Carotid baroreflex control of leg vascular conductance at rest and during exercise

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Keller, David M., Wendy L. Wasmund, D. Walter Wray, Shigehiko Oogoh, Paul J. Fadel, Michael L. Smith, and Peter B. Raven. Carotid baroreflex control of leg vascular conductance at rest and during exercise. J Appl Physiol 94: 542–548, 2003. First published October 18, 2002; 10.1152/japplphysiol.00817.2002.—We sought to test the hypothesis that the carotid baroreflex (CBR) alters mean leg blood flow (LBF) and leg vascular conductance (LVC) at rest and during exercise. In seven men and one woman, 25 ± 2 (SE) yr of age, CBR control of LBF and LVC was determined at rest and during steady-state one-legged knee extension exercise at ~65% peak O2 uptake. The application of 5-s pulses of +40 Torr neck pressure and −60 Torr neck suction significantly altered mean arterial pressure (MAP) and LVC both at rest and during exercise. CBR-mediated changes in MAP were similar between rest and exercise (P > 0.05). However, CBR-mediated decreases in LVC (%change) to neck pressure were attenuated in the exercising leg (16.4 ± 1.6%) compared with rest (33 ± 2.1%) and the nonexercising leg (23.7 ± 1.9%) (P < 0.01). These data suggest CBR control of blood pressure is partially mediated by changes in leg vascular tone both at rest and during exercise. Furthermore, despite alterations in CBR-induced changes in LVC during exercise, CBR control of blood pressure was well maintained. Using direct blood flow measurements, Collins et al. (5) have noted an exercise-induced change in hindlimb and kidney vasomotor responsiveness after bilateral carotid occlusion. Despite a similar pressor response elicited by bilateral carotid occlusion at rest and during treadmill exercise, the relative contribution of the hindlimb and kidney vascular beds to the overall increase in blood pressure was significantly altered, with the hindlimb contributing more and the kidney contributing less during exercise. These findings demonstrate a clear shift in the CBR control of the vasculature from rest to exercise. However, the greater reliance on active skeletal muscle vasoconstriction during exercise is not a universally accepted concept.

A large body of research has examined the functional consequence of sympathetic activation during exercise, and the presence of a metabolically induced inhibition of the full expression of sympathetic neural activation within exercising tissue has been consistently reported (2, 3, 14–16, 35, 37). This exercise-related alteration of vascular responsiveness to a given sympathetic stimulus compared with rest has been termed “functional sympatholysis.” Recent work suggests that this metabolic alteration of sympathetically mediated vasoconstriction is graded to the intensity of the exercise, becoming more evident at greater exercise intensities (3, 31, 37). The mechanisms for this graded attenuated vascular response to sympathetic activation have been associated with an exercise-induced production of nitric oxide (4, 32, 36), adenosine, and prostacyclin (20, 27) and their exercise intensity-related increases in concentration as well as with increases in muscle temperature (6), hypoxia (13), and metabolic acidosis (19).

CBR control of ABP is maintained from rest to exercise, despite drastic changes in the local distribution of blood flow. Therefore, an understanding of the responsiveness of the local vasculature to CBR stimulation remains an important question considering the potential for metabolic modulation of vascular control within the exercising tissue. Thus we sought to examine the importance of CBR-mediated changes in leg vascular conductance (LVC) of exercising and nonexercising tis-

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sue in the regulation of ABP in humans. We hypothesized that CBR stimulation would alter LVC at rest and that this response would be altered within the exercising, but not the nonexercising, muscle.

METHODS

Subjects. Seven men and one woman [age, 25 ± 2 (SE) yr; height, 179.7 ± 2.5 cm; weight, 73.6 ± 4.1 kg] voluntarily participated in the present investigation. Each of the subjects was acquainted with the testing protocols, and was informed of potential risks of participating in the present study, and provided written, informed consent, approved by the University of North Texas Health Science Center’s Institutional Review Board. All subjects were healthy, nonsmokers, free of known cardiovascular and respiratory disease, and not using any prescription or over-the-counter medications. Subjects were advised not to participate in any strenuous physical activity or to consume alcohol 24 h before any of the scheduled experiments. Subjects were also asked to refrain from the consumption of caffeinated beverages 12 h before any of the scheduled experiments. Each subject visited the laboratory on two separate occasions.

