Role of muscular factors in cardiorespiratory responses to static exercise: contribution of reflex mechanisms

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Jellamo, Ferdinando, M. Massaro, G. Raimondi, G. Peruzzi, and J. M. Legramante. Role of muscular factors in cardiorespiratory responses to static exercise: contribution of reflex mechanisms. J. Appl. Physiol. 86(1): 174–180, 1999.—We investigated the effects of muscle mass and contraction intensity on the cardiorespiratory responses to static exercise and on the contribution afforded by muscle metaboreflex and arterial baroreflex mechanisms. Ten subjects performed static handgrip at 30% maximal voluntary contraction (MVC) (SHG-30) and one-leg extension at 15% (SLE-15) and 30% (SLE-30) MVC, followed by postexercise circulatory occlusion (PECO). Mean arterial pressure (MAP) and heart rate (HR) responses were greater during SLE-30 than during SHG-30. The difference in MAP was maintained by PECO, and the part of the pressor response maintained by PECO, rate (HR) responses were greater during SLE-30 than during SHG-30. The difference in MAP was maintained by PECO, and the part of the pressor response maintained by PECO was greater after SLE-30 than after SHG-30 (88.3 ± 10.6 and 67.8 ± 12.7%, respectively, P = 0.02). There were no differences in MAP and HR responses between SHG-30 and SLE-15 trials. Baroreflex sensitivity was maintained during SHG-30 and SLE-15, whereas it was significantly reduced during SLE-30 and recovered back to the resting level during PECO. Minute ventilation and oxygen uptake increased more during SLE-30 than during both SHG-30 and SLE-15 trials. Minute ventilation remained significantly elevated above rest only during PECO following SLE-30. These data suggest that during static exercise the muscle mass and contraction intensity affect 1) the magnitude of the cardiorespiratory responses, 2) the contribution of muscle metaboreflex to the cardiorespiratory responses, and 3) the arterial baroreflex contribution to HR control.

static exercise; muscle metaboreflex; arterial baroreflex

THE CARDIOVASCULAR AND RESPIRATORY RESPONSES TO STATIC EXERCISE ARE WELL ESTABLISHED AND INCLUDE INCREASES IN ARTERIAL BLOOD PRESSURE (AP), HEART RATE (HR), AND PULMONARY MINUTE VENTILATION (VE) (7). HOWEVER, THE FINER MODULATORY EFFECTS EXERTED BY SOME FACTORS ASSOCIATED WITH THE MUSCLE CONTRACTION ON THE CARDIORESPIRATORY RESPONSES TO THIS KIND OF MUSCULAR ACTIVITY ARE STILL A MATTER OF DEBATE.

WHEREAS THERE IS A GENERAL AGREEMENT THAT THE MAGNITUDE OF AP AND HR RESPONSES IS RELATED TO THE RELATIVE INTENSITY OF CONTRACTION, Conflicting results have been reported concerning the dependency of the pressor and HR responses on the size of the active muscle mass (4, 14, 15, 17, 28–30). The influence of muscle mass on the respiratory responses has not been as extensively investigated. The only study addressing this issue reported the independence of Ve increase from the mass of muscle involved in static contractions (12).

Similarly debated are the control mechanisms underlying the cardiorespiratory responses to static exercise. Two theories of neural control have been proposed. In the first, activation of regions of the brain responsible for the recruitment of skeletal muscle motor units would activate concomitantly neuronal circuits within the brain stem controlling cardiovascular and respiratory functions, and this has been termed "central command" (7, 8). In the second theory, neural signals arising in contracting muscles would activate reflexly the cardiovascular and respiratory control areas in the brain stem ("exercise pressor reflex") (1, 16). Results from human studies have supported both these theories (3, 5, 13, 18, 19, 22) and have favored the concept that the two mechanisms are not mutually exclusive, i.e., there is redundancy of the control systems (16). Whereas it is reasonable to assume that one mechanism may produce almost the entire responses when the other is absent or markedly depressed, it is also possible that in subjects with all mechanisms intact the two mechanisms are not completely redundant (6) but that the relative contribution they afford may vary depending on factors associated with the muscle contraction, such as the type of exercise and the intensity of physical activity, which, in the case of static exercise, is determined by both the strength of contraction (i.e., the percentage of the maximal voluntary contraction (MVC)) that is expended and by the mass of contracting muscles (16).

