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

Kohei Sato and Tomoko Sadamoto
Research Institute of Physical Fitness, Japan Women’s College of Physical Education, Tokyo, Japan
Submitted 7 December 2009; accepted in final form 29 June 2010

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 (VO2peak) 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% VO2peak. The PetCO2 at 70% VO2peak (43.2 ± 1.6 Torr) was significantly lower than that at 50% VO2peak (45.3 ± 1.4 Torr). In parallel with the changes in PetCO2, QICA increased from resting level by 11.6 ± 1.5 and 18.4 ± 2.7% at 30 and 50% VO2peak (P < 0.01), respectively, and leveled off at 70% VO2peak. 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 (VO2peak): 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 VO2peak 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 (VO₂) over 30 s was taken as VO₂peak.

Exercise and experimental protocol. The subjects were seated on a semisupine cycle ergometer (Cateye-Ergociser EC-3700, Cateye) with a backrest inclination of ∼40–50°. 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 VO₂peak, 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 QICA 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 ∼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 (DICA) 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 DICA was calculated in relation to the blood pressure curve: DICA = (systolic diameter × 1/3) + (diastolic diameter × 2/3). Moreover, the time-averaged mean flow velocity obtained by the pulsed wave Doppler mode was defined as the mean blood flow velocity (VICA; m/s). The recordings of the VICA were taken from the average of ∼10 cardiac cycles to eliminate the effects caused by the breathing cycle. In VICA measurement, care was taken to ensure that the probe position was stable, that the insonation angle did not vary (in most cases, 60°), 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 DICA and VICA 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 DICA and VICA in the individual period. QICA was calculated by multiplying the cross-sectional area [π × (DICA/2)] with VICA: QICA = VICA × area × 60 (ml/min).

The QVA was measured with a similar Doppler ultrasound system (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 QVA was calculated as described for QICA. 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 QICA and QVA were 5.3 ± 1.2 and 5.8 ± 1.0% at rest, 6.1 ± 0.9 and 6.3 ± 1.2% at 30% VO₂peak, 5.9 ± 0.7 and 5.8 ± 1.0% at 50% VO₂peak, and 5.3 ± 0.7 and 6.3 ± 0.6% at 70% VO₂peak, respectively. Moreover, we carried out a test-retest experiment to confirm the reproducibility of QICA and QVA measurement at rest and during dynamic exercise.
exercise in the pilot study (n = 6). Such determinations of QICA and QVA are made with an average CV of 4.6 ± 1.0% for QICA and 5.3 ± 1.3% for QVA at rest, 6.3 ± 0.9 and 6.2 ± 1.3% at 30% VO2peak, 5.0 ± 0.9 and 4.9 ± 1.2% at 50% VO2peak, and 6.4 ± 0.8 and 6.5 ± 1.1% at 70% VO2peak, respectively. The intraclass correlation coefficient of the repeated measurements of QICA was 0.94, and that in QVA was 0.96, respectively. The CVs in QICA and QVA 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 electrocardiograph (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 (5). Furthermore, stroke volume and CO were determined from the blood flow at each workload and also expressed relative to rest. 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 QICA and the ratio of MAP at VA level to QVA were, respectively, taken as indexes 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 midsternal 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 [(QICA + QVA) × 2 (ml/min)] (7). The distribution of CO to brain was expressed as gCBF/CO × 100 (%). The relative contribution of QICA and QVA to gCBF was estimated as QICA/gCBF × 100 (%) and QVA/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. VO2, 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% VO2peak workload, PetCO2 was lower than at 50% VO2peak (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.

Table 1. Cardiorespiratory and cerebrovascular variables at rest, during dynamic exercise, and at recovery

