Carotid baroreflex regulation of sympathetic nerve activity during dynamic exercise in humans


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Fadel, P. J., S. Ogho, D. E. Watenpaugh, W. Wasmund, A. Olivencia-Yurvati, M. L. Smith, and P. B. Raven. Carotid baroreflex regulation of sympathetic nerve activity during dynamic exercise in humans. Am J Physiol Heart Circ Physiol 280: H1383–H1390, 2001.—We sought to determine whether carotid baroreflex (CBR) control of muscle sympathetic nerve activity (MSNA) was altered during dynamic exercise. In five men and three women, 23.8 ± 0.7 (SE) yr of age, CBR function was evaluated at rest and during 20 min of arm cycling at 50% peak O₂ uptake using 5-s periods of neck pressure and neck suction. From rest to steady-state arm cycling, mean arterial pressure (MAP) was significantly increased from 90.0 ± 2.7 to 118.7 ± 3.6 mmHg and MSNA burst frequency (microneurography at the peroneal nerve) was elevated by 51 ± 14% (P < 0.01). However, despite the marked increases in MAP and MSNA during exercise, CBR-Δ%MSNA responses elicited by the application of various levels of neck pressure and neck suction ranging from +45 to −80 Torr were not significantly different from those at rest. Furthermore, estimated baroreflex sensitivity for the control of MSNA at rest was the same as during exercise (P = 0.74) across the range of neck chamber pressures. Thus CBR control of sympathetic nerve activity appears to be preserved during moderate-intensity dynamic exercise.

mean arterial pressure; carotid baroreceptors; neck pressure; neck suction; arm exercise

It was reported by Bevegard and Shepherd (1) in 1966 that carotid baroreflex (CBR) regulation of arterial blood pressure (ABP) was unaltered during exercise in humans. The application of neck suction (NS) caused CBR-mediated decreases in heart rate (HR) and ABP that were similar at rest and during supine leg cycling. In an attempt to more completely define CBR function during dynamic exercise, Potts et al. (22) defined the open-loop stimulus-response relationship for CBR control of HR and ABP during leg cycling at 25 and 50% peak O₂ uptake (VоІpeak). These investigators demonstrated that the CBR was reset to the prevailing level of systemic pressure and was able to respond to transient changes in carotid sinus pressure (CSP) as effectively as at rest. This resetting of the CBR without a change in sensitivity has been confirmed for moderate-to high-intensity dynamic exercise (15, 17) as well as static exercise (3). Therefore, it appears that CBR function is preserved during exercise.

While CBR control of blood pressure remains operable during exercise, the mechanisms by which the CBR responds to changes in ABP may be different from those during rest. Several investigations have reported that efferent baroreflex control of HR was altered during dynamic exercise (7, 21, 24), and it has been suggested that during dynamic exercise the magnitude of CBR-mediated changes in HR was dependent on the level of cardiac vagal tone, such that the reflex tachycardia to neck pressure (NP) decreased during exercise, while the reflex bradycardia to NS was augmented (21). However, the effect of exercise on CBR control of efferent sympathetic nerve activity remains unclear, inasmuch as studies examining CBR-mediated changes in sympathetic nerve activity during exercise have been limited.

Eckberg and Wallin (5) noted that isometric handgrip exercise at 30% of maximum resulted in an attenuated muscle sympathetic nerve activity (MSNA) response to +30 Torr NP and an augmented MSNA response to −30 Torr NS. These investigators concluded that exercise caused small but significant alterations of CBR-mediated neural responses that appear to limit increases in MSNA. In contrast, Papelier et al. (18) reported that sustained activation of the muscle chemoreflex with postexercise ischemia caused diminished CBR-mean arterial pressure (MAP) responses to hypertension and enhanced responses to hypotension without alterations in the carotid-HR response. Although MSNA was not recorded, it was suggested that the augmentation in sympathetic nerve activity caused by muscle chemoreflex activation overpowered the CBR response to hypertension and added to the CBR-mediated vasoconstriction induced by hypotension. Although equivocal, these investigations suggest possible alterations in CBR control of MSNA during exercise.