This study was designed with a twofold aim in mind. The first was to systematically investigate in the same individuals the effects of muscle mass on both the cardiovascular and the associated respiratory responses to static exercise; and the second was to test the hypothesis that the contraction intensity and/or the size of active muscle mass may affect the relative contribution of reflex mechanisms to the cardiorespiratory responses to static exercise.

To accomplish these aims, we evaluated the cardiorespiratory responses to different intensities of arm and leg static exercise followed by postexercise circulatory occlusion to maintain the chemical stimulation of muscle afferents (i.e., metaboreflex activation) while avoiding marked perturbations of the neural mechanisms that are normally operating during exercise. Finally, since in addition to central and muscle reflex mechanisms the arterial baroreflexes recently have been hypothesized to be involved in cardiovascu-
lar regulation during exercise (9, 11, 26), we also investigated whether the arterial baroreflex modulation of sinus node is affected by the contraction intensity and the mass of statically exercising muscles.

METHODS

Ten healthy male sedentary volunteers, age 23–31 yr, participated in this study. Each subject gave informed written consent after receiving full details of the protocol, and was aware of any possible short-term discomfort involved.

All subjects were normotensive (sitting blood pressure <140/90 mmHg), taking no medication, and were free from cardiovascular and pulmonary diseases, based on medical history and physical examination at the time of the study. All subjects were nonsmokers and were not involved in regular physical activity. The protocol was approved by the Ethics Committee of the Department of Internal Medicine of the University of Rome.

General procedure. Exercises consisted of static handgrip (SHG) and static leg extension (SLE). All exercises were performed in the seated position, with the trunk supported by the movable-back chair of a commercially available, computer-based multifunctional dynamometer system designed for rehabilitative purposes (REV 9000, Technogym, Gambettola, Forlì, Italy). This apparatus allows both upper and lower limb exercises by changing the lever arms of the dynamometer, which are appropriately designed for the different limbs and provided by the manufacturer. Subjects underwent several preliminary sessions during which they were taught and carefully trained to perform MVC of forearm and quadriceps muscles while avoiding the contraction of muscle groups other than those specifically involved in the exercise.

SHG was performed at 30% of MVC (SHG-30 trial) with the dominant hand. MVC had been determined as the highest force developed by the subjects in three previous 5-s maximal contraction trials. The height of the dynamometer was adjusted to permit SHG to be performed with the arm extended, and the elbow was supported by a padded platform while the forearm was free. This setup configuration should further contribute to minimize any accessory muscle recruitment.

SLE was performed at 15% (SLE-15) and 30% (SLE-30) MVC. MVC had been previously determined as described for the SHG trial. During MVE trials, restraining belts were placed around the chest and abdomen to stabilize the body, and, again, to minimize contractions with other muscles (17). The subjects were not allowed to grasp with the hands any part of the dynamometric apparatus. The lever arm of the dynamometer was placed parallel to the limb, with the axis of rotation coinciding as closely as possible with the axis of rotation of the knee joint. The distal end of the lever arm was attached to the inferior third of the exercising leg, and the foot was not in contact with the floor. The knee angle was fixed at 80° (full extension considered 0°). The nonexercising leg was maintained flexed at 90° at the knee and not in contact with the floor.

