Carotid baroreflex function during prolonged exercise

Department of Integrative Physiology and Cardiovascular Research Institute, University of North Texas Health Science Center, Fort Worth, Texas 76107-2609

Carotid baroreflex function during prolonged exercise. J. Appl. Physiol. 87(1): 339–347, 1999.—The present investigation was designed to uncouple the hemodynamic physiological effects of thermoregulation from the effects of a progressively increasing central command activation during prolonged exercise. Subjects performed two 1-h bouts of leg cycling exercise with 1) no intervention and 2) continuous infusion of a dextran solution to maintain central venous pressure constant at the 10-min pressure. Volume infusion resulted in a significant reduction in the decrement in mean arterial pressure seen in the control exercise bout (6.7 ± 1.8 vs. 11.6 ± 1.3 mmHg, respectively). However, indexes of central command such as heart rate and ratings of perceived exertion rose to a similar extent during both exercise conditions. In addition, the carotid-cardiac baroreflex stimulus-response relationship, as measured by using the neck pressure-neck suction technique, was reset from rest to 10 min of exercise and was further reset from 10 to 50 min of exercise in both exercise conditions, with the operating point being shifted toward the reflex threshold. We conclude that the progressive resetting of the carotid baroreflex and the shift of the reflex operating point render the carotid-cardiac reflex ineffectual in counteracting the continued decrement in mean arterial pressure that occurs during the prolonged exercise.

Although the hemodynamic responses associated with prolonged exercise have been documented, the mechanisms involved in blood pressure regulation during prolonged exercise have not been fully elucidated. After the initial response to the onset of dynamic exercise, prolonged exercise at a constant workload is characterized by the redistribution of blood volume to the cutaneous circulation in response to thermoregulatory demands (4, 17) resulting in a progressive decrease in central blood volume (CBV), central venous pressure (CVP), and total peripheral resistance (TPR). This redistribution consequently results in a progressive decrease in stroke volume (SV) and mean arterial pressure (MAP) and a concomitant increase in heart rate (HR), a phenomenon which has been termed cardiovascular drift. The increase in HR also occurs progressively, presumably as a compensatory response to the decrease in central filling volume and SV, and results in the maintenance of cardiac output (Qc). However, despite the use of whole body surface cooling or saline infusion during prolonged exercise to return CBV to precardiovascular drift values, HR continues to increase, and a slight downward drift in MAP remains (11, 18). These data raise the question as to whether there is a loss of baroreflex regulation of arterial blood pressure during prolonged dynamic exercise.

Potts et al. (16) have previously demonstrated that at the onset of 25% maximal oxygen uptake (VO2max) and 50% VO2max exercise, the carotid baroreflex (CBR) was classically reset in direct relation to the intensity of exercise and that the operating point (i.e., prestimulus MAP) was relocated toward the threshold of the reflex. Recently, we have demonstrated that the CBR continued to be reset upward in relation to exercise intensity from 50 to 100% VO2max (10) and furthermore that the relocation of the operating point continued toward threshold in direct relation to the increasing exercise intensity. It has been proposed that the mechanism of resetting of the CBR at the onset of dynamic exercise is a result of the activation of the feed-forward mechanism or “central command” (16, 19). We submit 1) that with prolongation of exercise at a constant workload, further increases in central command with progressive motor fiber recruitment (5, 9) will be reflected by increases in HR and ratings of perceived exertion (RPE) and will result in a continual upward resetting of the CBR. In addition, we propose 2) that with exercise at a greater intensity than the 50% VO2max used by Potts et al. (16), the operating point would be further shifted toward or below the threshold pressure of the baroreflex. Therefore we hypothesize that, as prolonged steady-state exercise continues and cardiovascular drift becomes manifest, MAP would fall below the operating range of the progressively reset CBR, which would then become ineffectual in correcting the downward drift in MAP. Hence the objective of the present investigation was to demonstrate that the apparent loss of arterial blood pressure regulation seen during prolonged, constant-load dynamic exercise can be attributed to a progressive resetting of the CBR in relation to increases in central command. Furthermore, we suggest that the resetting is independent of the CBV displacement that occurs in response to the thermoregulatory stress incurred during prolonged moderate- to high-intensity dynamic exercise.