Previously, it was demonstrated that, at rest, 5-s periods of NP-NS produced CBR-mediated changes in...
MSNA that were described by a typical sigmoidal baroreflex relationship (23). However, the stimulus-response curve for CBR control of MSNA has yet to be characterized during dynamic exercise. Therefore, the purpose of the present investigation was to determine whether dynamic exercise altered CBR control of MSNA in humans. Our intent was to construct stimulus-response relationships for carotid baroreceptor control of MSNA using brief 5-s perturbations of CSP. Given the previous findings in human investigations that indicate a resetting of the CBR-HR and CBR-MAP stimulus-response curve to the prevailing ABP without a change in reflex sensitivity, we hypothesized that the CBR-MSNA stimulus-response curve would also be reset with unaltered sensitivity during dynamic exercise.

**METHODS**

**Subjects.** Five men and three women (means ± SE: age, 23.8 ± 0.7 yr; height, 174.7 ± 3.8 cm; weight, 71.3 ± 5.3 kg) voluntarily participated in the present investigation. Each subject was advised of the testing protocols and potential risks of participation in the study and provided written informed consent, which was approved by the University of North Texas Health Science Center Institutional Review Board. All subjects were nonsmokers, were free of any known cardiovascular or respiratory disease, and were not using prescription or over-the-counter medication. Strenuous physical activity and alcohol consumption were prohibited 24 h before any scheduled testing session, and subjects were asked to abstain from caffeinated beverages 12 h before any testing. A total of 20 subjects initially entered the study. However, in five subjects, placement of the femoral arterial catheter was unsuccessful; in three subjects, nerve recordings were not obtained; and in four subjects, we were unable to maintain nerve recordings during exercise. Only the eight subjects for whom we had nerve recordings at rest and during exercise were used for the analyses.

**Exercise testing.** Subjects were administered a seated incremental exercise test on an arm cycle ergometer (Intellifit, Houston, TX) mounted on a table for the determination of Vo2peak during arm cycling. The arm cycle work rate was set at 20 W for men and 10 W for women and was increased 20 W for men and women, respectively, each minute as the subject maintained an arm cycling rate of 60 rpm. The exercise test was terminated when the subject could no longer maintain a work rate of 60 rpm, despite strong verbal encouragement.

Subjects respired through a mouthpiece attached to a low-resistance turbine volume transducer (model VMM E-2A, Sensor Medics, Anaheim, CA) for measurement of breath volumes while respiratory gases were continuously sampled from the mouthpiece for determinations of fractional concentrations of O2, CO2, and N2 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 OptiPlex GXi) for on-line, breath-by-breath determination of respiratory gases. For each subject, the work rate at which 50% Vo2peak occurred during arm cycling was determined and used as the work rate for 20 min of dynamic arm exercise. The actual experimental protocol was scheduled on a separate day from the incremental exercise test.

**Experimental measurements.** All testing was performed with the subjects in an upright seated position. Cardiovascular variables were monitored beat-to-beat and recorded by a personal computer (PC) equipped with customized software as well as a second PC equipped with an on-line data acquisition program (DL-720, Dataga Instruments, Akron, OH). HR was monitored with a standard lead II electrocardiogram (ECG). The ECG signal was output to a pressure monitor (model 78342A, Hewlett-Packard, Andover, MA) interfaced with the PCs. ABP was measured directly from the femoral artery of the left leg using an 18-gauge (1.35-mm) 12-cm Teflon catheter connected to a pressure transducer (Maxxim Medical, Athens, TX) interfaced with the aforementioned pressure-monitoring system. Before placement of the femoral catheter, lidocaine (1%) was injected subcutaneously to minimize subject discomfort. The catheter was kept patent by a continuous drip of heparinized saline (4 U/ml at 2 ml/h), and before blood pressure measurements were obtained, the transducer was zeroed to the midaxillary line of the subject.

