Regulation of middle cerebral artery blood velocity during recovery from dynamic exercise in humans

Shigehiko Ogoh,1 James P. Fisher,2 Sushmita Purkayastha,1 Ellen A. Dawson,1 Paul J. Fadel,2 Michael J. White,3 Rong Zhang,4 Niels H. Secher,5 and Peter B. Raven1

1Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas; 2Department of Medical Pharmacology and Physiology, Dallas Cardiovascular Research Center, University of Missouri-Columbia, Columbia, Missouri; 3University of Birmingham, Birmingham, United Kingdom; 4Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, and UT Southwestern Medical Center, Dallas, Texas; and 5Department of Anesthesia, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

Submitted 20 July 2006; accepted in final form 23 October 2006

Ogoh S, Fisher JP, Purkayastha S, Dawson EA, Fadel PJ, White MJ, Zhang R, Secher NH, Raven PB. Regulation of middle cerebral artery blood velocity during recovery from dynamic exercise in humans. J Appl Physiol 102: 713–721, 2007. First published October 26, 2006; doi:10.1152/japplphysiol.00801.2006.—We sought to examine the regulation of cerebral blood flow during 10 min of recovery from mild, moderate, and heavy cycling exercise by measuring middle cerebral artery blood velocity (MCA V). Transfer function analyses between changes in arterial blood pressure and MCA V were used to assess the frequency components of dynamic cerebral autoregulation (CA). After mild and moderate exercise, the decreases in mean arterial pressure (MAP) and mean MCA V (MCA Vm) were small. However, following heavy exercise, MAP was rapidly and markedly reduced, whereas MCA Vm decreased slowly (−23 ± 4 mmHg and −4 ± 1 cm/s after 1 min for MAP and MCA Vm, respectively; means ± SE). Importantly, for each workload, the normalized low-frequency transfer function gain between MAP and MCA Vm remained unchanged from rest to exercise and during recovery, indicating a maintained dynamic CA. Similar results were found for the systolic blood pressure and systolic MCA V relationship. In contrast, the normalized low-frequency transfer function gain between diastolic blood pressure and diastolic MCA V (MCA Vd) increased from rest to exercise and remained elevated in the recovery period (P < 0.05). However, MCA Vd was quite stable on the cessation of exercise. These findings suggest that MCA V is well maintained following mild to heavy dynamic exercise. However, the increased transfer function gain between diastolic blood pressure and MCA Vd suggests that dynamic CA becomes less effective in response to rapid decreases in blood pressure during the initial 10 min of recovery from dynamic exercise.

Address for reprint requests and other correspondence: S. Ogoh, Dept. of Integrative Physiology, Univ. of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, TX 76107 (e-mail: sogoh@hsctunt.ed).
effective to regulate a transient decrease in CBF during moderate to heavy exercise (18).

It is probable that the most difficult challenge for the dynamic CA occurs during recovery from heavy-intensity exercise, when the effects of the muscle pump are severely reduced or stopped and cardiac output and MAP are suddenly and drastically reduced. Whether the divergent MCA Vm and MCA Vd responses and alterations in CA observed during dynamic exercise persist in recovery from exercise remains unknown. Addressing this question specifically may provide information regarding gray- or black-out (5, 8) immediately after exercise. Thus the goal of this study was to examine dynamic CA during a 10-min recovery period following dynamic exercise. This was accomplished by using transfer function analysis between arterial blood pressure and MCA Vm, MCA Vm, and MCA Vd, and after, during, and after three intensities of steady-state cycle exercise. We hypothesized that the transfer function gain between DBP and MCA Vd increases following cycling, indicating that dynamic CA is less effective in responding to rapid decreases in arterial pressure after dynamic exercise.

METHODS

Seven healthy subjects with a mean age of 25 ± 2 yr, height of 182 ± 7 cm, and weight of 72 ± 6 kg (means ± SD) were recruited for this study. All subjects were free of any known cardiovascular and pulmonary disorders and were not using prescribed or over-the-counter medications. Each subject provided written, informed consent, which conformed to the Declaration of Helsinki and was approved by The Ethics Committee of Copenhagen (KF01-369/97). Subjects were requested to abstain from caffeinated beverages for 12 h and strenuous physical activity and alcohol for at least 1 day before the experimental session. The present report represents the data from the “control” (non-drug) exercise sessions from an investigation that was designed to examine the influence of the autonomic nervous system on baroreflex control during exercise (19).

