observations.

**Limitations.** The present study has several limitations. First, we did not measure the CBF up to maximal exercise (100% \( \dot{V}O_{2\text{peak}} \)), because the CBF measurements during maximal exercise showed a large variation due to changes in the probe position and the insolation angle of the ultrasound beam during body movements. However, the CV and test-retest reproducibility in our CBF measurements indicated that the data obtained at rest and during submaximal exercise were reliable in this study. Second, the subjects in the present study were only 10 women. Thus, if data from male subjects were added, the cerebrovascular responses in ICA and VA systems during exercise could be generalized. Although there was no sex differences in the \( Q_{ICA} \) and \( Q_{VA} \) at rest (30, 32), further investigations are required in both systems during dynamic exercise. Third, we used photoplethysmography and Modelflow methods to estimate MAP and CO responses to exercise. Although these methods were validated in previous studies for an estimation of MAP and CO at rest and during dynamic exercise (5, 15, 16, 36), these techniques have some limitations (1, 12).

In summary, during dynamic exercise, the increase in the \( Q_{ICA} \) leveled off at moderate dynamic exercise over the intensity of 50% \( \dot{V}O_{2\text{peak}} \), whereas the \( Q_{VA} \) progressively increased up to the intensity of 70% \( \dot{V}O_{2\text{peak}} \). These results indicated that the cerebrovascular responses to dynamic exercise are different between ICA and VA systems. Moreover, the relative contribution of \( Q_{ICA} \) decreased and \( Q_{VA} \) increased to gCBF as exercise intensity increased, yet \( Q_{ICA} \) still accounted for the majority of cerebral perfusion.