The muscle tension at preset relative intensities during the whole period of forearm and leg static contractions was held constant with the aid of a visual feedback on the computer monitor driven by the dynamometer placed in front of the subjects. Determination of maximal efforts was done at the beginning of each experimental session. Ninety seconds were allowed between the three maximal-strength tests. On the experimental days, pneumatic cuffs were placed, as high as possible, on the exercising upper arm and thigh to allow postexercise circulatory occlusion (PECO) studies.

Recorded variables. The tension × time integral (TTI) during the whole period of static contractions was evaluated directly by the computer program by computing the area under the tension trace (11).

AP was continuously and noninvasively measured from the third finger of the nondominant hand by using the plethysmographic method of the unloaded arterial wall (Finapres, Ohmeda 2300 NIBP monitor, Englewood, CO). This device has been proven to provide excellent estimates of changes of intra-arterial pressure during the laboratory tests, including exercise (20). During the data-collection periods, the servo-reset mechanism of Finapres was turned off to permit continuous data acquisition.

The arm with the instrumented finger was held extended at the heart level by means of a pulley arrangement, with rubber slings sustaining the arm at the wrist with the elbow, also held by a padded support, while the forearm was free. This was done to avoid the effect of hydrostatic pressure on AP readings.

Three electrocardiogram electrodes were also placed on the chest to monitor the heart rhythm and the quality of QRS complex on the oscilloscope of a defibrillator (Hewlett-Packard 43120A).

Continuous monitoring of ventilation and gas exchange was performed by the aid of a breath-by-breath data-collection system, which includes a mass spectrometer and two pneumotachographs (Fleisch no. 3) pressure transducer sets (Hewlett-Packard 47304A) connected to a mouth-face mask two-way non-rebreathing valve assembly (Hans Rudolph, model 7921) (9). Flowmeter and mass spectrometer calibrations were always done before each experimental session by using a calibrated syringe and gas mixtures of known concentrations.

Spontaneous baroreflex analysis. This technique, which we employed to investigate the arterial baroreflex modulation of sinus node, has been already described in detail (9–11, 21).

Briefly, the beat-by-beat time series of systolic AP (SAP) and pulse interval (PI) are searched for three or more consecutive beats in which SAP and PI of the following beat change in the same direction (either increasing or decreasing). These sequences are identified as “baroreflex sequences.” A linear regression is applied to each individual sequence. Only those in which the coefficient of determination (r²) is >0.85 are accepted. The mean individual slope of the SAP/PI relationship, obtained by averaging all slopes computed within a given test period, is calculated and taken as a measure of the integrated spontaneous baroreceptor reflex sensitivity for that period. This technique has been recently proven to provide reproducible results during many laboratory tests, including static exercise (10).

Experimental protocol. On the experimental day, the protocol started at 9:30 AM in a laboratory at ambient temperature (22–24°C). The subjects were required not to eat or to drink coffee for at least 2 h. Each subject attended the laboratory on 2 consecutive days. On one day they performed SHG and on the other day SLE exercises. After instrumentation, the subjects sat quietly to relax in the room made dark and noiseless. Thereafter, the protocol began with a 4-min control period followed by 3 min of static exercise. Eight seconds before the cessation of exercises, the pneumatic cuff on the exercising arm or thigh was rapidly inflated to suprasystolic pressure values (250 mmHg) by a computer-driven pressure source, and the circulatory occlusion was maintained for 4 min in the postexercise period. This maneuver was followed by a 4-min recovery period. The order of forearm and leg exercises and, for the latter, of the 15 and 30% MVC trials was randomized. A resting period of 30 min was allowed between SLE-15 and SLE-30 trials.