Protocol. On the experimental day, the subjects arrived at the laboratory a minimum of 2 h following a light meal. Subjects were seated in a semi-recumbent position on a hospital bed that was modified to allow cycling exercise. Each subject performed three bouts of exercise at steady-state heart rates (HR) of 90 (EX90), 120 (EX120), and 150 (EX150) beats/min representing mild (39 ± 5 W, means ± SE), moderate (93 ± 9 W), and heavy (142 ± 11 W) workloads, respectively. After a 10-min rest period, the subjects initially worked at 10 W, and the workload was then adjusted to reach the target HR for each exercise bout. Once the target HR was achieved, subjects exercised for 6–8 min to ensure steady-state conditions before the spectral and transfer function analysis data were assessed. Following each exercise bout, all variables were continuously monitored and recorded for 10 min. Two 3-min data segments (minutes 1–3 and 6–8 after exercise) of the recovery period were used for transfer function analysis. The exercise bouts were performed in random order and separated by 30–40 min to enable sufficient recovery from the preceding exercise trial. If both HR and MAP were not returned to resting values after 40 min of recovery, the subjects rested and did not start the next exercise trial until both were achieved.

Measurements. Arterial blood pressure was measured by a catheter (1.1-mm inner diameter, 20 gauge) in the brachial artery of the nondominant arm and connected to a transducer (Baxter, Uden, the Netherlands) positioned at the level of the right atrium in the midaxillary line. The HR and the R-R interval were monitored using a lead II electrocardiogram. The signals were connected to a Dialogue 2000 monitor (IBC-Danica, Copenhagen, Denmark) interfaced with a personal computer equipped with customized data acquisition software for the beat-to-beat recording of variables. Arterial blood samples were obtained at rest, during and after (minute 5 after exercise) each bout of exercise, and immediately analyzed for pH, CO2 tension (Paco2), and lactate (ABL725, Radiometer, Copenhagen, Denmark). Beat-to-beat MAP, systolic blood pressure (SBP), and DBP were measured, and PP was calculated for each cardiac cycle.

The MCA Vm was obtained by transcranial Doppler ultrasonography (Multidop X, DWL, Sipplingen, Germany). A 2-MHz Doppler probe was placed over the temporal window and fixed with an adjustable headband and adhesive ultrasonic gel (Tensive, Parker Laboratories, Orange, NJ). Beat-to-beat MCA Vm, MCA Vm, and MCA Vd were measured, as well as MCA pulse blood flow velocity (MCA Vpp = MCA Vm − MCA Vd). The cerebrovascular resistance index (CVRi) was calculated by dividing MAP by MCA Vm and used as an estimate of changes in cerebrovascular resistance (17).

Data analysis. Analog signals of arterial pressure and the spectral envelope of MCA Vm were sampled at 200 Hz and digitized at 12 bits for off-line analysis. Beat-to-beat MAP, SBP, DBP, MCA Vm, MCA Vd, and MCA Vd were obtained from the analog signals and linearly interpolated and resampled at 2 Hz for spectral analysis of dynamic CA (26). For an estimate of dynamic CA, using the transfer function, the cross-spectrum between changes in MAP and MCA Vm, SBP, and MCAVs and DBP and MCA Vd were calculated and divided by the autospectrum of MAP, SBP, and DBP, respectively.

From the temporal sequences input x(t) and output y(t), the frequency-domain transforms x(f) and y(f) are computed with a fast Fourier transform. The transfer function H(f) between the two signals was calculated as H(f) = Sxy(f)/Sxx(f), where Sxx(f) is the input autospectrum of changes in x(t) and Sxy(f) is the cross-spectrum between the two signals. The transfer function magnitude |H(f)| and phase spectrum Φ(f) obtained from the real part HRe(f) and imaginary part HIm(f) of the complex transfer function becomes:

\[ |H(f)| = |HRe(f)^2 + HIm(f)^2|^{1/2} \]

\[ \Phi(f) = \tan^{-1}(HIm(f)/HRe(f)) \]

In addition, the transfer function H(f) was normalized to the mean values of input (x) and output (y) variables as H*(f) = Sxy(f)/Sxx(f)y, and the normalized gain was calculated as 20 log[H*(f)] to express values in decibels. A value of 0 indicates that the output varies by the same fraction of the mean value as the input, a negative value that it varies less and a positive value that it varies greater than the input.

