Resetting of the carotid arterial baroreflex during dynamic exercise in humans

K. H. Norton, R. Boushel, S. Strange, B. Saltin, and P. B. Raven

Department of Integrative Physiology and Cardiovascular Research Institute, University of North Texas Health Science Center, Fort Worth, Texas 76107-2609; and Copenhagen Muscle Research Center, Rigshospitalet, DK-2200 Copenhagen, Denmark

Norton, K. H., R. Boushel, S. Strange, B. Saltin, and P. B. Raven. Resetting of the carotid arterial baroreflex during dynamic exercise in humans. J. Appl. Physiol. 87(1): 332–338, 1999.—Recent investigations have demonstrated that at the onset of low-to-moderate-intensity leg cycling exercise (L) the carotid baroreflex (CBR) was classically reset in direct relation to the intensity of exercise. On the basis of these data, we proposed that the CBR would also be classically reset at the onset of moderate- to maximal-intensity L exercise. Therefore, CBR stimulus-response relationships were compared in seven male volunteers by using the neck pressure-neck suction technique during dynamic exercise that ranged in intensity from 50 to 100% of maximal oxygen uptake (VO2max). L exercise alone was performed at 50 and 75% VO2max, and L exercise combined with arm (A) exercise (L + A) was performed at 75 and 100% VO2max. O2 consumption and heart rate (HR) increased in direct relation with the increases in exercise intensity. The threshold and saturation pressures of the carotid-cardiac reflex at 100% VO2max were >75% VO2max, which were in turn >50% VO2max (P < 0.05), without a change in the maximal reflex gain (Gmax). In addition, the HR response value at threshold and saturation at 75% VO2max was >50% VO2max (P < 0.05) and 100% VO2max was >75% VO2max (P < 0.07). Similar changes were observed for the carotid-vasomotor reflex. In addition, as exercise intensity increased, the operating point (the prestimulus blood pressure) of the CBR was significantly relocated further from the centering point of the stimulus-response curve and was at threshold during 100% VO2max. These findings identify the continuous classic rightward and upward resetting of the CBR, without a change in Gmax during increases in dynamic exercise intensity to maximal effort.

Potential causal mechanisms for the resetting of the CBR include the feed-forward, centrally originated signals that activate in parallel the cardiovascular and somatomotor responses to exercise, i.e., central command, (4, 5, 9, 19) and the feedback reflexes which originate in the active skeletal musculature due to chemical and mechanical error signals, i.e., the exercise-pressor reflex (9, 19). It has been proposed that the immediate resetting of the CBR at the onset of dynamic exercise is primarily the result of the activation of central command (17, 19), a phenomenon that is directly related to the intensity of exercise or, more specifically, the activation of an appropriate number of motor fibers to execute the exercise (4, 5, 20). Central command has been proposed to interact with the CBR at the level of the neuron pool that receives the baroreflex afferents, thus producing a lateral shift in the CBR stimulus-response relationship, such that the reflex operates around the exercise-induced increase in blood pressure (19). Therefore, increases in exercise intensity to maximal effort would result in increases in indexes of central command, such as heart rate (HR), along with the increase in O2 uptake (VO2), and may be reflected by a continued rightward resetting of the CBR (9). However, modulation of the CBR can also occur by activation of the exercise-pressor reflex (13), which has been proposed to produce an upward vertical shift in the CBR stimulus-response relationship due to increased sympathetic activation (19). Therefore we proposed to analyze the vertical and horizontal components of the resetting of the CBR stimulus-response relationship during dynamic exercise ranging in intensity from moderate to maximal exercise.