Maximal exercise testing. On the first visit, each subject performed a graded, one-legged knee extension maximal exercise test by using a modified Krogh bicycle ergometer for the determination of a maximum workload and peak $\dot{V}O_2$ uptake ($\dot{V}O_2$ peak) during one-legged knee extension. The kick rate for the maximal exercise test was set at 30 extensions per minute (epm), and after each 1-min stage the load was increased by ~3 lb. per stage. Subjects were provided visual feedback of the workload achieved throughout the exercise test via a light-emitting diode display (lb.), and a metronome provided auditory feedback as to the rate of the contraction and relaxation phases of the exercise. The exercise test was terminated when the subject could no longer maintain a kick rate of 30 epm despite strong verbal encouragement.

Subjects respired through a mouthpiece attached to a low-resistance turbine volume transducer (model VMM, Sensor Medics, Anaheim, CA) for the measurement of breath volumes while respiratory gases were continuously sampled from the mouthpiece for determinations of fractional concentrations of $O_2$, $CO_2$, and $N_2$ with mass spectrometry (model MGA1100B, Perkin-Elmer, St. Louis, MO). The analog signals of the mass spectrometer were subjected to analog-to-digital conversion and computer analysis (Dell OptiFlex GXI) for on-line, breath-by-breath determination of respiratory gases.

Experimental protocol. On a separate day (at least 48 h after performing the graded maximal exercise test), the subjects performed dynamic, one-legged knee extension exercise at a workload equal to ~65% $\dot{V}O_2$ peak of the maximal workload achieved during the final stage of the graded maximal exercise test. Subjects were encouraged in a similar fashion as during their graded maximal exercise test, in order for the subject to maintain a consistency of each knee extension. The rate of kicking was modified to 20 epm for the exercise performed on the experimental day to further extend the time in which the exercising leg (EL) was relaxed to optimize the FLV of the Doppler ultrasound measures during the relaxation phase.

Measurements and procedures. All testing was performed with subjects in a semirecumbent ~60° back-supported seated position, resulting in an ~120° leg-to-torso angle to optimize one-legged exercise performance as well as blood flow measurements. Cardiovascular variables were monitored beat-to-beat and were recorded on a personal computer equipped with customized software (Necusuc3) that collects and records data on each R wave. Heart rate (HR) was monitored with a standard lead II electrocardiogram (ECG). The ECG signal was output to a monitor (model 78342A, Hewlett-Packard, Andover, MA) interfaced with the personal computer. ABP was measured by using photoplethysmography (Finapres model 2300, Ohmeda) on the middle finger of the right hand of each subject and calibrated to match the diastolic blood pressure achieved from brachial auscultation. Subjects were fitted with a malleable lead neck collar for the application of neck pressure (NP) and neck suction (NS). CBR function was assessed at rest and during one-legged knee extension exercise after steady-state $O_2$ consumption ($\dot{V}O_2$) had been achieved (~5 min). During the initial exercise bout only, breath-by-breath measurements of $\dot{V}O_2$ were collected during the first 6.5 min, as well as during the final 2 min. All exercise trials were limited to ~20 min (19.4 ± 0.6 min) so as to eliminate any confounding effects of fatigue or cardiovascular drift on CBR function (22). In an effort to minimize skin blood flow, laboratory temperature on experimental days was maintained between 20–22°C.