The squared coherence function MSC(f) was estimated as:

\[ MSC(f) = \frac{S_{xy}(f)^2}{S_{xx}(f)S_{yy}(f)} \]

where Sxy(f) is the autospectrum of changes in y(t). The squared coherence function reflects the fraction of output power that can be linearly related to the input power at each frequency. Similar to a correlation coefficient, it varies between 0 and 1 and reflects the statistical reliability of transfer function analysis between input and output.

Spectral power, mean value of transfer function gain, phase, and coherence function were calculated in the very low- (VLF; 0.02–0.07 Hz), low- (LF; 0.07–0.20 Hz), and high-frequency (HF; 0.20–0.30 Hz) ranges to reflect dynamic characteristics of pressure-flow relationship identified by transfer function analysis (26, 27). Blood pressure fluctuations in the HF range are induced primarily by respiration, whereas those in the VLF and LF ranges are independent of the respiratory frequency and damped by CA (7). Thus, in this study, we used the VLF and LF ranges to identify the dynamic CA during exercise.

Statistical analysis. One-way ANOVA with repeated measures (SigmaStat, Jandel Scientific Software, SPSS, Chicago, IL) was used to assess the differences in the steady-state hemodynamics, spectral power of arterial pressure, and MCA Vm, and transfer function gain, phase, and coherence function between the rest and three exercise.
bouts. Two-way ANOVA (time × workload) with repeated measures was used to assess the differences in these variables between exercise and recovery periods. A Student Newman-Keuls test was employed post hoc when main effects were significant (P < 0.05). Data are expressed as means ± SE.

RESULTS

Exercise. The amplitude of the arterial pressure waveform increased from rest to heavy exercise in association with similar increases in the amplitude of the MCA V waveform. Changes in MCA Vm and MCA Vpp during cycling were associated with the exercise-induced increases in SBP and PP, respectively, in an intensity-dependent manner from rest to heavy exercise (Table 1). In contrast, the small changes in MCA Vm and MCA Vd were not in proportion to the changes in MAP and DBP, respectively. For example, during EX150, the relative change in MCA Vm from rest (+13%; P < 0.05) was smaller than that in MAP (+29%; P < 0.05). The small increase in MCA Vm during heavy exercise was mirrored by an increase in CVRi (P < 0.05). During EX120 and EX150, CVRi increased by 7 and 15%. Arterial PaCO2 decreased slightly during EX150 and EX120 (5.08 ± 0.12 kPa), respectively, but was not different from that at rest (5.05 ± 0.18 kPa). However, PaCO2 decreased slightly during EX150 (4.89 ± 0.18 kPa, P > 0.05).

During all exercise bouts, the VLF and LF transfer function phase between MAP and MCA Vm, as well as the VLF and LF phase between SBP and MCA Vm and between DBP and MCA Vd, remained stable and did not differ from the resting values (Tables 2 and 3). The normalized LF transfer function gain was unchanged from rest to exercise. Similarly, the normalized LF transfer function gain between MAP and MCA Vm, as well as between SBP and MCA Vm, remained unchanged from rest to exercise. In contrast, the normalized LF