METHODS AND PROCEDURES

Subjects

Seven healthy men (aged 25.4 ± 0.75 yr) gave written informed consent for this investigation, which was approved by the Ethics Committee of the Fredriksberg Municipalities. 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

Each subject performed two graded exercise tests at least 2 days before participation in the experiment. The primary test
was a maximal exercise test for the determination of maximal O₂ uptake (Vo₂max) during upright, seated, back-supported leg cycling exercise. The second test involved the measurement of Vo₂ during arm ergometry performed at several graded exercise workloads to determine the arm exercise workload which would elicit a Vo₂ of ~25% of the leg cycling Vo₂max. On the experimental day, each subject performed four bouts (10–15 min each) of constant-load dynamic exercise in a 20°C, 40–60% relative humidity environment, in the same body position that was used during the preliminary exercise tests. Each exercise bout was separated by a rest period of sufficient length of time to return HR and mean arterial pressure (MAP) to baseline values. Exercise bout 1 consisted of leg cycling exercise at 50% of the predetermined leg cycling Vo₂max (50% L). Exercise bout 2 consisted of leg cycling at the same workload, with the addition of arm-cranking exercise at a workload that elicited 25% of the leg cycling Vo₂max, such that the whole-body Vo₂ was ~75% of leg Vo₂max (75% L + A). Exercise bout 3 (75% L) consisted of leg cycling alone at a workload eliciting the same Vo₂ as was attained during the bout 2 combined exercise. Finally, exercise bout 4 consisted of leg cycling at the same workload as in bout 3, with the addition of arm-cranking exercise at a workload that elicited 25% of the leg cycling Vo₂max, such that the whole-body Vo₂ approximated leg Vo₂max (Max L + A). Presentation of exercise bouts 1–4 to each subject was randomized on the experimental day. Table 2 lists the absolute Vo₂ measures and wattage achieved for each level of exercise. During each exercise bout, HR, Vo₂, and MAP were continuously monitored and recorded. At rest and after attainment of steady-state exercise in each experimental exercise bout, CBR stimulus-response curves were constructed by using a modification of the neck pressure-neck suction (NP-NS) protocol previously developed by Potts et al. (17). Measurements

Maximal exercise test and Vo₂ measures. Subjects who were determined acceptable by physical examination performed two graded exercise tests for the determination of Vo₂. The test for leg Vo₂max was performed in the upright posture on a constant-load cycle ergometer. The arm ergometry exercise test was performed in the seated position, with a constant-load cycle ergometer that was modified for arm ergometry. During each maximal exercise test, the subject exercised to volitional fatigue, and measurements included the rate of Vo₂ (using breath-by-breath open-circuit spirometry [Medgraphics CPX/D, MN]) and continuous electrocardiogram monitoring by using a 12-lead monitoring system. Subjects returned to the laboratory no less than 2 days after maximal-exercise testing for performance of the experimental exercise bouts.

HR and arterial blood pressure. During each experimental test, HR was continuously monitored via electrocardiogram. Arterial blood pressure was measured directly via a catheter placed into the right femoral artery. The pressure was monitored by using disposable pressure transducers (Baxter) that were interfaced with a pressure monitor (Dainika Elektronik, Dialogue 2000). 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 HR, were recorded beat-by-beat on-line by using a personal computer (Zitech Pro, Pentium 90) and customized software (sampling rate, 250/s).

CBR function. CBR function during exercise was analyzed via a slight modification of the NP-NS method previously reported by Potts et al. (17). To accommodate the high workloads used in the present experiments, the modification was 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 lighter exercise workloads (17). On the basis of data from Eckberg et al. (3) which 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 at high exercise workloads with appropriate repeatability. Furthermore, operating-point pressures were established for each stimulus and defined as the prevailing MAP before neck pressure or neck suction was applied. The carotid sinus pressure that resulted from the applied stimuli was estimated by adding the recorded neck chamber pressure or suction to the prestimulus MAP attained two beats before the beginning of the maneuver. In addition, the time required to construct a stimulus-response curve during the 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% Vo₂max 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 have been reported previously (10).