Leg blood flow. Femoral artery mean blood flow velocity (MBV) was determined by using pulsed Doppler ultrasound velocimetry. Blood flow velocity spectra and arterial diameters were obtained by a Doppler ultrasound unit (model RT 6800, General Electric) operating in pulsed mode. A probe with an operating frequency of 2.5 MHz was placed on the skin over the common femoral artery 2–3 cm distal to the inguinal ligament. The angle of the transducer crystal relative to the skin was 45°. All Doppler data were recorded onto VHS tape and further analyzed by using custom software. Beat-by-beat MBV was calculated by integrating the total area under the instantaneous MBV profile during each cardiac cycle. MBV and femoral artery diameter were measured from the femoral artery of either the EL or the nonexercising leg (NEL) during the first bout of one-legged exercise, after which subjects recovered for ~35 min before performing a second bout of identical one-legged exercise. During the second bout, MBV and femoral artery diameter were collected from either the EL or NEL not measured in the first exercise bout. Femoral artery diameter was measured by using the same 2.5-MHz probe at a site matching that at which velocity was measured. Average femoral artery diameter was determined at rest and during one-legged knee extension exercise in the EL and the NEL. All resting MBV and resting femoral artery diameter data were measured from one leg of each of the subjects (i.e., right or left) before any exercise trials were performed. Femoral artery diameter was not changed to 5-s pulses of either NP or NS, and the following formula was used to calculate mean leg blood flow (LBF): $LBF = \pi \cdot \text{radius}^2 \cdot \text{MBV}$.

CBR responsiveness. CBR control of MAP, MBV, and HR were assessed by applying single 5-s pulses of NP (+40 Torr) and NS (~60 Torr), as described by Potts et al. (26). Under resting conditions, NP and NS were applied during a 10- to 15-s breath hold at end expiration to minimize the respiratory modulation of HR and MAP. During exercise, NP and NS were applied without the presence of a breath hold (8). A minimum of 45 s was allowed to pass between each NP and NS trial to allow physiological variables to return to prestimulus values.

Peak responses for MAP and HR were determined as the greatest change in each variable that occurred from the application of NP and NS, and changes from each trial were averaged to provide a mean response for each subject. Changes in MBV and femoral artery diameter were deter-
Table 1. Physiological responses to one-legged knee extension exercise

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Nonexercising Leg</th>
<th>Exercising Leg</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBV, cm/s</td>
<td>13.6 ± 2.4</td>
<td>23.8 ± 2.8</td>
<td>61.2 ± 4.8</td>
</tr>
<tr>
<td>LBF, ml/min</td>
<td>457.7 ± 68.3</td>
<td>823.0 ± 82.0</td>
<td>2475.2 ± 278.3</td>
</tr>
<tr>
<td>Femoral diameter, mm</td>
<td>8.6 ± 0.2</td>
<td>8.5 ± 0.1</td>
<td>9.2 ± 0.2</td>
</tr>
<tr>
<td>LVC, ml·mmHg⁻¹·min⁻¹</td>
<td>4.1 ± 0.6</td>
<td>7.1 ± 0.7</td>
<td>21.8 ± 2.2</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>89.2 ± 3.6</td>
<td>95.5 ± 2.1</td>
<td>92.5 ± 2.7</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>74.2 ± 6.1</td>
<td>85.9 ± 4.1</td>
<td>84.4 ± 4.4</td>
</tr>
<tr>
<td>Oxygen uptake, ml/min</td>
<td>337.9 ± 18.0</td>
<td>557.7 ± 45.4</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE. MBV, mean blood flow velocity; LBF, leg blood flow; LVC, leg vascular conductance; MAP, mean arterial pressure; HR, heart rate. *Significantly different from rest, \( P < 0.05 \). †Significantly different from rest and nonexercising leg, \( P < 0.05 \).

RESULTS

\( \dot{V}_O_2 \) during one-legged knee extension exercise. The \( \dot{V}_O_2 \) peak during one-legged knee extension exercise for the group was \( 882.9 ± 65.3 \) ml/min (\( 12.0 ± 0.5 \) ml·kg⁻¹·min⁻¹). The steady-state exercise \( \dot{V}_O_2 \) during one-legged knee extension exercise was \( 557.7 ± 45.4 \) ml/min (\( 7.5 ± 0.3 \) ml·kg⁻¹·min⁻¹), i.e., \( -63.3 ± 2.2\% \) of \( \dot{V}_O_2 \) peak.