**Sympathetic nerve recordings.** Postganglionic MSNA was recorded with standard microneurographic techniques, as described previously (27, 31). A tungsten microelectrode was inserted into the peroneal nerve near the popliteal fossa of the right leg. The nerve signal was processed by a preamplifier and an amplifier (nerve traffic analyzer model 662C-3, Department of Bioengineering, University of Iowa, Iowa City, IA) with a total gain of 90,000. Amplified signals were band-pass filtered (700–2,000 Hz), rectified, and discriminated. Raw nerve signals were integrated by a resistance-capacitance circuit with a time constant of 0.1 s. Muscle sympathetic nerve recordings were recognized by their pulse-synchronous burst pattern and increased burst frequency with end-expiratory breath holds and Valsalva maneuvers without any responses to arousal or skin stroking. These characteristics were used to discriminate between muscle and skin sympathetic nerve fibers.

**Procedures.** On the experimental day, after being instrumented with ECG leads and a femoral arterial catheter, subjects were seated in a chair positioned in front of the arm cycle ergometer, and proper seat and ergometer adjustments were made. At this point, to verify the work rate (50% Vo2peak during arm cycling) and to identify optimal leg positioning to minimize movement of the right leg, which was to be instrumented for MSNA measurements, breath-by-breath measurements of O2 uptake (Vo2) were collected during 6 min of exercise at the desired work rate. Work rate and leg-positioning adjustments for each subject were made accordingly. After this initial validation exercise bout, the peroneal nerve of the right leg was instrumented for continuous recordings of MSNA. After a nerve recording site was obtained, subjects were fitted with a malleable lead neck collar for the application of NP and NS. CBR responsiveness was then assessed at rest and during steady-state arm exercise at 50% Vo2peak (after ~6 min of exercise).

**CBR responsiveness.** CBR control of MSNA and MAP was assessed by applying random-ordered single 5-s pulses of NP and NS to the anterior two-thirds of the subject’s neck, a technique previously described in detail (22). Briefly, NP and NS ranging from +45 to −80 Torr were applied to simulate a reflex response to +45, +30, +15, 0, −10, −20, −40, −60, and −80 Torr. Under resting conditions, each level of pressure and suction was delivered to the carotid sinus for 5 s during a 10- to 15-s breath hold at end expiration. The breath hold was performed to minimize the respiratory-related modulation of HR and MAP; however, slight but consistent increases in MSNA were noted during the breath hold in some
subjects. Therefore, multiple control trials (ambient pressure
in the collar) were performed, and the average of these trials
was used as the baseline prestimulus MSNA value for each
subject. During exercise, the breath hold was eliminated,
inasmuch as Eckberg et al. (4) reported no differences be-
tween the responses to neck collar stimuli during inspiration
and expiration at a breathing frequency of >24 breaths/min.
In addition, our laboratory previously identified the repea-
tability of applying NP and NS without a breath hold during
high-intensity exercise (16). Four to five perturbations were
performed at each level of NP-NS trials at rest, whereas during
exercise only two to three perturbations were performed. The
reduced time for carotid sinus stimulation during exercise
(~12–14 min) was designed to allow subjects to be at steady
state before CBR testing began and also to minimize any
confounding effects of cardiovascular drift on CBR function
(6). A minimum of 45 and 30 s of recovery was allotted
between NP-NS trials at rest and during exercise, respec-
tively, to allow all physiological variables to return to pre-
stimulus values.

Peak and nadir MAP responses were determined as
the greatest changes in MAP that occurred from the application
of each NP and NS stimulus, respectively, and were averaged
to provide a mean response for each subject. The largest
changes in MAP typically occurred after the NP-NS had been
turned off, which corresponded to ~7 s from the start of
the application of NP and NS (see arterial pressure tracings in
Figs. 2 and 3). This is primarily due to the latency of the
CBR-mediated change in MSNA of ~1.22–1.54 s (8) and the
transduction time of ~5.5 s from the burst of MSNA to a
subsequent change in vascular resistance and alteration in
ABP (30).

The MSNA responses during each 5-s period of NP and
NS were identified according to their appearance and timing
in relation to preceding R waves and calculated as total
activity over the 5-s period, which was computed as the
product of burst frequency and mean burst amplitude and
expressed in arbitrary units. At rest, the MSNA responses
for each level of NP and NS were averaged to provide a
mean response for each subject, which was then expressed
as a percent change from the mean MSNA (Δ%MSNA)
value obtained during the breath hold alone (control tri-
als). During steady-state exercise, the average MSNA
value for each level of NP and NS was compared with a
mean baseline value determined from a segment taken at
the beginning and end of the CBR stimulation period and
presented as a percent change in total activity. Estimated
changes in CSP were calculated as prestimulus MAP minus
neck chamber pressure and used to build CBR stimu-
lus-response curves for MSNA and MAP.