In the present investigation, the resulting parameters of threshold, saturation, and maximal gain values obtained from the logistic model (7) of each CBR stimulus-response curve were compared by using one-way ANOVA with repeated measures across exercise conditions. 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

Carotid-Cardiac Baroreflex Response to Dynamic Exercise

No significant differences were seen in the carotid-cardiac baroreflex maximal gain, or sensitivity, be-

| Table 1. Subject information |  |
|---|---|---|---|---|
| Age, yr | 25.4 ± 0.7 | Height, cm | 182.6 ± 2.0 | Weight, kg | 84.6 ± 3.9 |
| Vo₂max, ml·min⁻¹·kg⁻¹ | 45.7 ± 2.6 |  |

Values are means ± SE. Vo₂max, maximal oxygen uptake during leg cycling.

| Table 2. Absolute Vo₂ and watts for each exercise stage |  |
|---|---|---|---|---|---|---|
| | 50% L | 75% L | 75% L + A | Max L + A |
| Vo₂, l/min | 1.71 ± 0.1 | 2.6 ± 0.3 | 2.6 ± 0.8 | 3.8 ± 0.2 |
| Watts | 137.8 ± 8.1 | 208.8 ± 8.1 | 212.0 ± 22.5 | 264.8 ± 15.3 |

Values are means ± SE, S% of Vo₂max, during leg cycling: L, leg-only exercise; A, arm exercise; L + A, combined leg and arm exercise.
Table 3. Derived variables for carotid-cardiac baroreflex stimulus-response relationship

<table>
<thead>
<tr>
<th>Condition</th>
<th>Threshold, mmHg</th>
<th>HR at Threshold, beats/min</th>
<th>Saturation, mmHg</th>
<th>HR at Saturation, beats/min</th>
<th>CP-OP, mmHg</th>
<th>Gain, beats·min⁻¹·mmHg⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>66.1 ± 8.6</td>
<td>77.0 ± 5.5</td>
<td>131.3 ± 11.0</td>
<td>57.4 ± 1.7</td>
<td>3.7 ± 1.6</td>
<td>-0.33 ± 0.07</td>
</tr>
<tr>
<td>50% L</td>
<td>80.5 ± 8.0*</td>
<td>126.3 ± 3.2*</td>
<td>143.4 ± 8.0*</td>
<td>116.7 ± 2.9*</td>
<td>8.6 ± 2.8*</td>
<td>-0.24 ± 0.05</td>
</tr>
<tr>
<td>75% L + A</td>
<td>100.1 ± 11.4*</td>
<td>161.1 ± 1.7*</td>
<td>161.3 ± 6.2*</td>
<td>156.9 ± 2.1*</td>
<td>11.3 ± 1.6</td>
<td>-0.23 ± 0.05</td>
</tr>
<tr>
<td>75% L</td>
<td>94.4 ± 7.9†</td>
<td>170.9 ± 6.6†</td>
<td>154.7 ± 8.5†</td>
<td>160.9 ± 6.3†</td>
<td>10.8 ± 0.6</td>
<td>-0.22 ± 0.03</td>
</tr>
<tr>
<td>Max L + A</td>
<td>109.8 ± 11.6††</td>
<td>189.1 ± 4.9††</td>
<td>173.0 ± 9.3††</td>
<td>172.5 ± 9.3††</td>
<td>20.7 ± 1.9†</td>
<td>-0.26 ± 0.04</td>
</tr>
</tbody>
</table>