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>30% VO2peak</th>
<th>50% VO2peak</th>
<th>70% VO2peak</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2, ml/min</td>
<td>236 ± 9</td>
<td>1335 ± 68*</td>
<td>1728 ± 77*</td>
<td>377 ± 27*</td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>77 ± 2</td>
<td>102 ± 3*</td>
<td>114 ± 2*</td>
<td>83 ± 2</td>
<td></td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>60 ± 2</td>
<td>127 ± 3*</td>
<td>159 ± 3*</td>
<td>79 ± 3*</td>
<td></td>
</tr>
<tr>
<td>CO, 1/min</td>
<td>4.4 ± 0.5</td>
<td>11.5 ± 0.4*</td>
<td>16.1 ± 0.6*</td>
<td>6.5 ± 0.2*</td>
<td></td>
</tr>
<tr>
<td>PetCO2, Torr</td>
<td>40.3 ± 0.9</td>
<td>45.3 ± 1.4*</td>
<td>43.2 ± 1.6*</td>
<td>42.7 ± 2.6*</td>
<td></td>
</tr>
<tr>
<td>QICA, ml/min</td>
<td>295 ± 20</td>
<td>349 ± 25*</td>
<td>344 ± 21*</td>
<td>311 ± 23*</td>
<td></td>
</tr>
<tr>
<td>Change from rest, %</td>
<td>1.6 ± 1.5</td>
<td>18.4 ± 2.7</td>
<td>17.2 ± 2.0</td>
<td>5.1 ± 2.2</td>
<td></td>
</tr>
<tr>
<td>DICA, cm</td>
<td>0.48 ± 0.02</td>
<td>0.49 ± 0.02</td>
<td>0.49 ± 0.02</td>
<td>0.48 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>VRICA, cm/s</td>
<td>28.0 ± 2.5</td>
<td>31.1 ± 2.8*</td>
<td>31.7 ± 2.7*</td>
<td>29.6 ± 2.8</td>
<td></td>
</tr>
<tr>
<td>QVA, ml/min</td>
<td>95 ± 5</td>
<td>126 ± 7*</td>
<td>132 ± 8*</td>
<td>109 ± 7*</td>
<td></td>
</tr>
<tr>
<td>Change from rest, %</td>
<td>1.0 ± 3.1</td>
<td>32.8 ± 3.6</td>
<td>39.5 ± 3.4</td>
<td>15.8 ± 4.0</td>
<td></td>
</tr>
<tr>
<td>DVA, cm</td>
<td>0.32 ± 0.01</td>
<td>0.33 ± 0.01*</td>
<td>0.33 ± 0.01*</td>
<td>0.33 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>VRVA, cm/s</td>
<td>19.9 ± 0.9</td>
<td>24.5 ± 1.0*</td>
<td>25.3 ± 1.0*</td>
<td>21.2 ± 0.7</td>
<td></td>
</tr>
<tr>
<td>CVRICA, mmHg/ml·min·1·min⁻¹</td>
<td>0.26 ± 0.02</td>
<td>0.30 ± 0.03*</td>
<td>0.34 ± 0.03*</td>
<td>0.27 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>CVRVA, mmHg/ml·min·1·min⁻¹</td>
<td>0.81 ± 0.05</td>
<td>0.82 ± 0.05</td>
<td>0.87 ± 0.05</td>
<td>0.76 ± 0.05</td>
<td></td>
</tr>
<tr>
<td>gCBF, ml/min</td>
<td>779 ± 40</td>
<td>950 ± 52*</td>
<td>952 ± 45*</td>
<td>840 ± 47*</td>
<td></td>
</tr>
<tr>
<td>Change from rest, %</td>
<td>12.9 ± 1.5</td>
<td>21.9 ± 2.5</td>
<td>22.5 ± 2.0</td>
<td>7.6 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>gCBF/CO X 100, #</td>
<td>17.7 ± 1.2</td>
<td>10.3 ± 0.7*</td>
<td>8.4 ± 0.6*</td>
<td>13.0 ± 0.8*</td>
<td></td>
</tr>
<tr>
<td>QICA/gCBF, %</td>
<td>75.2 ± 1.8</td>
<td>73.0 ± 2.0</td>
<td>71.9 ± 1.8*</td>
<td>73.4 ± 2.0</td>
<td></td>
</tr>
<tr>
<td>QVA/gCBF, %</td>
<td>24.8 ± 1.8</td>
<td>25.7 ± 2.0</td>
<td>27.0 ± 2.0</td>
<td>28.1 ± 1.8*</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE. VO2, oxygen uptake; VO2peak, peak VO2; MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; PetCO2, end-tidal partial pressure of CO2; QICA and QVA, blood flow in internal carotid arteries (ICA) and vertebral arteries (VA), respectively; VO2, VA, mean blood flow velocities in the ICA and VA, respectively; DICA and DVA, mean diameter in ICA and VA, respectively; CVRICA and CVRVA, index of cerebrovascular resistance in the ICA and VA, respectively; gCBF, global cerebral blood flow [(QICA + QVA) / gCBF]; gCBF/CO X 100 (%), the distribution of CO to brain; QICA/gCBF (%), the relative contribution of QICA to gCBF; QVA/gCBF (%), the relative contribution of QVA to gCBF. *Different from rest (P < 0.05).
Differential responses between the QICA and QVA during dynamic exercise. The increase in QICA leveled off over an intensity of 50% $V_{\text{O}_2\text{peak}}$, whereas the continuous increase in QVA occurred until an intensity of 70% $V_{\text{O}_2\text{peak}}$, and that the CVRICA increased with increasing exercise load, whereas CVRVA remained stable throughout the graded intensities. These results confirmed our hypothesis that the cerebral vascular 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.