Data analyses. CBR stimulus-response curves for MAP
were fit for each subject to a four-parameter logistic function
described by Kent et al. (11), which uses the following equa-

\[
\text{MAP} = A_1 + e^{[A_2/(\text{ECSP} - A_3)]^{A_4}} + A_4
\]

where \(A_1\) is the MAP response range (maximum – minimum),
\(A_2\) is the gain coefficient, \(A_3\) is the centering point (CP) or
CSP required to elicit equal pressor and depressor responses,
\(A_4\) is the minimum MAP response, and ECSP represents
estimated change in CSP. Individual data were fit to this
model by nonlinear least-squares regression, which mini-
mized the sum-of-squares error to predict a curve of “best fit”
for each data set. The gain of the CBR-MAP stimulus-
response curve was derived from the first derivative of the
logistic function of Kent et al., and the maximal gain (\(G_{\text{max}}\))
was calculated as the gain at the CP (\(A_3\)). In addition, a CBR
threshold (i.e., point where no further increase in MAP oc-
curred, despite reductions in CSP) and saturation (i.e., point
where no further decrease in MAP occurred, despite in-
creases in CSP) were identified. All parameters were aver-
ged and presented as group means. Unfortunately, the
CBR-MSNA responses were unable to be modeled by the
logistic model of Kent et al. because of the large variability
in the individual MSNA responses. This increased variability
prevented the logistics model from selecting a curve of best fit
for each subject and deriving typical baroreflex parameters.
Therefore, to derive an estimate of CBR-MSNA reflex sensi-
tivity at rest and during exercise, a simple linear regression
analysis was used.

Statistical analyses. Comparisons of physiological vari-
ables, CBR-MAP stimulus-response parameters, and CBR-
MSNA reflex sensitivity between rest and exercise were
made utilizing paired \(t\)-tests. An analysis of covariance was
employed to determine significant differences in CBR-
\(\Delta\%\)MSNA values between rest and exercise. In addition, a
\(t\)-test was used to identify significant differences between
the \(V_{\text{O}_2\text{peak}}\) values during arm cycling of the men and
women. Statistical significance was set at \(P < 0.05\). Values are
means ± SE.

RESULTS

\(V_{\text{O}_2\text{peak}}\) during arm cycling. The average \(V_{\text{O}_2\text{peak}}\)
during arm cycling for the group was 29.1 ± 2.5
\(\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}\), with the men demonstrat-
ing significantly higher values than the women (33.7 ± 1.5 vs.
21.3 ± 1.8 \(\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}\)). The steady-state exercise
work rate at 50% \(V_{\text{O}_2\text{peak}}\) during arm cycling was
16.8 ± 1.1 \(\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}\) (equivalent to 44 ± 2 W)
for the men and 11.4 ± 0.8 \(\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}\) (equivalent
to 20 ± 0 W) for the women.

Physiological responses to arm exercise. The MSNA
and cardiopulmonary responses to steady-state dy-
namic arm exercise at 50% \(V_{\text{O}_2\text{peak}}\) are presented in
Table 1. MSNA expressed as total activity or burst
activity at rest and during exercise, a simple linear regression
analysis was used.

<table>
<thead>
<tr>
<th>Table 1. Physiological responses to 50% (V_{\text{O}_2\text{peak}}) arm cycling</th>
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<tr>
<td><strong>MSNA</strong></td>
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<tr>
<td>Total activity, (\dagger) units/min</td>
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<tr>
<td>Burst frequency, bursts/min</td>
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<td>MAP, mmHg</td>
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<tr>
<td>HR, beats/min</td>
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<td>Oxygen uptake, ml/min</td>
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Values are means ± SE. \(V_{\text{O}_2\text{peak}}\) peak \(O_2\) consumption; MSNA, muscle sympathetic nerve activity; MAP, mean arterial pressure; HR, heart rate. *Significantly different from rest (\(P < 0.05\)). \(\dagger n = 5\), different nerve site was used for 3 subjects during exercise.
significantly elevated from rest to steady-state exercise (Table 1).