Values are means ± SE. HR, heart rate; %, percentage of VO_2max, during leg cycling. Threshold and saturation values in mmHg represent the position of the stimulus-response relationship relative to the x-axis (i.e., carotid sinus pressure) of the reflex function curve, whereas threshold and saturation values in beats/min indicate position of the curve relative to the y-axis (i.e., heart rate). CP, centering point is carotid sinus pressure at point of maximal gain of the modeled baroreflex function curve; OP, operating point is carotid sinus pressure at which the prethreshold mean arterial pressure is located on the carotid baroreflex function curve; CP-OP, difference in carotid sinus pressure (in mmHg) between locus of the CP and OP. Note that as the workload increased, OP moved toward the threshold at a lower carotid sinus pressure, making the CP-OP difference larger. *Significance compared with previous state; †significance compared with last similar stage, i.e., L vs. L or L + A vs. L + A. Statistical analysis was performed by using ANOVA; P < 0.05. ‡Significant at P < 0.07.
analyzed because of an inability to model the baroreflex-function curves for each exercise bout performed by the other three subjects. Although rhythmic variation in MAP recordings, due to the effect of the movement of the exercising leg on the intravascular catheter, can hinder modeling of carotid-vasomotor stimulus-response curves, a primary difficulty in the present investigation lay in obtaining reliable threshold values for these curves. This would imply that stronger or more prolonged neck pressure stimuli may have been required to achieve maximal reflex vasomotor responses during these exercise types and intensities. However, Papelier et al. (13) also demonstrated a steepening of the leftward portion of the carotid-vasomotor baroreflex (and not the carotid-cardiac baroreflex) during postexercise leg muscle ischemia induced by thigh cuff inflation. This alteration was attributed by the authors to an activation of the muscle chemoreflex, which 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 (11, 13, 19).

Therefore, the inability to model the baroreflex stimulus-response relationship during certain bouts of exercise may also be attributable to chemoreflex activation.

No significant differences were seen in the carotid-vasomotor baroreflex maximal gain, or sensitivity, at any exercise intensity. However, significant lateral and vertical shifts (i.e., the y-axis coordinate or MAP response to the corresponding threshold or saturation pressure value) were seen in the location of the threshold and saturation of the carotid-vasomotor baroreflex with increases in exercise intensity, with the exception of vertical shifts from rest to 50% L exercise (Table 4). These shifts occurred regardless of the type of exercise being performed, i.e., L or combined L + A exercise. Interestingly, the threshold, saturation, and corresponding y-axis response values for 75% L + A were observed to be greater than the values for 75% L for each subject. However, due to the small numbers of subjects and measurement variance, this observation did not result in any statistically significant differences.

The position of the operating point of the carotid-vasomotor baroreflex during the resting condition was 79.9 ± 7.8 mmHg, and during the four exercise bouts (50% L, 75% L + A, 75% L, and maximal exercise), the positions were 90.1 ± 5.2, 104.5 ± 5.0, 107.5 ± 4.9, and 111.3 ± 3.2 mmHg, respectively. In addition, the operating point of the carotid-vasomotor baroreflex was significantly shifted away from the centering point toward the threshold of the reflex with progressive increases in exercise workload in a manner similar to that reported for the carotid-cardiac baroreflex (Tables 3 and 4). No significant difference was found between the position of the operating points relative to the centering points of the L only and combined L + A exercise bouts at 75% $\dot{V}$O$_{2\text{max}}$.

Because the data from only four subjects of the total seven subjects were analyzed so that a one-way repeated-measures ANOVA could be used across all conditions for each subject, the attainment of statistical significance indicated the strength of the data of this investigation.

**DISCUSSION**

The findings of the present investigation support our hypothesis that the CBR stimulus-response relationship was classically reset upward and rightward in relation to increases in work intensity. This conclusion supports the investigations of Melcher and Donald (8) in the dog model, as well as those of Potts et al. (17) and Papelier et al. (12) in the exercising human. Each of those investigations also demonstrated a reset, but functional and equally sensitive, baroreflex during exercise compared with during the resting condition. However, the present investigation further demonstrates that this phenomenon occurs over a wide range of exercise intensities, up through exercise at $\dot{V}$O$_{2\text{max}}$ [vs. the submaximal exercise workloads of 50% $\dot{V}$O$_{2\text{max}}$ and ~75% $\dot{V}$O$_{2\text{max}}$ utilized in the investigations of Potts et al. (17) and Papelier et al. (12), respectively]. In addition, the data of the present investigation extend the findings of Potts et al. (17), in that the relocation of the operating point (the prestimulus MAP) away from the centering point (point of maximal gain) and toward the threshold of the reflex occurred, in relation to exercise intensity, through exercise intensities up to $\dot{V}$O$_{2\text{max}}$. Physiologically, the relocation of the operating point toward threshold provides a greater range of response to hypertensive events stimulated by the activation of the exercise pressor reflex, as suggested by the work of Sheriff et al. (23).