Table 1. Steady-state cardiovascular and hemodynamic variables at rest, during heavy dynamic exercise, and recovery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>EX150</th>
<th>R1–3</th>
<th>R6–8</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beats/min</td>
<td>63 ± 4</td>
<td>139 ± 1*</td>
<td>100 ± 5†</td>
<td>76 ± 4‡</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>90 ± 3</td>
<td>116 ± 5*</td>
<td>94 ± 2†</td>
<td>90 ± 3‡</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>123 ± 4</td>
<td>174 ± 8*</td>
<td>139 ± 4†</td>
<td>124 ± 3‡</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>68 ± 3</td>
<td>81 ± 3*</td>
<td>72 ± 2†</td>
<td>69 ± 3‡</td>
</tr>
<tr>
<td>PP, mmHg</td>
<td>55 ± 2</td>
<td>93 ± 6*</td>
<td>67 ± 4†</td>
<td>55 ± 1‡</td>
</tr>
<tr>
<td>MCA Vm, cm/s</td>
<td>62 ± 5</td>
<td>70 ± 6*</td>
<td>61 ± 5†</td>
<td>60 ± 4‡</td>
</tr>
<tr>
<td>MCA Vd, cm/s</td>
<td>97 ± 7</td>
<td>133 ± 10*</td>
<td>114 ± 10†</td>
<td>93 ± 7‡</td>
</tr>
<tr>
<td>MCA Vpp, cm/s</td>
<td>39 ± 4</td>
<td>36 ± 3</td>
<td>37 ± 4</td>
<td>38 ± 3</td>
</tr>
<tr>
<td>CRV, mmHg·cm⁻¹·s</td>
<td>1.52 ± 0.13</td>
<td>1.75 ± 0.18*</td>
<td>1.61 ± 0.14‡</td>
<td>1.56 ± 0.13†</td>
</tr>
</tbody>
</table>

Values are means ± SE. EX150, heavy dynamic exercise; R1–3, minutes 1–3 of recovery; R6–8, minutes 6–8 of recovery; HR, heart rate; MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MCA Vm, middle cerebral artery mean blood velocity; MCA Vd, middle cerebral artery diastolic blood velocity; MCA Vpp, middle cerebral artery pulse blood velocity; CVRi, cerebrovascular resistance index. *Significantly different from rest (P < 0.05). †Significantly different from EX150 (P < 0.05). ‡Significantly different from R1–3 (P < 0.05).

Table 2. Spectral power, transfer function gain, phase, and coherence in very-low-frequency range

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Rest</th>
<th>EX150</th>
<th>R1–3</th>
<th>R6–8</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLF BP power spectra</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>3.67 ± 1.64</td>
<td>5.32 ± 1.97</td>
<td>7.98 ± 1.80</td>
<td>3.48 ± 0.63</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>4.56 ± 2.01</td>
<td>5.31 ± 1.84</td>
<td>10.17 ± 3.05</td>
<td>2.73 ± 0.51</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>3.94 ± 1.54</td>
<td>3.97 ± 1.86</td>
<td>5.34 ± 1.16</td>
<td>3.05 ± 0.39</td>
</tr>
<tr>
<td>VLF MCA V power spectra</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCA Vm, cm³/s²</td>
<td>3.60 ± 0.55</td>
<td>4.50 ± 0.89</td>
<td>9.14 ± 1.39†</td>
<td>7.14 ± 1.65</td>
</tr>
<tr>
<td>MCA Vd, cm³/s²</td>
<td>4.59 ± 1.28</td>
<td>8.21 ± 2.62</td>
<td>10.59 ± 2.79</td>
<td>7.25 ± 1.77</td>
</tr>
<tr>
<td>MCA Vpp, cm³/s²</td>
<td>2.04 ± 0.09</td>
<td>3.93 ± 0.59</td>
<td>6.69 ± 1.30</td>
<td>5.02 ± 1.17</td>
</tr>
<tr>
<td>VLF phase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean, radian</td>
<td>0.23 ± 0.30</td>
<td>0.88 ± 0.16</td>
<td>0.56 ± 0.17</td>
<td>0.42 ± 0.30</td>
</tr>
<tr>
<td>Systole, radian</td>
<td>0.25 ± 0.30</td>
<td>0.35 ± 0.41</td>
<td>0.12 ± 0.37</td>
<td>0.57 ± 0.33</td>
</tr>
<tr>
<td>Diastole, radian</td>
<td>0.54 ± 0.14</td>
<td>0.01 ± 0.05</td>
<td>0.61 ± 0.16</td>
<td>0.29 ± 0.20</td>
</tr>
<tr>
<td>VLF normalized gain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean, db</td>
<td>2.41 ± 1.01</td>
<td>0.42 ± 0.98</td>
<td>2.09 ± 1.34</td>
<td>3.76 ± 0.72</td>
</tr>
<tr>
<td>Systole, db</td>
<td>1.73 ± 0.92</td>
<td>0.21 ± 2.21</td>
<td>−0.58 ± 1.63</td>
<td>2.10 ± 1.28</td>
</tr>
<tr>
<td>Diastole, db</td>
<td>3.27 ± 0.99</td>
<td>4.85 ± 0.84</td>
<td>4.43 ± 1.25</td>
<td>5.49 ± 0.83</td>
</tr>
<tr>
<td>VLF coherence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean, U</td>
<td>0.65 ± 0.06</td>
<td>0.55 ± 0.02</td>
<td>0.59 ± 0.04</td>
<td>0.62 ± 0.05</td>
</tr>
<tr>
<td>Systole, U</td>
<td>0.57 ± 0.06</td>
<td>0.57 ± 0.05</td>
<td>0.61 ± 0.05</td>
<td>0.52 ± 0.02</td>
</tr>
<tr>
<td>Diastole, U</td>
<td>0.71 ± 0.04</td>
<td>0.60 ± 0.04</td>
<td>0.65 ± 0.04</td>
<td>0.70 ± 0.04</td>
</tr>
</tbody>
</table>