**CBR control of MSNA.** The stimulus-response relationship for CBR control of MSNA at rest and during arm cycling is presented in Fig. 1. The CBR-Δ%MSNA responses elicited by the application of NP and NS from +45 to −80 Torr were not significantly different between rest and exercise. In addition, estimated baroreflex sensitivity across the range of neck chamber pressures was similar at rest and during exercise (−1.24 ± 0.21 and −1.24 ± 0.18 Δ%MSNA/mmHg, P = 0.74). Sample recordings depicting maintained CBR control of MSNA during exercise are presented in Figs. 2 and 3.

**CBR control of MAP.** The stimulus-response relationship for CBR control of MAP at rest and during steady-state dynamic arm cycling is presented in Fig. 4. The logistic parameters describing the CBR-MAP relationship are shown in Table 2. Carotid sinus threshold and saturation pressures were significantly increased from rest to steady-state exercise. In addition, during exercise the OP and CP were significantly increased from rest, and the OP tended to move away from the CP toward the threshold region of the reflex (CP-OP relationship = 0.01 ± 2.6 at rest and 3.8 ± 1.2 during exercise, P = 0.14). The \( G_{\text{max}} \) of the CBR-MAP stimulus-response relation-

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**Fig. 1.** Reflex responses in muscle sympathetic nerve activity (MSNA) elicited by perturbations to the carotid sinus baroreceptors at rest and during arm cycling at 50% peak \( \dot{V}O_2 \) uptake (\( \dot{V}O_{2\text{peak}} \)). MSNA is calculated as total activity and presented as a percent change from baseline. **A:** changes in MSNA across the full range of neck chamber pressures at rest and during arm cycling at 50% \( \dot{V}O_{2\text{peak}} \). Values are means ± SE. **B:** typical carotid baroreflex stimulus-response curve presented as percent changes in MSNA (Δ% MSNA) plotted against estimated carotid sinus pressure (ECSP) calculated as the prestimulus mean arterial pressure (MAP) minus chamber pressure. Values are means ± SE. No differences in carotid baroreflex-MSNA responses were found between rest and exercise.

**Fig. 2.** MSNA and arterial blood pressure (ABP) responses of 1 subject to application of −80 Torr neck suction at rest (A) and during arm cycling at 50% \( \dot{V}O_{2\text{peak}} \) (B). Data segment includes a representative period of nerve activity during each condition followed by a segment during which neck suction was applied. ChP, neck chamber pressure.

**Fig. 3.** MSNA and ABP responses of 1 subject to application of +30 Torr neck pressure at rest (A) and during arm cycling at 50% \( \dot{V}O_{2\text{peak}} \) (B). Data segment includes a representative period of nerve activity during each condition followed by a segment during which neck pressure was applied.
The major accomplishment of this investigation was that, for the first time, CBR-mediated changes in MSNA have been quantified during steady-state dynamic exercise in humans. More importantly, our findings indicate that CBR control of sympathetic nerve activity was reset to function at the higher arterial pressures induced by dynamic arm exercise without a change in reflex sensitivity. In addition, similar to dynamic leg exercise, the CBR-MAP stimulus-response curve responding range was displaced upward, and the operating range was shifted to the right during the steady-state arm cycling (i.e., parallel resetting).