From recent investigations, the concept has arisen of a complex interaction between central command and the reflexes initiated by the stimulation of chemically and mechanically sensitive receptors in the exercising muscles. Iellamo et al. (6) have identified the unique effects of the stimulation of each of these muscle receptors on baroreflex control of HR. Additionally,

---

**Table 4. Derived variables for the carotid-vasomotor baroreflex stimulus-response relationship**

<table>
<thead>
<tr>
<th></th>
<th>Threshold, mmHg</th>
<th>MAP at Threshold, mmHg</th>
<th>Saturation, mmHg</th>
<th>MAP at Saturation, mmHg</th>
<th>CP-OP, mmHg</th>
<th>Gain, mmHg/mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>57.7±7.1</td>
<td>94.6±6.9</td>
<td>109.8±6.6</td>
<td>71.1±7.9</td>
<td>1.0±0.5</td>
<td>-0.50±0.63</td>
</tr>
<tr>
<td>50% L</td>
<td>73.7±4.9*</td>
<td>97.7±6.7</td>
<td>128.8±7.5*</td>
<td>77.5±6.6</td>
<td>6.4±1.3*</td>
<td>-0.47±0.36</td>
</tr>
<tr>
<td>75% L</td>
<td>96.4±5.3*</td>
<td>113.4±8.7*</td>
<td>156.4±5.3*</td>
<td>94.1±8.9</td>
<td>13.5±0.4*</td>
<td>-0.45±0.06</td>
</tr>
<tr>
<td>75% L + A</td>
<td>93.1±5.1†</td>
<td>107.2±9.3†</td>
<td>146.2±5.8†</td>
<td>87.3±7.7†</td>
<td>13.0±0.8†</td>
<td>-0.50±0.68</td>
</tr>
<tr>
<td>Max L + A</td>
<td>112.1±5.2†</td>
<td>130.4±7.1†</td>
<td>172.3±3.2†</td>
<td>110.5±5.5†</td>
<td>18.4±0.9†</td>
<td>-0.53±0.68</td>
</tr>
</tbody>
</table>

Values are means ± SE. MAP, mean arterial pressure. *Significance from previous stage; †significance from last similar stage, i.e., L vs. L or L + A vs. L + A. All statistical analysis performed by using ANOVA; P < 0.05.
Potts and Li (16) have demonstrated that, in anesthetized dogs, the effect of the stimulation of fibers that carry afferent signals from skeletal muscle may depend on the basal level of baroreceptor activity. However, the relative effects of central command and the exercise-pressor reflex on CBR resetting during dynamic exercise remain unclear. Rowell and O’Leary (20) have postulated that central command activation produces a rightward lateral shift in the CBR stimulus-response relationship through an interaction at the level of the neuron pool that receives the baroreflex afferents, such that the reflex operates around the exercise-induced increase in blood pressure. In addition, they proposed that activation of the exercise-pressor reflex would produce an upward vertical shift in the CBR stimulus-response relationship due to increased sympathetic activation (20). However, although A exercise is known to elicit higher lactate accumulations (14), HR (14, 15), and ratings of perceived exertion (15) than L exercise at the same absolute VO2, the potential for a disproportionate activation of the muscle metaboreflex in conjunction with a heightened central command activation did not result in significant differences in the resetting of the CBR during L and combined L + A exercise.