METHODS AND PROCEDURES

To uncouple the effects of increases in central command from the global hemodynamic responses to prolonged exercise, volunteer subjects performed 1 h of dynamic leg cycling exercise at 65% VO2max with 1) no intervention and 2) maintenance of cardiac filling volume via the continuous infusion of a solution of 6% dextran in saline. At 10 and 50 min of exercise, CBR stimulus-response curves were generated by using a variable-pressure neck collar, as previously demonstrated in our laboratory (16). We anticipated that maintenance of cardiac filling volume would oppose the compensatory component of the increase in HR (compensating for the fall in SV) during the exercise bout; however, the central-command-related increases in HR would remain. In addition, although the infusion of dextran in saline counter-
acts the fall in SV by maintaining central filling volume, the decrease in TPR due to cutaneous vasodilation during the exercise would remain. Therefore we anticipated that some degree of diminution of MAP would occur and would proceed uncorrected due to the relocation of the operating arterial pressure in relation to the progressively reset CBR.

**Subjects**

Eight healthy subjects (aged 27.9 ± 1.6 yr) gave written informed consent for participation in this investigation, which was approved by the Institutional Review Board of the University of North Texas Health Science Center at Fort Worth. All subjects were free of known cardiovascular and pulmonary disorders and were not taking any prescribed medications. Subject data are summarized in Table 1.

**Protocol**

At least 2 days before participating in the experimental protocol, each subject performed a graded exercise test for the determination of VO\(_{2}\max\) during semirecumbent leg cycling exercise. On the experimental day, each subject performed two 1-h bouts of constant-load dynamic leg cycling exercise at ~65% VO\(_{2}\max\) in the semirecumbent position. The exercise consisted either of constant-load leg cycling exercise with no intervention or of constant-load leg cycling with continuous intravenous infusion of a solution of 6% dextran in saline. The infusion rate of the dextan solution was varied so that CVP did not fall below the pressure value recorded at 10 min of exercise. The exercise bouts were performed in an environment at 24°C with 40–60% relative humidity and were separated by a rest period of sufficient length (at least 3 h) to return HR and MAP to approximate baseline values. CBR stimulus-response curves were constructed at rest, after attainment of steady-state exercise (after ~10 min of constant-load exercise), and during the last 10–12 min of each experimental exercise bout, by using a modification of the neck pressure-neck suction (NP-NS) protocol previously developed by Potts et al. (16). For the experimental bouts with infusion of dextran in saline, the infusions were begun after the first exercise NP-NS protocol (i.e., at 20 min of exercise) and were maintained throughout the exercise bout at an infusion rate that would maintain CVP at the level no lower than that attained immediately before the execution of the first exercise NP-NS protocol. During each exercise bout, HR, O\(_2\) uptake (VO\(_2\)), MAP, and CVP were continuously monitored and recorded. In addition, at 10-min intervals, temperature at the auditory canal, Qc, and RPE were assessed. Venous blood samples were also drawn periodically for the measurement of venous hemoglobin, hematocrit, O\(_2\) content, O\(_2\) saturation, and concentrations of lactate and catecholamines (norepinephrine and epinephrine). The concentration of atrial natriuretic peptide (ANP) was also assessed in the blood samples to discern the effects of the infusion of the dextan solution on the cardiac stretch receptors.

**Measurements**

Maximal exercise stress test and VO\(_2\) measures. Subjects who were determined to be acceptable means of physical examination performed a graded exercise test for the determination of VO\(_{2}\max\). The subjects exercised in the 70° semirecumbent back-supported posture at progressively increasing workloads on a constant-load cycle ergometer until they reached volitional fatigue. During the test, measurements included the rate of VO\(_2\) (using breath-by-breath open-circuit spirometry) and continuous electrocardiogram monitoring (using a 12-lead monitoring system). Subjects returned to the laboratory no less than 2 days after maximal exercise testing for the performance of the experimental exercise bouts.