Values are means ± SE. BP, blood pressure; VLF, very low frequency. †Significantly different from EX150 (P < 0.05).
transfer function gain between DBP and MCA Vd increased from rest during EX90, EX120, and EX150 (P < 0.05).

Recovery. During recovery from each exercise condition, HR gradually decreased with the slowest reduction following EX150 (Table 1). During recovery from EX90 and EX120, the decreases in MAP and DBP were small, as were the decreases in MCA Vm and MCA Vd. After mild and moderate exercise, however, the decreases in SBP were −10 ± 2 and −24 ± 4 mmHg (P < 0.05) at minute 2 of recovery (R2), and the decreases in MCA Vs were −11 ± 4 and −28 ± 5 cm/s (P < 0.05), respectively (see Fig. 2). In contrast, following EX150, the decrease in MCA Vm and MCA Vs occurred slowly, despite rapid and marked reductions in MAP and SBP (Figs. 1 and 2). At minute 1 of recovery (R1), the reductions in MAP and SBP were −23 ± 3 and −29 ± 5 mmHg, respectively, but the reductions in MCA Vm and MCA Vs were only −4 ± 1 and −5 ± 4 cm/s, respectively. MCA Vd did not decrease during the recovery from EX150 despite a decrease in DBP. As a consequence of the changes in SBP and DBP, PP gradually became smaller during recovery after each exercise bout, and this reduction in pulse-wave amplitude was dependent on the workload (Fig. 3). MCA Vpp was also gradually reduced during recovery after each exercise bout. However, there was no significant difference in MCA Vpp from R1 to R3 between moderate and heavy exercise conditions. Although the CVRi was not altered during recovery from the EX90 and EX120 conditions, after EX150 the CVRi was rapidly reduced at R1 and was maintained at the lower value during R2 to R8 (P < 0.05). Compared with rest, PaCO2 was only slightly reduced during the recovery from EX90 and EX120 (4.85 ± 0.11 and 4.81 ± 0.13 kPa, respectively), whereas the decrease in PaCO2 was more pronounced after EX150 (4.61 ± 0.15 kPa; P < 0.05).

During the recovery period following all exercise bouts, the VLF and LF transfer function phase between MAP and MCA Vm as well as between SBP and MCA Vs and between DBP and MCA Vd did not differ from exercise (Tables 2 and 3; Fig. 4). The normalized VLF transfer gains were also unchanged from exercise to recovery. In addition, the normalized LF transfer function gain between MAP and MCA Vm as well as between SBP and MCA Vs did not differ from the exercise
values. However, the increase in the normalized LF transfer function gain between DBP and MCA $V_d$ that occurred from rest to exercise ($P < 0.05$) was maintained during recovery from each exercise workload, indicating that dynamic CA in the diastolic phase remained impaired during recovery. Importantly, the coherence between changes in arterial pressure and MCA $V$ remained above 0.5 during exercise and recovery, indicating that a statistically significant relationship was maintained.