Effect of exercise on CBR-MSNA responses. The finding that the CBR-Δ%MSNA responses were not significantly different between rest and steady-state exercise indicated that CBR control of MSNA was preserved during dynamic exercise. In contrast, Eckberg and Wallin (5) reported that baroreflex control of MSNA was slightly altered during brief isometric handgrip exercise, with a heightened ability to inhibit MSNA with NS and a diminished capacity to increase MSNA with NP. The reason for differences between results of Eckberg and Wallin and the present investigation is unclear. However, the different types of exercise or the posture of the subjects during experiments may have been responsible. The differences in physiological responses between static and dynamic exercise have been well documented (14). However, CBR responsiveness as determined from CBR-MAP and CBR-HR responses have been reported to be unaltered during static and dynamic exercise in humans (3, 15, 17, 22). These reports suggest that CBR control was not dependent on the type of exercise being performed. Therefore, the more likely explanation for the differences between investigations may be due to the subjects being in a supine position in the study of Eckberg and Wallin and in the seated position in the present investigation. The seated position results in a higher resting baseline MSNA than the supine position, presumably due to cardiopulmonary unloading (28). Thus it is plausible that the greater and smaller MSNA responses to 30 Torr NP and NS, respectively, at rest than with handgrip exercise in the study of Eckberg and Wallin were a consequence of the low baseline MSNA in the resting supine position, whereas in the present investigation the seated position resulted in higher MSNA values at rest, which were more comparable to those obtained during steady-state exercise. Thus, at rest and during exercise, MSNA was adequate to demonstrate notable decreases with the application of NS.

The influence of subject posture on CBR control of MSNA may be further realized by a comparison of the resting CBR-MSNA responses in the present investigation with carotid MSNA responses obtained at rest in a group of subjects in the supine position. Rea and Eckberg (23) reported that sympathetic nerve activity responses to changes in CSP from +40 to −65 Torr were asymmetric, with increases in MSNA during NP being much greater than reductions in MSNA with NS. In contrast, as depicted in Fig. 1, we found more symmetric changes in MSNA with the application of NP and NS. We suggest that these differences were a result of the higher baseline values of MSNA induced by the seated position, which permitted more graded responses to the application of various levels of NS pressures. Whether this was a result of a central interaction between the cardiopulmonary baroreceptors and the CBR or a consequence of higher baseline nerve activity remains unknown.

Even though Eckberg and Wallin (5) reported differences in CBR-MSNA responses during isometric exercise, the differences were minor, and when they were evaluated completely, CBR control of MSNA was maintained. These findings, combined with several human (3, 15, 17, 22) and animal studies (13) that have reported continued baroreflex control of arterial pressure at various intensities of exercise, suggest that the control of blood pressure via the sympathetic nervous system was unaltered during exercise. By utilizing a range of pressure inputs from +45 to −80 Torr, the present investigation has identified the stimulus-re-

### Table 2. Carotid-MAP baroreflex function curve parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rest</th>
<th>Arm Cycling at 50% VO_2peak</th>
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<tr>
<td>Threshold, mmHg</td>
<td>70.3 ± 5.6</td>
<td>97.5 ± 5.4*</td>
</tr>
<tr>
<td>Saturation, mmHg</td>
<td>113.5 ± 6.1</td>
<td>145.7 ± 1.5*</td>
</tr>
<tr>
<td>Operating point, mmHg</td>
<td>91.9 ± 3.1</td>
<td>117.4 ± 3.5*</td>
</tr>
<tr>
<td>Centering point, mmHg</td>
<td>91.9 ± 5.1</td>
<td>121.6 ± 3.3*</td>
</tr>
<tr>
<td>G_max, mmHg/mmHg</td>
<td>−0.62 ± 0.05</td>
<td>−0.65 ± 0.07</td>
</tr>
<tr>
<td>Response range, mmHg</td>
<td>26.0 ± 3.0</td>
<td>29.8 ± 3.1</td>
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<tr>
<td>Minimum MAP response, mmHg</td>
<td>80.1 ± 2.7</td>
<td>99.3 ± 4.8*</td>
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Values are means ± SE. MAP, mean arterial pressure; G_max, maximal gain. Response range equals maximum minus minimum MAP response. *Significantly different from rest (P < 0.05).
spontaneous relationship for CBR control of MSNA during arm cycling. Although we were unable to model the MSNA responses using the logistic model of Kent et al., examination of Fig. 1 indicated that the CBR-MSNA stimulus-response curve was relocated to higher CSP (i.e., to the right) during exercise. However, parallel resetting describes an upward relocation on the response axis as well as a rightward relocation on the operating axis of the CBR stimulus-response curve (22). Even though an upward relocation was not evident in Fig. 1, if absolute values for MSNA total activity were used, the upward relocation would be apparent, inasmuch as MSNA was elevated ~50% during steady-state exercise (Table 1). However, the intersubject variability of total activity among subjects combined with the use of different nerve sites during exercise compared with rest in three subjects warranted the use of Δ%MSNA changes for group comparisons.