**Cardiovascular variables.** HR and VO\(_2\) were continuously monitored via electrocardiogram and a customized breath-by-breath mouthpiece apparatus, respectively. Qc was measured at 10-min intervals by using the acetylene rebreathing method (21), with SV being calculated from the division of Qc by HR. Arterial blood pressure and CVP were measured directly via catheters inserted by a consulting physician into the radial artery and brachial vein, respectively, of each subject. Placement of the dual lumen CVP catheter at the fourth intercostal space was confirmed with the use of fluoroscopy. Both pressures were monitored by using disposable pressure transducers (Cobe) interfaced with pressure monitors (Hewlett-Packard 78342A). The pressure transducers were calibrated and established at zero reference pressure at the midaxillary and third intercostal space before and after the experiment, and catheters were appropriately connected to a pressurized saline bag for saline flush. Mean, systolic, and diastolic blood pressure, along with CVP and HR, were recorded beat-by-beat on-line by using a personal computer (Gateway 2000, sampling rate 100/s) and customized software. VO\(_2\) was similarly recorded breath-by-breath by using a personal computer (Dell Optiplex Gxi, sampling rate 250/s) and customized software. In addition, at 10-min intervals, venous blood samples were taken from the second port of the dual lumen CVP catheter and RPE (Borg scale) were supplied by the subject (1). At the same time periods, body temperature was measured by using a Thermoscan Instant Thermometer, which utilizes a sealed auditory canal position to measure the infrared heat radiation from the tympanic membrane and provides a calculated temperature reading that is adjusted to an oral measurement.

Venous blood samples. Venous blood samples were drawn from the second port of the dual lumen CVP catheter at rest, at 10, 20, 50, and 60 min of exercise and after 10 min of recovery from the exercise. These samples were subjected to hematocrit analysis (microcentrifuge), and the hemoglobin concentration (g/dl), O\(_2\) saturation (%), and O\(_2\) content (ml/dl) of each sample were measured and recorded (IL 282 CO-Oximeter). Also, the concentration of lactate in each venous blood sample was recorded (YSI 2300 Stat). In addition, the catecholamines, epinephrine and norepinephrine, were separated in each of these samples via isocratic high-pressure liquid chromatography, and the plasma concentrations (pmol/ml) of epinephrine and norepinephrine were quantified electrochemically at 650 mV. Finally, the plasma concentration (pmol/ml) of ANP was measured using a radioimmunoassay kit (Peninsula Laboratories).

CBR. CBR function during exercise was analyzed via a slight modification of the NP-NS method previously reported by Potts et al. (16), in which brief (5-s) pressure and suction stimuli are applied to the carotid sinus region of the subject’s neck and the peak HR and MAP responses to the individual stimuli are recorded. To accommodate the high workloads used in the present experiments, the modifications were designed to enable the subjects to breathe freely during the 5-s carotid sinus stimuli, in contrast to the end-expiratory breath hold maneuver previously used at rest and during

**Table 1. Subject information**

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>VO(_{2}\max), ml·min(^{-1})·kg(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.9 ± 1.6</td>
<td>177.8 ± 1.7</td>
<td>75.1 ± 2.2</td>
<td>48.3 ± 3.6</td>
</tr>
</tbody>
</table>

Values are means ± SE. VO\(_{2}\max\), maximal O\(_2\) uptake during leg cycling.
lighter exercise workloads (16). On the basis of data from Eckberg et al. (3), who demonstrated that, at a breathing frequency of 24 breaths/min, no difference existed between the responses to neck collar stimuli during inspiration and expiration, we predicted that, by choosing the peak HR and MAP response to each stimulus, CBR stimulus-response curves could be modeled, with appropriate repeatability, at high exercise workloads. In addition, the time required to construct a stimulus-response curve during exercise was reduced to a maximum of 10–12 min to minimize the confounding effects of cardiovascular drift on CBR function. Before the present investigation was conducted, the repeatability of the modified NP-NS technique was established. The HR responses (carotid-cardiac baroreflex) to several levels of carotid sinus stimulation were recorded after 10 min of dynamic leg cycling exercise at 68% \( V_{\text{O2max}} \) in one subject during four separate bouts of exercise. The gain, threshold, and saturation values for each of the four individual CBR stimulus-response curves, as well as the means, SE, coefficients of variation, and 95% confidence intervals of these values are listed in Table 2.