Physiological responses to one-legged knee extension exercise. HR and MAP responses to steady-state one-legged knee extension exercise are presented in Table 1. Baseline HR was increased during exercise compared with rest \( (P < 0.05) \). However, MAP was not significantly elevated during exercise. These changes in HR and MAP were consistent throughout the exercise bouts because steady-state measurements recorded at 5–6 min (83 ± 4 beats/min and 95 ± 2 mmHg, respectively) were not significantly different from measurements obtained during the last minute of exercise (86 ± 4 beats/min and 94 ± 2 mmHg; \( P > 0.05 \)). The LBF and LVC responses to steady-state exercise are presented in Fig. 1. Compared with rest, the steady-state LBF increased by \(-75\%\) in the NEL \( (P = 0.037) \) and by \(-450\%\) in the EL \( (P < 0.001) \) during exercise. Femoral artery diameter increased from 8.6 mm at rest to 9.2 mm in the EL during steady-state exercise \( (P = 0.035) \), but it was unchanged in the NEL \( (P = 0.915) \). LVC increased by \(-73\%\) during exercise in the NEL \( (P < 0.01) \) and by \(-530\%\) in the EL \( (P < 0.001) \) compared with rest.

CBR control of HR and MAP. CBR-mediated changes in HR and MAP at rest and during one-legged exercise are presented in Table 2. The application of 5 s of \(+40\) Torr NP increased HR and MAP at rest by \(-10\%\) and \(-13\%,\) respectively \( (P < 0.05) \), and during exercise by \(-9\%\) and \(-13\%,\) respectively \( (P < 0.05) \). Conversely, stimulation of carotid baroreceptors with 5 s of \(-60\) Torr NS decreased HR and MAP at rest by \(-23\%\) and \(-12\%,\) respectively \( (P < 0.05) \), and during exercise by

Fig. 1. A: changes in leg blood flow in response to one-legged knee extension exercise. B: changes in leg vascular conductance in response to one-legged knee extension exercise. NEL, non-exercising leg; EL, exercising leg. *Significantly different from rest, \( P < 0.05 \). †Significantly different from NEL, \( P < 0.05 \).
~21 and ~14%, respectively (P < 0.05). There was no difference in the range of response for both HR and MAP between rest and exercise (P > 0.05).

CBR control of LBF. CBR-mediated changes in LBF at rest and during one-legged exercise are presented in Fig. 2 and Table 2. The CBR responses elicited by the application of NP decreased LBF at rest by ~25% (P < 0.001). Compared with baseline, NP reduced LBF by ~16% (P < 0.001) in the NEL and by ~8% in the EL (P < 0.001). The CBR response elicited by the application of NS increased LBF at rest (~6%; P < 0.001), in the NEL (~11%; P = 0.035), and in the EL (~4%; P < 0.001).

CBR control of LVC. The stimulus-response relationship for CBR control of LVC expressed in absolute units (ml·mmHg⁻¹·min⁻¹) at rest and during exercise is presented in Fig. 3. The range of response to +40 Torr NP and ~60 Torr NS was 2.0 ± 0.3 ml·mmHg⁻¹·min⁻¹ at rest. This range of response to NP and NS was significantly increased during exercise in the EL (6.9 ± 0.6 ml·mmHg⁻¹·min⁻¹) compared with rest (P < 0.05) but not in the NEL (3.4 ± 0.4 ml·mmHg⁻¹·min⁻¹) (P = 0.099).

The stimulus-response relationship for CBR control of LVC expressed as a percent change from prestimulus steady-state values (%ΔLVC) at rest and during exercise is presented in Fig. 4. The CBR response elicited by the application of NP decreased LVC at rest (~33%; P < 0.001) and in both the NEL (~24%; P < 0.001) and EL (~16%; P < 0.001). The CBR response elicited by the application of NS increased LVC at rest (~18%; P < 0.001) and in both the NEL (~25%; P < 0.001) and the EL (~16%; P = 0.004). The percent decrease in LVC elicited by the application of NP in the EL was significantly less than at rest and in the NEL (P = 0.003). The CBR range of response for %ΔLVC (%ΔLVC to NS minus %ΔLVC to NP) was no different between rest and the NEL during exercise (P = 0.775). However, the LVC range of response in the EL was decreased compared with rest (P < 0.001) and the NEL (P < 0.001).