Exercise Intensity

DiCarlo and Bishop (1) have examined the time course of the resetting of the arterial baroreflex in exercising rabbits. These researchers have demonstrated an immediate resetting of the reflex, at the onset of exercise, which persists when the exercise pressure response is attenuated by intravenous infusion of nitroglycerin. These data suggest that central command may mediate resetting of the operating point of the arterial baroreflex toward higher pressures, thus contributing to the characteristic sympathoexcitatory response elicited at the onset of exercise. Their investigation also demonstrated that an intact arterial baroreflex was required for the sympathoexcitatory response to exercise to be expressed, because it was absent in sinoaortic-denervated rabbits (1). Additionally, Ebert (2) has shown that the anticipation of static exercise in humans results in an alteration in cardiac output and carotid-vascular responses to neck pressure and neck suction stimuli. These findings support the role of a quicker acting, feed-forward type of mechanism, such as “central command,” as the primary mechanism responsible for the resetting of the CBR during dynamic exercise. In the present investigation, as in the investigations of Potts et al. (17), Papelier et al. (12), and Melcher and Donald (8), baroreflex resetting occurred in direct relation to increases in exercise intensity, which in turn is related to increases in central command activation, with the recruitment of greater numbers of motor fiber units to perform the higher intensity of exercise.

A + L Exercise

In the present investigation, the addition of A exercise to L exercise presented a complex physiological picture. Not only does arm work elicit different chemical, thermal, and perceptive responses to exercise than does leg work (14, 15), the additional muscle mass must receive an adequate proportion of cardiac output to sustain the exercise (21). The question of how cardiac output is distributed to exercising muscle during high-intensity dynamic exercise was raised by Secher et al. in 1977 (22). These investigators found that the addition of arm-cranking exercise to leg-cycling exercise resulted in an increase in HR and VO2 without a concomitant increase in MAP or pulse pressure. However, leg vascular conductance was decreased during the addition of arm exercise. Therefore, for a maintenance of a relatively similar MAP between the two exercise bouts, arm vasodilation and leg vasoconstriction must have been balanced, in conjunction with the observed modest rise in cardiac output. The question of the origin of the signal that elicited the increased leg vascular resistance in the face of the increased exercise workload can possibly be explained by our reflex-resetting model. An augmented central command activation with increased active muscle mass (addition of arm-cranking exercise to leg-cycling exercise, i.e., increased numbers of active muscle fibers) will result in an upward and rightward shift in the CBR stimulus-response curve. If, after a transient rise, MAP returned to a value similar to that observed during leg exercise alone, as in the investigation of Secher et al. (22), the MAP would then lie nearer to the threshold of the reset baroreflex function curve, which would be perceived as a hypotensive stimuli and would result in an activation of the efferent sympathetic limb of the autonomic nervous system and produce a reduced vascular conductance in the leg musculature.

Potential Limitations

In the present investigation, we used brief, external carotid sinus stimuli to construct open-loop, stimulus-response relationships for the CBR during moderate to maximal intensities of exercise. These 5-s stimuli produced rapid reflex HR and MAP responses. Although these responses may not represent the full expression of baroreflex responsiveness to a longer stimuli, the maximal HR and MAP response to each stimulus were used to construct repeatable (10) reflex stimulus-response relationships which were then modeled by using the logistic function, described by Kent et al. (7), that we have used in our laboratory in previous investigations (17). The brevity of the carotid-sinus stimuli facilitated the minimalization of the influence of the extracarotid baroreceptors, such that the reflex responses recorded during and immediately after the stimuli were attributed to the noninvasively isolated carotid arterial baroreflex. In addition, the reflex responses in HR in relation to the carotid sinus stimuli have been termed the carotid-cardiac baroreflex, whereas the reflex responses in MAP in relation to these stimuli have been termed the carotid-vasomotor baroreflex. We have used this terminology because, due to the brevity of the carotid sinus stimuli, we have assumed that the reflex alterations in blood pressure
would be primarily caused by reflex-induced changes in peripheral vascular resistance. Raven et al. (18) have demonstrated that, during the 5-s stimuli, the resultant change in HR affects cardiac output, and thus MAP, in the face of a constant stroke volume. However, after the stimulus, the MAP response persists, despite a return of HR to baseline. This indicates that peripheral vascular resistance, not cardiac output, primarily affected the peak MAP response that occurs after the termination of the stimuli. This interpretation reflects the latency of response of the sympathetic nervous system, which achieves 50–80% of complete sympathetic effector response within 5 s (26).