In the present investigation, the resulting parameters of threshold, saturation, and maximal gain values obtained from the logistic model (8) of each CBR stimulus-response curve were compared by using two-way ANOVA with repeated measures across exercise condition. Student-Newman-Keuls post hoc pairwise comparisons were used to further analyze group mean differences. Statistical significance was accepted at a \( P \) value of <0.05.

**RESULTS**

Cardiovascular variables. The maintenance of a consistent thermal stress between the two exercise conditions was of primary importance to our investigation. Accordingly, the increases in body temperature during the hour of exercise (−2°C) were not significantly different between the two exercise conditions at any time of measurement. The alterations in several cardiovascular variables recorded during the exercise bouts are reported below as percent change from the measurement taken at 10 min of exercise. The absolute measurement values for each of these variables recorded at 10 min of exercise are listed in Table 3.

In the control condition, 1 h of exercise resulted in a significant (52.7 ± 9.8%) fall in CVP between 10 and 60 min of exercise. In addition, SV, TPR, and MAP declined significantly with exercise time (15.2 ± 2.2, 11.59 ± 1.3, and 13.4 ± 1.7%, respectively; see Fig. 1). Figure 1 also illustrates that HR rose significantly (12.5 ± 2%) throughout the exercise protocol, and, as a result, \( Q_C \) was maintained over this period, i.e., no significant differences were found in \( Q_C \) from 10 to 60 min of exercise. There were no significant differences in

**Table 2. Derived variables for the carotid-cardiac stimulus-response relationships**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Gain, beats·min(^{-1})·mmHg(^{-1})</th>
<th>Threshold, mmHg</th>
<th>Saturation, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>−0.146</td>
<td>99.5</td>
<td>165.7</td>
</tr>
<tr>
<td>2</td>
<td>−0.142</td>
<td>84.6</td>
<td>162.6</td>
</tr>
<tr>
<td>3</td>
<td>−0.143</td>
<td>87.8</td>
<td>166.8</td>
</tr>
<tr>
<td>4</td>
<td>−0.147</td>
<td>96.6</td>
<td>160.7</td>
</tr>
<tr>
<td>Mean</td>
<td>−0.145 ± 0.038</td>
<td>92.4 ± 4.3</td>
<td>163.9 ± 2.7</td>
</tr>
<tr>
<td>CV, %</td>
<td>2.63</td>
<td>4.65</td>
<td>1.70</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.0038</td>
<td>6.87</td>
<td>4.43</td>
</tr>
</tbody>
</table>

Mean, mean ± SE; CV, coefficient of variation ([SE/mean] × 100); 95% CI, 95% confidence interval.

**Table 3. Absolute measurements of cardiovascular variables at 10 min of exercise**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>141.2 ± 2.4</td>
<td>145.5 ± 2.6</td>
</tr>
<tr>
<td>Central venous pressure, mmHg</td>
<td>3.1 ± 0.7</td>
<td>3.8 ± 0.6</td>
</tr>
<tr>
<td>Total peripheral resistance, mmHg·l(^{-1})·min(^{-1})</td>
<td>5.4 ± 0.9</td>
<td>5.9 ± 0.3</td>
</tr>
<tr>
<td>Stroke volume, ml/beat</td>
<td>128.5 ± 7.6</td>
<td>121.7 ± 8.4</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>106.5 ± 4.5</td>
<td>103.6 ± 2.1</td>
</tr>
<tr>
<td>Cardiac output, liters</td>
<td>181 ± 11</td>
<td>176 ± 11</td>
</tr>
<tr>
<td>Arteriovenous oxygen difference, ml/l</td>
<td>120 ± 8</td>
<td>120 ± 9</td>
</tr>
</tbody>
</table>

Values are means ± SE.

The maintenance of a consistent thermal stress between the two exercise conditions was of primary importance to our investigation. Accordingly, the increases in body temperature during the hour of exercise (−2°C) were not significantly different between the two exercise conditions at any time of measurement. The alterations in several cardiovascular variables recorded during the exercise bouts are reported below as percent change from the measurement taken at 10 min of exercise. The absolute measurement values for each of these variables recorded at 10 min of exercise are listed in Table 3.