**DISCUSSION**

The data of the present investigation support our initial hypothesis that CBR stimulation with the use of NP and NS would effectively decrease and increase LVC, respectively, at rest and during exercise. Fur-

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### Table 2. CBR control of HR, MAP, and LBF at rest and during exercise

<table>
<thead>
<tr>
<th>Condition</th>
<th>HR, beats/min</th>
<th>MAP, mmHg</th>
<th>LBF, ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>74.2 ± 6.1</td>
<td>89.2 ± 3.6</td>
<td>457.7 ± 68.3</td>
</tr>
<tr>
<td>Nonexercising leg</td>
<td>85.9 ± 4.1*</td>
<td>101.3 ± 3.5</td>
<td>351.3 ± 59.3</td>
</tr>
<tr>
<td>Exercising leg</td>
<td>84.4 ± 4.4*</td>
<td>108.1 ± 1.7</td>
<td>707.0 ± 83.5</td>
</tr>
<tr>
<td>+40 Torr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>82.3 ± 6.2‡</td>
<td>105.1 ± 2.5</td>
<td>2,475.0 ± 262.8‡</td>
</tr>
<tr>
<td>Nonexercising leg</td>
<td>92.6 ± 4.4**</td>
<td>78.4 ± 2.4‡</td>
<td>2,315.8 ± 278.3‡‡</td>
</tr>
<tr>
<td>Exercising leg</td>
<td>91.8 ± 4.5**</td>
<td>82.4 ± 2.5‡</td>
<td>909.8 ± 94.4**</td>
</tr>
<tr>
<td>−60 Torr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>56.8 ± 5.6‡</td>
<td>78.4 ± 2.4‡</td>
<td>2,551.5 ± 249.8‡‡</td>
</tr>
<tr>
<td>Nonexercising leg</td>
<td>68.0 ± 3.5‡‡</td>
<td>80.6 ± 2.7‡</td>
<td>909.8 ± 94.4**</td>
</tr>
<tr>
<td>Exercising leg</td>
<td>66.1 ± 3.9‡‡</td>
<td>82.4 ± 2.5‡</td>
<td>909.8 ± 94.4**</td>
</tr>
</tbody>
</table>

Values are means ± SE. CBR, carotid baroreflex. *Significantly different from rest, P < 0.05. †Significantly different from rest and NEL, P < 0.05. ‡Significantly different from baseline, P < 0.05.
thermore, the CBR-mediated percent reduction in LVC to NP was attenuated in the EL compared with both rest and the NEL, indicating a modulation of sympathetically mediated alterations in LVC within active muscle during exercise. It is apparent from these data that alterations in LVC play a significant role in mediating CBR-induced changes in ABP both at rest and during exercise. Moreover, despite alterations in CBR-mediated changes in LVC during exercise, CBR control of blood pressure was well maintained.

Although our laboratory has previously identified the predominance of alterations in total vascular conductance compared with cardiac output in mediating CBR changes in blood pressure at rest, the present study extends these findings by identifying a prominent role of the CBR in the regulation of skeletal muscle blood flow both at rest and during exercise (23). Under resting conditions, NP and NS caused reflex-mediated decreases and increases in LVC, respectively. Similarly, during exercise, the application of NP caused decreases in LVC within the NEL as well as the EL. However, the decrease in the EL was significantly less compared with the response in the NEL or at rest, indicating a reduced responsiveness to CBR-mediated sympathoexcitation within the exercising muscle. These data are in line with previous reports of an exercise-induced attenuation of the expected sympathetically mediated vasoconstriction (3, 13, 15, 16, 34, 35). However, when the CBR changes in LVC were expressed as absolute units of conductance (ml·mmHg⁻¹·min⁻¹), it was apparent that the reduction in LVC in EL was greater than in the NEL as well as that observed at rest. These data confirm the recent report of Collins et al. (5) in which they identified a greater CBR-mediated reduction in vascular conductance of the dog hindlimb during exercise compared with rest as well as an inactive vascular bed (i.e., renal). Our data and those of Collins et al. and O'Leary et al. (24) clearly demonstrate the importance of sympathetic control of vascular conductance within skeletal muscle in mediating CBR-induced changes in blood pressure.

However, whether sympathetic-mediated responses are greater or attenuated in exercising muscle is a point of continued debate.