**DISCUSSION**

The present study provides insight into the regulation of CBF in the recovery from dynamic exercise. First, decreases in
MCA \textit{V}\textsubscript{m} and MCA \textit{V}\textsubscript{s} occurred slowly, despite rapid and marked reductions in MAP and SBP after heavy exercise. In addition, the normalized LF transfer function gain between MAP and MCA \textit{V}\textsubscript{m} and between SBP and MCA \textit{V}\textsubscript{s} remained unchanged from rest, indicating a maintained dynamic CA for mean and systolic CBF regulation following exercise. However, although MCA \textit{V}\textsubscript{d} remained relatively stable on the cessation of exercise, the normalized LF transfer function gain between DBP and MCA \textit{V}\textsubscript{d} was increased from rest. These data suggest that, even though overall CBF was well maintained following mild to heavy dynamic exercise, dynamic CA for diastolic CBF regulation may be impaired, and thus CBF may be unable to respond to sudden decreases in blood pressure.

In the present study, we observed the different responses of CA to exercise and its recovery in the VLF and LF ranges (Tables 1 and 2). The VLF transfer function phase and gain were unchanged during exercise and recovery from rest, indicating that CA in the VLF was not influenced by these conditions. A previous study in rats (13) demonstrated that CA is more active in the VLF than that in the LF at rest. Thus, we considered the possibility that changes in the VLF range may be important when moving from rest to exercise. However, no differences were found in this frequency range. This finding may be related to the mechanism of different responses of CA to exercise and its recovery across frequency ranges. Moreover, it remains unclear whether CA is more active in the VLF than that in the LF range at rest or during exercise and recovery in humans.

The findings provide important information regarding gray- or black-out incidents that occur immediately at the cessation of exercise (5, 8) and are consistent with previous studies (2, 22) that have reported that syncope was related to impaired regulation of the diastolic phase of MCA \textit{V}. When blood pressure decreases during syncope, MCA \textit{V}\textsubscript{d} diminishes, whereas MCA \textit{V}\textsubscript{s} may be well maintained (22). In addition, during head-up tilt, MCA \textit{V}\textsubscript{s} and MCA \textit{V}\textsubscript{d} fall significantly. However, the magnitude of the fall, especially in MCA \textit{V}\textsubscript{d}, is
larger in patients with syncope or presyncope (2) than in healthy subjects. These findings indicate the presence of a compromised regulation at the diastolic phase of MCA V is a possible precipitating factor in the onset of syncope. Thus an impaired MCA Vd regulation after exercise may be a trigger for postexercise-mediated syncope events.

During exercise, dynamic CA becomes less able to regulate transient decreases in MCA V (8, 18, 21). Pott et al. (21) demonstrated that, during the catch phase of the rowing stroke, MCA Vm increases in parallel with MAP, but during the return phase MCA Vm declines to a nadir below the resting values, even though reductions in MAP remain above its resting values. Similarly, Edwards et al. (8) suggested that, during repetitive resistance exercise, the fluctuations in arterial pressure that occurred with each muscle contraction were too rapid to be countered by CA.

In regard to dynamic exercise, Brys et al. (4) reported that dynamic CA is unaltered during incremental exercise compared with rest by using transfer function analysis between MAP and MCA Vm. However, it is possible that autoregulatory control of the cerebral vasculature (dynamic CA) may influence the waveform response of MCA V to the waveform of arterial pressure. Thus it is possible that, especially during heavy exercise, when PP exceeds the range of static CA, a difference in the response of MCA V to arterial pressure between systolic and diastolic phases may occur even though MCA Vm is well controlled. Ogoh et al. (18) considered the impact of exercise-induced increases in PP (change in the waveform of arterial pressure) on dynamic CA by using the systolic and diastolic phases of MCA V within each cardiac cycle. In that analysis, the transfer function gain between MAP and MCA Vm and between SBP and MCA Vm remained unchanged from rest to exercise, whereas the transfer function gain between DPB and MCA Vd increased from rest to heavy exercise. These findings indicated that, despite marked increases in PP during exercise, the ability of the cerebral vasculature to modulate blood flow around the exercise-induced increase in MCA Vm is maintained but that cerebral circulation appears to be less effective in responding to rapid decreases than to increases in blood pressure. From these findings, we hypothesized that dynamic CA would be impaired in its regulation of the diastolic CBF during the recovery from dynamic exercise. We reasoned that such impairment would make cerebral perfusion vulnerable to the rapid decreases in arterial pressure that occur on cessation of exercise. However, our data indicate that, even though dynamic CA was impaired at the diastolic phase of MCA V profile, averaged MCA Vd was well maintained following dynamic exercise despite the rapid decrease in arterial pressure, particularly following heavy exercise. Conversely, spectral power of LF MCA Vd increased from EX150 to recovery, indicating an enhanced instability of beat-to-beat diastolic CBF after dynamic exercise (Fig. 4). Collectively, these findings suggest that static CA was well maintained, whereas dynamic CA at the diastolic phase was altered during recovery from dynamic exercise. We suspect that this discrepancy may be related to the different time scales used for measuring averaged MCA Vd (over 3 min) and the beat-to-beat changes in MCA Vd in this study.