In the control condition, 1 h of exercise resulted in a significant (52.7 ± 9.8%) fall in CVP between 10 and 60 min of exercise. In addition, SV, TPR, and MAP declined significantly with exercise time (15.2 ± 2.2, 11.59 ± 1.3, and 13.4 ± 1.7%, respectively; see Fig. 1). Figure 1 also illustrates that HR rose significantly (12.5 ± 2%) throughout the exercise protocol, and, as a result, \( Q_C \) was maintained over this period, i.e., no significant differences were found in \( Q_C \) from 10 to 60 min of exercise. There were no significant differences in
CVP at rest or during the first 20 min of exercise between the two exercise bouts. However, when infusion of a dextran solution was begun at 20 min of exercise and maintained throughout the exercise period (mean infusion volume, 419 ± 45 ml), CVP rose continuously (50.4 ± 10.3% during the 40 min of infusion), such that CVP was significantly greater at 40, 50, and 60 min of exercise with volume infusion than at the same periods of control exercise. Volume infusion resulted in the maintenance of SV during the exercise bout, i.e., no significant differences were found in SV from 10 to 60 min of exercise. However, TPR continued to fall to a statistically similar extent as during the control condition (Fig. 1). As a result, a significant decrement was seen in MAP with exercise time. However, by minute 50, this decrement was significantly less than in the control condition (total MAP decrease of 6.7 ± 1.8%) (Fig. 1). In addition, HR rose to the same extent as in the control condition as a function of exercise time (12.3 ± 2.0%) and Qc also increased significantly over the hour of exercise (9.4 ± 2.2%) due to the maintenance of SV, see Fig. 1. Figure 1 also illustrates a significant increase in the arteriovenous O2 difference (a-vO2) from 10 to 60 min of the control exercise bout (12.1 ± 2.7%) which was absent during exercise with volume infusion. The disparity between the (a-vO2) of the control vs. the infusion-exercise bouts, which was statistically significant at 60 min of exercise, was presumed to be due to the effect of the increase in flow (Qc) on O2 extraction. However, despite a significant difference in O2-carrying capacity at 60 min (control: 20.41 ± 0.96 vs. infusion: 18.54 ± 0.92 ml/dl, P = 0.012), the resultant difference in percent O2 extraction was not significant (0.96 ± 0.052 vs. 0.92 ± 0.069%, P = 0.65).

Indexes of Central Command

The indexes of central command measured in the current investigation were statistically similar between the two exercise bouts, as clearly illustrated in Fig. 2. HR rose 12.5 ± 2.2% in the control condition and 12.3 ± 2.0% in the volume-infusion experiment. RPEs also rose significantly with exercise time in the control and volume-infusion bouts (34.9 ± 4.4 and 32 ± 4.7%, respectively).

\[ \dot{V}O_2 \]

In addition, \( \dot{V}O_2 \) was observed to drift upward similarly during both exercise bouts. Percent change in this measurement was calculated from 20 min rather than from 10 min due to an increase in \( \dot{V}O_2 \) at the 10-min value, presumably due to anticipation of the impending NP-NS protocol, which was administered between 10 and 20 min of exercise (Fig. 2).

Blood Measurements

Venous blood samples were drawn during the resting period before each exercise bout; at 10, 20, 50, and 60 min of exercise; and after 10 min of recovery from the exercise. The infusion of an average of 419 ± 45 ml of dextran solution significantly reduced the measured hematocrit at 50 and 60 min of exercise, as well as during recovery, compared with the control condition. Accordingly, hemoglobin content (g/dl) was also significantly less in these blood samples. The infusion did not significantly affect the O2 saturation nor the O2 content of the venous blood, although a nonsignificant trend existed for an increased venous O2 saturation during exercise with volume infusion. This trend corresponded to a nonsignificant trend for a decreased (a-vO2) during volume infusion, as Qc was higher during this condition compared with control. In addition, the plasma concentrations of epinephrine and norepinephrine were similar during the two exercise conditions, as was the concentration of ANP; this indicates that the cardiac stretch receptors were not affected by this degree of volume infusion. Figure 3 illustrates the measurements of hematocrit, hemoglobin, epinephrine, norepinephrine, and lactate in the venous blood samples.