In the present study, we report an attenuated LVC response to NP in the exercising leg compared with the NEL and rest when the data are presented as a percent change, but a greater response to NP is indicated when the data are expressed in absolute units of conductance. What is the appropriate interpretation of this data? According to Poiseuille’s law, under constant perfusion pressure, a given percent change in the radius of a vessel consistently produces the same percent change in conductance, regardless of the baseline blood flow, or baseline conductance (2). Therefore, by using percent changes in conductance, vasoconstrictor and vasodilator responses can be accurately compared between conditions even when baseline blood flows are markedly different, such as between rest and exercise. Thus, taking into account the fivefold increase in leg blood flow without a significant increase in blood pressure during one-legged exercise, we believe that percent changes are more accurate for comparison of the vascular responses to sympathetic activation between rest, the NEL, and the EL. In regard to the presence of metabolically altered vascular responsiveness in the present study, we suggest that there is a clear attenuation of the CBR-mediated LVC response to sympathetic activation induced by NP in the EL. However, this interpretation is dependent on the sympathetic stimulus being similar between rest and exercise. Previously, our laboratory has reported that CBR control of MSNA was similar at rest and during arm cycling exercise (9). Although the MSNA measurement was performed in a nonexercising limb, which is necessary for the obtainment of this signal, it is generally well accepted that sympathetic outflow is similar between contracting and noncontracting skeletal muscle (17). Thus the percent increase in sympathetic activity induced by NP appears to be similar in resting and exercising muscle. Although it is plausible that CBR control of MSNA is affected by the mode of exercise (i.e., arm cycling vs. 1-legged exercise), in the present study a reduced responsiveness to NP was observed in the EL compared not only with rest but also with the NEL during one-legged exercise, in which it is unlikely that any differential sympathetic response would explain the observed differences. Regardless of any mathematical or methodological concerns, the finding of an attenuated response to NP is in agreement with previous (3, 15, 35) and more recent work confirming the existence of a metabolic attenuation of the vascular response to sympathetic stimulation in humans (7, 37).

It is apparent that the coexistence of two opposite mechanisms of effect, which have historically been thought to be mutually exclusive, are a function of definition and viewpoint and not one of physiology. Two fundamentals of the physiology of exercise are that 1) there exists a tight coupling of O₂ delivery to meet the metabolic demand of the exercising tissue and this is reflected by the linear relationship between VO₂, and cardiac output; and 2) ABP is the regulated vari-

Fig. 4. Carotid baroreflex modulation of leg vascular conductance expressed as a percent change from steady-state values at rest and during one-legged knee extension exercise. *Significantly different from rest, P < 0.05. †Significantly different from NEL, P < 0.05.
able and that it is the sympathetic control of the vasculature that predominates (30). Clearly, if during exercise the full expression of sympathetically mediated vasoconstriction occurred in the active tissue, then a disproportionate reduction in flow would occur, thereby limiting the delivery of \( \text{O}_2 \) to the exercising muscles. Instead the mechanisms of an altered vascular response to sympathetic activation, which appears to be directly linked to the metabolic activity of the tissue, result in an intensity-related attenuation of the effects of sympathetic neural activation within active muscle, as previously suggested (3, 31, 37). Thus the functional outcome is that a balance exists between sympathetic neural activation and the exercise-induced vasodilator metabolites and hormones, such that blood flow to the active muscle is tightly regulated to maintain the metabolic demands of the exercising muscle. At the same time, it is likely that alterations within the baroreflex arc (i.e., resetting) (10, 11, 21, 25, 26, 28, 29) as well as changes in end-organ responsiveness within different vascular beds (5) allow for the continued regulation of ABP during exercise.