Differential responses between the QICA and QVA during dynamic exercise. The increase in QICA leveled off over an intensity of 50% $V_{\text{O}_2\text{peak}}$, during cycling exercise, which was consistent with the previous report (11). However, the QVA increased progressively with graded intensities of exercise up to 70% $V_{\text{O}_2\text{peak}}$. These different cerebral vascular responses between ICA and VA during dynamic exercise are probably mediated by several factors and/or mechanisms. The first possible explanation is that the neurometabolic demand in the brain was regionally different between the territories covered by the ICA and the territories covered by the VA system and thereby resulted in different cerebral vascular responses between ICA and VA. The previous animal studies support this explanation (4, 8). Delp et al. (4) reported that the blood flow in the cortical areas showed less increase to maximal exercise than that in the brain stem, spinal cord, and the cerebellum. A second possibility is that anatomic differences might exist between ICA and VA systems. In line with this explanation, the histological studies of Edvinson et al. (6) have shown regional differences concerning density of β-adrenergic, cholinergic, and serotoninergic innervation of the intracerebral vessels, which may have different influences on the cerebral vascular resistance. In addition, pharmacological studies have suggested regional differences in the sensitivity to vasoactive substances, e.g., noradrenaline (9). The third factor is the difference in cerebral CO2 reactivity (3, 18, 35) and/or autoregulatory control (10, 21) between ICA and VA systems in humans. The present study indicates that cerebral CO2 reactivity during moderate exercise is reduced in the VA system compared with the ICA system (35). In addition, previous studies have demonstrated impaired autoregulation in the VA system compared with the ICA system (10). Thus, several factors probably contributed to the different cerebral vascular responses observed between the ICA and VA systems during dynamic exercise in the present study. Further research is required to clarify the detail mechanisms.

gCBF responses during dynamic exercise. We found that gCBF, calculated as the sum of QICA and QVA, elevated ~20%
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% $V\text{O}_2\text{peak}$, but not during a higher intensity over 70% $V\text{O}_2\text{peak}$ (11, 17, 22, 26, 33). The increase in gCBF during dynamic exercise reflected $Q_{\text{ICA}}$ leveling off at moderate exercise intensity and is attributed to hyperventilation-induced decreases in $P\text{ETCO}_2$ (11, 17, 22, 26, 33). 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% $V\text{O}_2\text{peak}$), because the CBF measurements during maximal exercise showed a large variation due to changes in the probe position and the insonation 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 $Q_{\text{ICA}}$ and $Q_{\text{VA}}$ at rest (30, 32), further investigations are required in both systems during dynamic exercise. Third, we used photoplethysmography and Model-flow 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 $Q_{\text{ICA}}$ leveled off at moderate dynamic exercise over the intensity of 50% $V\text{O}_2\text{peak}$, whereas the $Q_{\text{VA}}$ progressively increased up to the intensity of 70% $V\text{O}_2\text{peak}$. These results indicated that the cerebrovascular responses to dynamic exercise are different between ICA and VA systems. Moreover, the relative contribution of $Q_{\text{ICA}}$ decreased and $Q_{\text{VA}}$ increased to gCBF as exercise intensity increased, yet $Q_{\text{ICA}}$ still accounted for the majority of cerebral perfusion.

**ACKNOWLEDGMENTS**

We especially thank Hiroyuki Yamamoto (GE Yokogawa Medical Systems, Tokyo, Japan) and Ai Hirasawa (Research Institute of Physical Fitness, Japan Women’s College of Physical Education) for expert technical assistance.

**GRANTS**

This study was supported by a research grant from the Academic Frontier Project at the Japan Women’s College of Physical Education.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**REFERENCES**