Finally, measures of lactic acid (in mmol/l) indicated that the concentration of this metabolite was significantly higher at 10 and 20 min of control exercise compared with the exercise with volume infusion (Fig. 3). As infusion of the dextran in saline solution had not begun at this time, we submit that this discrepancy may be an effect of order because the volume infusion exercise bouts were consistently performed after several hours of recovery from the control exercise bouts. This order was necessary to prevent the confounding effects of increased blood volume on the hemodynamic responses to exercise in the control condition because the experiment was designed to be undertaken in one experimental day to minimize the invasive procedures experienced by the volunteer subjects.
Carotid-Cardiac Baroreflex

Modeling of the carotid-cardiac baroreflex stimulus-response relationship demonstrated that the reflex was significantly shifted rightward on the carotid sinus pressure axis from rest to 10 min of exercise and also from 10 to 50 min of exercise in both exercise conditions. Figure 4, A-C, illustrates each shift in the carotid-cardiac baroreflex threshold, centering point, and saturation. Figure 4D shows that no reflex shift was accompanied by a significant decrement in reflex gain, and Fig. 4E shows the operating point pressure at rest and at 10 and 50 min of exercise. The operating point of the carotid-cardiac baroreflex was significantly relocated from rest, at which time there was no significant difference between the operating point and centering point pressures, to 10 min of exercise and further from 10 to 50 min of exercise. These shifts occurred away from the reflex centering point and toward the threshold of the reflex such that there was no significant difference between the operating point and threshold pressures at 50 min of exercise (Fig. 4F).

Carotid-Vasomotor Baroreflex

We were unable to obtain threshold, saturation, and gain values for the individual carotid-vasomotor stimulus-response relationships elicited by the NP-NS protocol due to the inability to attain convergence in the modeling procedure. However, Fig. 5 illustrates the mean responses of the eight subjects to each level of carotid sinus perturbation at rest as well as at 10 and 50 min of exercise in both exercise conditions. The mean stimulus-response relationships constructed at rest for both conditions followed the usual sigmoidal shape. Therefore, the model of Kent et al. (8) was used to calculate threshold, saturation, and gain values for these curves. These values were similar during rest before the two exercise bouts [81.7, 120.9, and -0.30, respectively, in the control condition, and 72.1, 109.1, and -0.33, respectively, in the volume-infusion condition (the resting measurement was before infusion)]. However, we were unable to adequately model the mean or individual responses at 10 and 50 min of exercise to the logistic equation of Kent et al. (8). Interestingly, the shape of those carotid-vasomotor curves no longer fit the typical sigmoidal shape but appeared to become progressively steeper on the left-hand, or pressure stimulus, portion of the curve and in the volume-infusion condition flatter on the right-hand, or suction stimulus, portion of the curve. To quantify this observation, the individual curves were divided into left- and right-hand portions, constituting the three lowest and four highest carotid sinus pressures, respectively. Table 4 describes the slope of the entire carotid-vasomotor baroreflex stimulus-response relationship for each condition at 10 and 50 min of exercise. In addition, Table 4 describes the slope for the left- and right-hand portions of the curves individually.

DISCUSSION

Prolonged Exercise and Cardiovascular Drift

In the present investigation, 1 h of leg cycling exercise at 65% VO_{2\text{max}} elicited the cardiovascular and hemodynamic responses that have been previously documented for prolonged moderate- to high-intensity dynamic exercise (4, 20) (Fig. 1). The progressive decrease in MAP seen during prolonged exercise, after the initial increase at exercise onset, has been attributed to a redistribution of circulating blood volume to the cutaneous circulation in response to thermoregulatory demands (18). Accordingly, our data illustrate that CVP decreased significantly from 10 to 60 min of...
exercise, presumably due to a greater percentage of $Q_c$ being distributed to the cutaneous circulation. This fall in CBV resulted in a decreased cardiac filling volume, which was reflected by a concomitant reduction in SV and a compensatory increase in HR. When CVP, and thus SV, were maintained via a continuous infusion of a solution of 6% dextran in saline during the prolonged exercise protocol, a progressive decrement in MAP remained (6.71 ± 1.83%), albeit to a lesser degree than in the control condition, presumably due to the fall in TPR (11.59 ± 1.30%), corresponding to cutaneous vasodilation. As previously reported (11), no significant difference existed in the rise in HR between the two exercise conditions. $Q_c$ was relatively constant throughout the control exercise condition; however, due to the maintenance of CBV and SV, $Q_c$ increased appreciably during the volume-infusion condition (9.4 ± 2.2%) in relation to the increase in HR (Fig. 1). The fact that TPR and MAP continued to decrease throughout the exercise with infusion, despite a maintained or increased CBV, SV, and $Q_c$, taken in conjunction with the data of previous investigations (6, 11, 18), indicates that thermoregulatory blood-volume redistribution was an important component of the cardiovascular drift. However, these data also raise the question as to whether baroreflex control of blood pressure was diminished or fatigued during the prolonged exercise, particularly in the light of a maintained increase in HR despite the countermeasures used in the present and previous investigations (6, 11).