Analysis of the CBR-Δ%MSNA stimulus-response curves constructed for each subject indicated that the relocation of the response curve to operate at the higher pressures induced by exercise occurred without a change in reflex sensitivity. These findings are in agreement with previous investigations that have reported a resetting of the CBR-MAP stimulus-response curve without changes in the $G_{\text{max}}$ of the reflex (15, 22). Thus it appeared that, despite marked increases in MSNA and MAP during exercise, CBR control of MSNA was preserved. These data clearly demonstrate the ability of the CBR to control sympathetic nerve activity during exercise, as initially implicated in the classical work of Donald and colleagues (2, 13, 29). Through a series of investigations performed on the anesthetized and conscious dog, these investigators identified the importance of the CBR in the control of vascular resistance during exercise. The present investigation confirms and extends these findings by identifying the preserved ability of the CBR to control sympathetic neural outflow during dynamic exercise in humans.

Effect of exercise on CBR-MAP responses. In addition to the MSNA responses, we also measured CBR-mediated changes in MAP. During steady-state arm exercise, the CBR-MAP OP, CP, and minimal response were significantly increased from rest (Table 2). Furthermore, the CBR-MAP threshold and saturation pressures were elevated by exercise without any change in maximal reflex gain. Collectively, these alterations in the CBR-MAP stimulus-response curve represent the classic rightward and upward resetting of the CBR without changes in reflex sensitivity (Fig. 4). Whereas this resetting of the CBR-MAP curve has been identified during dynamic leg exercise from low to maximal intensity (15, 22), this is the first study to confirm resetting of the CBR during dynamic arm exercise. This is of considerable interest, inasmuch as arm exercise evokes metabolic, thermal, circulatory, and perceptive responses different from those elicited by leg exercise, thereby leading to a greater cardiovascular strain during arm exercise (19, 20). Thus, at a similar percentage of $V_{\text{O}_2,\text{peak}}$, blood pressure, ratings of perceived exertion, and HR were higher during arm than during leg exercise (19). However, despite these differences, the CBR appropriately resets to regulate blood pressure at the prevailing systemic pressure.

Interestingly, a comparison of the CBR-MAP stimulus-response curve from the present investigation with that reported by Norton et al. (15) for a group of subjects performing leg cycling at 50% of maximal $V_{\text{O}_2}$ in the seated position indicates that the CBR-MAP response curve was reset rightward and upward during both forms of exercise performed at the same relative workload. The major difference was that the stimulus-response curve was clearly relocated further upward and rightward during arm exercise. This indicates that the CBR resetting was independent of exercise mode and intensity and occurred in direct relationship to the prevailing exercise pressure.

It has been suggested that central command (a feedforward mechanism that acts through central processes to activate in parallel the cardiovascular and somatomotor responses to exercise) and the exercise pressor reflex (a negative-feedback reflex that originates in the active skeletal muscle and responds to chemical and mechanical stimuli) are involved in CBR resetting during exercise (10, 25). Nevertheless, the extent to which these two neural mechanisms affect resetting of the CBR remains unclear. Both appear to be more active during arm than during leg exercise, as indicated by the greater metabolic strain (exercise pressor reflex) and perceived effort (central command) of small muscle mass exercise (19, 20). However, recent findings that indicate that lactate and hydrogen ions may not contribute to the stimulation of the exercise pressor reflex challenge the role of a greater exercise pressor activation during arm exercise (12). The primary metabolic differences between leg and arm exercise were delayed $O_{\text{2}}$ kinetics and greater recruitment of fast-twitch glycolytic muscle fibers, which lead to elevated concentrations of plasma lactic acid at any given work rate during arm exercise (19). Therefore, it is possible that the metabolic strain may not have potentiated the exercise pressor reflex. However, the consistently higher HR and ratings of perceived exertion at any given steady-state $V_{\text{O}_2}$ during arm exercise compared with leg exercise indicated an elevated central command (19, 20). Inasmuch as our laboratory recently demonstrated that central command actively reset the CBR during dynamic exercise (9), we suggest that an elevated central command was the primary reason for the augmented resetting of the CBR-MAP stimulus-response curve during arm exercise compared with leg exercise.