Several physiological mechanisms also may be responsible for the observed differences between the averaged static and the beat-to-beat dynamic regulation of MCA V in recovery from dynamic exercise. One possible reason is postexercise-induced cerebral vasodilatation associated with withdrawal of exercise-induced sympatho-excitation. The postexercise-induced decrease in DBP was only −9 mmHg at R1 in the EX150 condition. Thus it is possible that cerebral vasodilatation compensated for this small decrease in DBP even though dynamic CA was impaired. Similarly, Koch et al. (12) reported that MCA Vd increased during recovery from resistance exercise despite large reductions in SBP. This phenomenon cannot be explained by alteration in CA alone, because an effective CA most likely would maintain MCA V unchanged or slightly decreased rather than increased under these conditions. Instead, this finding may be related to cerebral metabolic vasodilatation and sympathetic withdrawal during recovery, independent of changes in CA. Another possible reason could be the response of MCA Vd to dynamic exercise. The MCA Vd tended to decrease during exercise (Fig. 1 and Table 1). Thus, during recovery, MCA Vd tended to increase, returning to resting baseline from dynamic exercise that is controlled by a regulatory mechanism not influenced by an impaired CA at the diastolic phase of MCA V.

Although sympathetic activity is considered to have little influence on the cerebral vasculature, it is apparent that autonomic neural control of the cerebral vasculature plays a role in the beat-to-beat regulation of CBF (1, 11, 20, 24, 27). Ainslie et al. (1) observed a strong correlation between increases in muscle sympathetic nerve activity and CVRi during isocapnic conditions. The calculated CVRi values provide some insight into the dynamics of cerebrovascular reactivity during and after exercise. In the present study, CVRi increased during dynamic exercise, most notably during the heavy exercise workload (EX150) (Table 1). It is likely that this increase in CVRi counterbalanced the impact of further increases in arterial blood pressure and therefore kept MCA V constant at a moderately elevated CBF during exercise (12). The increase in MCA V was small compared with that in MAP during EX150 (+13% vs. +29%, respectively). Ogoh et al. (16) suggested that the importance of a sympathetically mediated vasoconstriction of the cerebral vasculature was to protect the blood-brain barrier when the limits of CA are exceeded. However, this protective effect of the sympathetically mediated vasoconstriction is decreased immediately after exercise. After EX150, the CVRi was rapidly reduced during minute 1 of recovery (R1) and was maintained at a lower value throughout recovery (Fig. 3). Koch et al. (12) demonstrated that MCA Vpp increased after dynamic resistance exercise despite decreases in perfusion pressure and PP. Similarly, in the present study, the pulse wave of MCA V decreased slowly during recovery from heavy cycling exercise despite acute decreases in perfusion pressure and PP. This phenomenon may be related to the off-response of sympathetic nerve activity associated with the cessation of exercise. Thus the vasodilatory effect of the reduced sympathetic activity on the cerebral vasculature counterbalances the acute decrease in arterial blood pressure and consequently maintains CBF.

The changes in cardiac output affect MCA Vm both at rest and during exercise, and its regulation is independent of CA (16). However, during recovery from dynamic exercise, the divergent response in MCA Vd (increase) and MCA Vd (no change) are observed despite decreases in cardiac output. This finding indicates that there is a difference in the effect of
cardiac output on MCA V regulation between the systolic and diastolic phase. It seems that MCA Vd is influenced more by changes in cerebral vasomotion than MCA Vs.