Carotid Arterial Baroreflex

In the present investigation, the construction of carotid-cardiac baroreflex stimulus-response curves during the control exercise bouts indicated that the baroreflex was indeed classically reset from the resting condition to the onset of the exercise, as well as being further reset by the prolongation of the bout to 1 h (Fig. 4). The shifts seen in the carotid-cardiac baroreflex reflex due to prolongation of exercise time were similar to those seen by Potts et al. (16), Papelier et al. (13), and Norton.
et al. (10) in response to increases in exercise intensity. In addition, the modeling of the baroreflex stimulus-response curves illustrated that prolongation of exercise, much like increases in exercise intensity (10, 16), results in a relocation of the reflex operating point (i.e., prestimulus MAP) toward threshold and away from the centering point of the reflex. The rightward shift of the carotid-cardiac baroreflex threshold and saturation values were in direct relation to the increases seen in the indexes of central command (i.e., HR, RPE). In fact, the increase in HR and the rightward shift in reflex threshold both approximated a change of 12.5% from 10 to 60 min of exercise under the control condition. In the dextran-infusion experiments, in which CVP was maintained and even increased during the hour of exercise, the threshold and saturation pressures of the carotid-cardiac baroreflex relationships were similarly reset (Fig. 4). Again, the data indicate that there was no significant difference in reflex gain during this protocol. Importantly, the maintenance of CVP, and thus SV, had no significant effect on the upward drift in HR during the exercise bout. In addition, RPE drifted upward to an equal extent as during the control condition. Taken together, these data indicate that central command activation was similar in the two exercise conditions. Accordingly, the rightward shifts in the reflex threshold and saturation values were also directly related to the rise in HR, RPE, and also VO2 during the infusion experiments. In evidence, HR and the reflex threshold increased ~12.3 and 12.5%, respectively, during the hour of exercise with volume infusion.

The individual carotid-vasomotor baroreflex stimulus-response relationships could not be modeled in this investigation; however, the data summarized in Fig. 5 show that the reflex appears to be reset rightward and upward, similar to the carotid-cardiac baroreflex. In addition, although the stimulus-response curves generated at rest during both conditions conformed to the typical sigmoid shape, the curves at 10 and 50 min of exercise appeared to become progressively steeper in response to positive pressure stimuli and in the volume-infusion condition flatter in response to negative (suction) stimuli (Table 4). A similar alteration in the carotid-vasomotor baroreflex (and not the carotid-cardiac baroreflex) was found by Papelier et al. (14) during postexercise leg muscle ischemia induced by thigh cuff inflation and was attributed by the authors to an activation of the muscle chemoreflex. This reflex is thought to have a modulatory effect, predominantly on the efferent, or response arm of the vasomotor component of the CBR, via the activation of the sympathetic nervous system (12, 14, 19). The change in shape of the carotid-vasomotor baroreflex curves in the present investigation may also be attributable to chemoreflex activation. Conceivably, the steeper slope of the lefthand portion of the curve, that indicates an increased gain of response to hypotensive stimuli, may be an effort to increase blood pressure and alleviate a chemical error signal in the exercising muscles. However, the increased gain of the left side of the relationship did not result in a correction of the downward drift in MAP seen in the present investigation. Therefore, we must speculate that the assumed activation of the muscle reflex was not sufficient to counteract the effect of the