Gallagher et al. (9) reported a significantly greater upward and rightward shift in the CBR-MAP stimulus-response curve when vencuronium bromide (Norcuron) was used to induce partial neuromuscular blockade and thereby increase central command during dynamic leg cycling at 20% $V_{\text{O}_2,\text{peak}}$. This augmentation in CBR resetting was very similar to the greater resetting noted in the comparison of the CBR-MAP stimulus-response curves during arm cycling at 50%...
resetting of the CBR during arm exercise. Additionally, includes involvement of the exercise pressor reflex in the muscle mass exercise. However, this by no means excludes involvement of the exercise pressor reflex in the resetting of the CBR during arm exercise. Additionally, it is plausible that increases in pulse pressure owing to changes in cardiac output and systemic vascular resistance alter the magnitude of baroreceptor input and passively contribute to the resetting of the CBR.

**Potential limitations.** In the present investigation, we utilized sympathetic measurements from an inactive skeletal muscle bed to describe overall CBR control of sympathetic outflow. This does not preclude the possibility that CBR-mediated changes in sympathetic nerve activity differ among vascular beds; however, it has been suggested that the release of sympathetic nerve activity was uniform throughout the body (26). Therefore, we suggest that the MSNA measurements of the present investigation provided an effective approximation of CBR control of sympathetic neural outflow at rest and during arm exercise. Another potential limitation was our inability to model the CBR-MSNA responses by using the logistic function described by Kent et al. (11) to predict a curve of best fit and determine the typical parameters and derived variables to describe CBR control of MSNA. However, with the use of arbitrary units to quantify MSNA, it is unclear how much information would be obtained from the parameters and variables derived from the curve of best fit. We were able to estimate the responsiveness of CBR control of MSNA by fitting each subject’s data to a simple linear regression model. However, this model does not take into account the typical sigmoidal baroreflex relationship, and therefore, by including points from the plateau regions of the curves in the linear regression analysis, the derived slopes and, thus, CBR responsiveness were likely underestimated. Nevertheless, the conclusion that CBR responsiveness was similar at rest and during exercise appears valid, inasmuch as no significant differences were found between rest and exercise in the MSNA responses elicited at any given neck chamber pressure (Fig. 1). While the findings of the present investigation identify the importance of the CBR in the reflex control of MSNA, the influence of alterations in HR elicited by the NP-NS cannot be overlooked, inasmuch as these changes must also contribute to the CBR regulation of MAP at rest and during exercise (15, 17, 22). Finally, in this closed-loop experiment, immediate changes in HR and systemic blood pressure induced by the application of NP-NS may have influenced the CBR-mediated MSNA response calculated over the 5-s NP-NS period by altering input to extracarotid baroreceptors and possibly the carotid baroreceptors themselves. Therefore, we cannot exclude possible influences of immediate changes in blood pressure induced by NP-NS on the sympathetic responses measured at rest and during exercise in the present investigation. However, any such effects would be similar at rest and during exercise, inasmuch as the alterations in MAP induced by NP-NS were not significantly different between rest and exercise.

In summary, we demonstrated that, across a range of pressures from +45 to −80 Torr, CBR-mediated changes in sympathetic nerve activity were not significantly different between rest and exercise. Moreover, estimated baroreflex sensitivity for the control of MSNA at rest appeared similar to that obtained during steady-state dynamic arm exercise. Thus CBR control of sympathetic outflow was reset to function at the higher arterial pressures induced by dynamic exercise. In addition, the CBR-MAP stimulus-response curve was shifted upward and to the right during steady-state arm cycling, which appears to be augmented compared with steady-state leg exercise performed at the same relative workload. We speculate that this augmentation results from a greater activation of central command during exercise performed with a small muscle mass. We conclude that CBR control of sympathetic nerve activity and MAP was maintained during moderate-intensity dynamic exercise.

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