CO₂ is the most powerful regulator of cerebral vascular tone. Moreover, lower body negative pressure-induced sympathetic nerve activation has no influence on the cerebral vascular response to CO₂ (14). Ogoh et al. (17) suggested that the CBF response to PₐCO₂ and the PₐCO₂ modification of CA were attenuated during exhaustive exercise. Although it is difficult to estimate the effect of PₐCO₂ on CBF regulation from the data in the present study, postexercise-induced hyperventilation, especially after heavy exercise, would result in the decrease in PₐCO₂, being more effective in decreasing MCA V. However, MCA Vm, MCA Vs, and MCA Vpp decreased more slowly after heavy exercise. This finding suggests that the effect of PₐCO₂ on MCA V was attenuated during the recovery from exercise, particularly after higher intensity dynamic exercise.

Potential limitations. A potential limitation of the transcranial Doppler ultrasonography is that the diastolic phase of the velocity profile may not be faithfully represented. To ensure that the flow-velocity profile of the MCA V was accurately measured, the flow-velocity wave was obtained with a resonance frequency range of 12–25 Hz. This resonance frequency range is identified to adequately encompass systolic and diastolic pressure wave monitoring using an arterial catheter and a pressure transducer (10). In addition, exercise increases blood flow in regions of the brain associated with movement (9); thus changes in cerebral regional blood flow may influence MCA V after exercise. However, MCA V was well maintained following mild to heavy exercise. This finding suggests that regional changes in cerebral perfusion may not be reflected in MCA, especially during exercise, and confirms previous work (9). Another limitation of this study was that we only measured PₐCO₂ once 4–5 min after exercise. However, this could not be avoided because of the required duration of data collection needed for the transfer function analyses. Regarding intense exercise, end-tidal CO₂ increased a few seconds after the end of exercise and then returned to its preexercise value (25). However, with dynamic resistance exercise, end-tidal CO₂ was maintained at its exercise value 30 s after exercise and then slowly decreased to a lower value than rest (12). In our previous study (6), PₐCO₂ was measured during recovery from light and exhaustive dynamic exercise; however, there were no significant changes in PₐCO₂ during recovery within 10 min following each exercise condition. Thus, in the present study, an impaired dynamic CA was not related to PₐCO₂ during recovery from exercise.

In the present study, we used transfer function analysis to demonstrate the dynamic relationship between diastolic pressure and MCA Vd and between systolic pressure and MCA Vs to estimate CA at diastolic and systolic phases. Our concept for this separate analysis is based on the potential for the mean value to miss information in regard to the waveform and a potential influence of PP, especially during exercise, as we have previously demonstrated (18). We found differences between the diastolic and systolic phases in the transfer function analysis. However, we would like to point out that this does not mean that “systolic autoregulation” and “diastolic autoregulation” are separate mechanisms. Rather, our findings suggest that the influence of CA on MCA Vd is different from MCA Vs during exercise and recovery. These differential CA influences may be important physiologically because previous studies have already demonstrated that there is a different response of MCA V to change in perfusion pressure between systolic and diastolic phases during specific conditions, such as orthostatic stress (2, 22) and exercise (18, 21). Although both transfer function phase and gain are used as an index of dynamic CA, changes in gain were not consistent with changes in phase in the present study. However, the phase estimate reflects the time relationship, whereas the gain reflects the amplitude relationship between arterial blood pressure and MCA V. Therefore, it is possible that changes in gain are not associated with changes in phase.

In summary, dynamic CA at the mean and systolic phase of the MCA V profile remained effective during recovery from exercise, whereas the normalized LF transfer function gain between DBP and MCA Vd was increased, indicating an impaired CA in the diastolic phase. Nevertheless, averaged MCA Vm, MCA Vs, and MCA Vd over a time interval of 3 min all remained relatively stable on the cessation of exercise. Thus, even though overall CBF was well maintained following mild to heavy dynamic exercise, the data indicate that dynamic CA may be less able to maintain brain perfusion in response to sudden decreases in blood pressure.

ACKNOWLEDGMENTS

The authors appreciate the time and effort expended by all the volunteer subjects. We thank Peter Nissen for expert technical assistance.

GRANTS

This study was supported in part by National Heart, Lung, and Blood Institute Grant HL-045547, a grant from Copenhagen Muscle Research Center, British Heart Foundation Grant PG/03/148/16352, and a Physiological Society Travel Award.

REFERENCES