### Table 4. Slopes of carotid-vasomotor stimulus-response relationships at 10 and 50 min of exercise

<table>
<thead>
<tr>
<th>Portion</th>
<th>10 min</th>
<th>50 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire</td>
<td>-0.16 ± 0.03</td>
<td>-0.15 ± 0.05</td>
</tr>
<tr>
<td>Left</td>
<td>-0.16 ± 0.04</td>
<td>-0.30 ± 0.03*</td>
</tr>
<tr>
<td>Right</td>
<td>-0.03 ± 0.003</td>
<td>-0.09 ± 0.003*</td>
</tr>
<tr>
<td>Infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire</td>
<td>-0.15 ± 0.004</td>
<td>-0.19 ± 0.006*</td>
</tr>
<tr>
<td>Left</td>
<td>-0.21 ± 0.006</td>
<td>-0.29 ± 0.006*</td>
</tr>
<tr>
<td>Right</td>
<td>-0.075 ± 0.002</td>
<td>-0.038 ± 0.002*</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significant difference between values at 10 and 50 min; P < 0.05.
rightward resetting of the stimulus-response relationship that may occur in response to a progressively increasing central command. This change in shape was the primary cause of the inability to model the carotid-vasomotor baroreflex relationship by using the logistic equation developed by Kent et al. (8). However, movement artifacts that primarily affect the directly measured arterial pressure may have compounded the within-subject variability of the blood pressure measurement.

In the present investigation, the carotid-cardiac baroreflex was progressively reset rightward and upward during the prolonged exercise bout. In addition, the operating point of the carotid-cardiac baroreflex was relocated away from the centering point and toward the threshold of the baroreflex in direct relation to exercise time and, thus, central command activation. Therefore, we propose that, as the thermoregulatory stress associated with prolonged steady-state exercise developed in the control condition and cardiovascular drift became manifest, MAP fell below the operating range of the reset CBR, rendering it ineffectual in correcting the downward drift in MAP. The same resetting occurred in the volume-infusion exercise bouts, presumably resulting in the same scenario of drift in MAP, albeit to a lesser degree than in the control condition because of the maintenance of CVP and SV.

The resetting of the carotid-cardiac baroreflex during the prolonged exercise was shown to occur in direct relation to increases in the indexes of central command and VO$_2$ due to the need for progressive motor fiber recruitment (7, 20). These data, along with those of other investigations such as Potts et al. (16), Norton et al. (10), and DiCarlo and Bishop (2), support the role of central command in CBR resetting during dynamic exercise. Also, the increasing VO$_2$ in relation to motor fiber recruitment may play a role in the resetting via an increased muscle afferent input to the cardiovascular center (15, 19). In addition, the alterations in the shape of the carotid-vasomotor baroreflex support an additional role for the exercise pressor reflex in modulating baroreflex control of blood pressure under certain exercise conditions (14) and may reflect the occlusive interaction between the exercise pressor reflex and the carotid-vasomotor reflex recently identified by Potts et al. (15).

In summary, the present investigation was successful in uncoupling the global hemodynamic responses to the thermal stress associated with prolonged exercise from the effects of baroreflex resetting. This resetting results in an increased range of response of the carotid-cardiac reflex to hypertension. However, it renders the reflex ineffectual in counteracting a fall in arterial pressure, such as occurs during prolonged exercise with the manifestation of cardiovascular drift.

This study was supported in part by the Life Sciences Division of the National Aeronautics and Space Administration (NASA) of the United States of America under NASA Grant No. NCT-70409, NASA Specialized Center of Research and Training Grant NAGW-3582, NASA Grant NAG 5-4668, and the American College of Sports Medicine-NASA Space Physiology Student Research Award.

This work was part of K. H. Norton’s dissertation as submitted to the University of North Texas Health Science Center for the fulfillment of the requirements for the degree of Doctor of Philosophy.

Address for reprint requests and other correspondence: P. B. Raven, University of North Texas Health Science Center, Department of Integrative Physiology, 3500 Camp Bowie Blvd., Fort Worth, TX 76107-2699.

REFERENCES