Similar to the findings of Strange et al. (33), we demonstrated a CBR-mediated increase in LVC to NS during exercise. However, Strange et al. did not report CBR-mediated changes in vascular conductance at rest or during exercise in an inactive vascular bed. Interestingly, the data of the present investigation identified that the percent increase in LVC during NS was significantly greater, whereas the response to NP was slightly reduced, in the NEL compared with rest. These alterations in CBR control within the NEL occurred without any changes in the CBR range of response for \( \Delta \text{LVC} (\% \Delta \text{LVC to NS minus } \% \Delta \text{LVC to NP}) \) between rest and the NEL. We suggest that these alterations in CBR responses within the NEL may be due to a resetting of the CBR curve noted with exercise (21, 29), which results in a reduced responsiveness to hypotensive stimuli (NP) and an augmented responsiveness to hypertensive stimuli (NS). In contrast to the NEL, LVC responses to NS within the EL were not different from rest; however, a clear attenuation of the decrease in LVC induced by NP was observed in all subjects in the EL compared with rest. Furthermore, the CBR range of response for \( \% \Delta \text{LVC in the EL was significantly decreased not only compared with rest but also compared with the NEL} \). Thus it is unlikely that resetting could solely explain the alterations noted within the EL, and as such a modulation of sympathetically mediated vasoconstriction was present in the EL. Importantly, this reduced LVC response to NP was noted compared with the NEL, thereby reflecting differences related primarily to end-organ responses to sympathetic neural activation of NP in the exercising leg. Nevertheless, despite an attenuated response to sympathetic activation in the EL, CBR control of blood pressure was well maintained during exercise.

During exercise, LBF was significantly elevated in both the EL and the NEL, by \( \sim 450 \) and \( 75\% \), respectively. The increase in LBF in the EL can easily be explained by increased activity of the muscle pump, as well as metabolically and shear stress induced-vasodilation resulting from the exercise and the increased cardiac output. However, the increase in LBF in the NEL is likely the primary result of increased cardiac output. It is expected that the steady-state sympathetic nerve activity associated with exercise in the present investigation was not adequate enough to cause sufficient vasoconstriction in the NEL and, therefore, shunt blood to the exercising tissue. The result was the observed increase in LBF in the NEL. In support of this finding, Green et al. (12), using Doppler ultrasound technology, have recently demonstrated similar increases in brachial artery blood flow during dynamic leg cycling.

Potential limitations in the design and interpretation of the present investigation should be considered. Although we were able to identify the importance of the skeletal muscle vasculature in CBR control of blood pressure at rest and during exercise, we did not fully model the CBR-LVC response curves and determine the typical parameters and variables derived from the curve of best fit (18). These data would more completely define CBR-mediated LVC responses both at rest and during exercise and, therefore, more specifically address the degree to which resetting occurs within the active and inactive muscle during exercise. Clearly, these are important questions for future research. A measurement of MSNA was not made in the present study, and, therefore, the degree to which sympathetic nerve activity increased during the one-legged exercise is unknown and whether the sympathetic nerve activity response to NP and NS was similar at rest, in the NEL, and in the EL is unclear. However, considering that no significant increases in blood pressure were observed with exercise, it is unlikely that sympathetic nerve activity was greatly increased. Furthermore, our laboratory has previously reported that CBR-mediated changes in MSNA were similar at rest and during exercise (9). One methodological limitation in regard to LBF is that the femoral artery supplies not only skeletal muscle but also other tissues such as bone and skin. However, with respect to changes in vascular responsiveness, the data of the present study would indicate a metabolic modulation originating from the active skeletal muscle.

In summary, we have demonstrated that the skeletal muscle vasculature is important in mediating CBR-induced changes in blood pressure both at rest and during exercise. Furthermore, CBR-mediated reductions in LVC to the sympathoexcitation induced by NP was attenuated in the EL compared with both rest and the NEL, indicating a modulation of sympathetically mediated alterations in LVC within active muscle during exercise. However, despite these alterations in CBR-mediated changes in LVC, CBR control of blood pressure was well maintained during exercise. Thus it appears that a balance exists between CBR control of the vasculature and exercise-induced inhibition of sympathetically mediated responses within active skeletal muscle. We suggest that this provides the precise regulation of skeletal muscle blood flow to maintain the
metabolic demands of the exercising muscle while at the same time allowing for the continued regulation of ABP during exercise.

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P. J. Fadel is currently an individual National Institutes of Health-National Research Service Award postdoctoral fellow in the Division of Hypertension at the University of Texas Southwestern Medical Center, Dallas.

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