The results of this investigation are similar to those of Potts et al. (17) and Papelier et al. (12) in that the baroreflex was reset at the onset of exercise in relation to exercise intensity. However, the present investigation extends these findings to maximal exercise. In addition, a disparity exists between the results of Papelier et al. and those of the present investigation. This disparity may be related to the experimental techniques used in each study. Papelier et al. used longer carotid sinus perturbations (20 s) to elicit reflex stimulus-response relationships in humans during exercise at intensities up to ~75% \( V_{\text{O}_2\text{max}} \). They found no alteration in the relationship of the operating point to the reflex responses to positive and negative pressure stimuli. Also, Papelier et al. used a NP-NS protocol wherein the operating pressure was fixed at zero neck pressure and the carotid sinus stimuli were equally distributed around the operating point pressure. In addition, because no modeling of the stimulus-response relationship was utilized, it is not possible to calculate whether the operating point had moved in relation to the reflex centering point or threshold, regardless of its location relative to the reflex responses to the carotid sinus stimuli. In other words, although the operating point may have remained at the same location relative to a stimulus response, the response value itself may have been closer to or at the threshold of the reflex as exercise intensity increased, thus resulting in the operating point being relocated in relation to the threshold as well.

In contrast, we plotted the operating pressure within the modeled curves and clearly demonstrate its relocation within the reset baroreflex-function curve. We suggest that our random-order presentation of short carotid sinus stimuli allowed us to model the baroreflex function curves and thereby demonstrate the relocation of the operating point toward the threshold of the reset baroreflex. The data of the present study clearly indicate that the operating point progressively relocates toward the threshold pressure and away from the centering point of the reflex-function curve in direct relation to the intensity of exercise (Tables 3 and 4). We propose that, as parasympathetic activity gradually decreases with increasing workload, further tachycardia via this mechanism becomes limited as the workload increases toward maximum (17). The identification of the shift in the operating point toward threshold with increasing vagal withdrawal suggests that this may be mediated by increasing central command. It should be noted that a discrepancy existed between the operating point pressures established for the carotid-cardiac and carotid-vasomotor baroreflexes at rest and during each exercise intensity. These differences are attributable to a limitation in the technique employed, wherein different stimulus-response sets may have been used to quantify HR from those utilized to establish MAP, because each stimulus does not always produce a valid HR and MAP response. Due to the moment-to-moment alterations in arterial blood pressure inherent in the pulsatile nature of the system, it is likely that the discrepancy arose because the prestimulus pressure was established at different time points. Regardless of the limitations in the methodology used, it is clear that the operating point relocated progressively closer to the threshold and farther from the centering point as the intensity of the exercise increased.

In conclusion, the results of this investigation support the concept of continued regulation of arterial blood pressure by the CBR during exercise. The carotid-cardiac and carotid-vasomotor reflexes were reset upward and rightward in direct relation to the intensity of exercise, with a concomitant shift of the reflex operating point away from the centering point and toward the threshold of the reflex (Tables 3 and 4). This resetting positions the reflex to respond to changes in systemic arterial pressure from the prevailing pressure of the steady-state dynamic exercise, with a particular augmentation in the range of response to hypertension.

The authors thank the subjects for their interest and cooperation. In addition, we thank Inge Holm for coordination of K. Norton’s stay in Copenhagen and Lisa Marquez for secretarial support in preparation of the manuscript.

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 NGT-70409, NASA Specialized Center of Research and Training Grant NAGW-3582, and NASA Grant NAGS-4668; by the American College of Sports Medicine; NASA Space Physiology Student Research Award; by the Danish National Research Scholarship; and by National Heart, Lung, and Blood Institute Grant HL-45547.

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. Present address of K. H. Norton: Laboratory of Cardiovascular Science, Gerontology Research Center, NIA/NIH, 4940 Eastern Ave., Baltimore, MD 21224.

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

Received 19 September 1997; accepted in final form 23 February 1999.

REFERENCES