Data acquisition and analysis. During the experimental sessions, the output of the Finapres system was transmitted via the RS 232 serial port and processed by software pro-
grams written in our laboratory to obtain beat-by-beat information on SAP, mean arterial pressure (MAP), PI, and HR. Details on respiratory and gas-exchange data-acquisition system have been already published (9). Reported data in the different experimental periods (i.e., rest, exercise, PECO, and recovery) represent the averaged values recorded in each given period, except for respiratory and gas-exchange responses during exercise representing peak values. Respiratory and gas-exchange data from one subject during SHG-30 trial were lost due to technical problems, so respiratory and gas-exchange results from SHG-30 experiments were calculated from nine subjects. The significance of differences in a variable among the different experimental periods within each exercise trial and of differences in a variable (or in the change from control) within a given experimental period among the different exercise trials was evaluated by analysis of variance. If significant F values were found, the Bonferroni test was used to determine differences between means for significant main effects. Relationships between variables were evaluated by the use of linear regression analysis. Values are presented as means ± SE. Differences were considered statistically significant when P was < 0.05.

RESULTS

Resting values for all cardiovascular and respiratory variables were within normal limits and did not differ significantly among the three exercise trials (Tables 1 and 2). TTI was significantly greater during SLE-30 (7,463.9 ± 504.3 N·s) than during both SLE-15 (4,889.9 ± 401.3 N·s) and SHG-30 trials (3,714.8 ± 306.0 N·s) (P < 0.05 for both), whereas the difference between the latter two was not statistically significant.

Cardiovascular responses to exercise and PECO (Table 1 and Fig. 1). MAP and HR increased significantly above resting levels during all three exercise trials. MAP and HR responses to SHG-30 and SLE-15 were not significantly different (12.5 ± 2.1 vs. 12.4 ± 2.0 mmHg and 4.4 ± 1.3 vs. 6.4 ± 1.7 beats/min for MAP and HR, respectively), whereas MAP and HR increases induced by SLE-30 (23.1 ± 3.5 mmHg and 17.1 ± 3.2 beats/min, respectively) were significantly greater (P < 0.05) than those for either the SHG-30 or the SLE-15 trial.

There was a significant, direct relationship between TTI and individual increases (i.e., changes from control) in MAP (r = 0.68, P < 0.001) and HR (r = 0.64, P < 0.001).

During PECO, HR returned to control values, whereas MAP remained significantly increased above rest in all three trials. The part of the pressor response that was maintained by PECO was significantly greater (P < 0.05) for SLE-30 than for both SHG-30 and SLE-15 trials, whereas no significant differences were observed between these latter two (19.4 ± 2.9, 8.0 ± 1.6 and 7.9 ± 2.0 mmHg for SHG-30, SLE-30, and SLE-15 trials, respectively).

Table 1. Cardiovascular responses and baroreflex sensitivity during leg and forearm static exercise

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise</th>
<th>PECO</th>
<th>Recovery</th>
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<tbody>
<tr>
<td>MAP, mmHg</td>
<td>88.3 ± 3.2</td>
<td>114.4 ± 4.5*</td>
<td>107.8 ± 5.1*</td>
<td>89.6 ± 3.8</td>
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<tr>
<td>HR, beats/min</td>
<td>75.4 ± 4.0</td>
<td>92.5 ± 4.2*</td>
<td>81.4 ± 5.1</td>
<td>77.8 ± 4.8</td>
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<tr>
<td>BRS, ms/mmHg</td>
<td>14.0 ± 2.5</td>
<td>7.9 ± 1.3*</td>
<td>12.5 ± 2.9</td>
<td>15.6 ± 3.2</td>
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<table>
<thead>
<tr>
<th></th>
<th>SLE-15</th>
<th>SHG-30</th>
</tr>
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<tbody>
<tr>
<td>MAP, mmHg</td>
<td>91.6 ± 2.3</td>
<td>97.0 ± 2.3*</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>76.1 ± 4.3</td>
<td>80.5 ± 4.6*</td>
</tr>
<tr>
<td>BRS, ms/mmHg</td>
<td>13.6 ± 2.7</td>
<td>12.1 ± 2.6</td>
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<table>
<thead>
<tr>
<th></th>
<th>SLE-30</th>
</tr>
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<tbody>
<tr>
<td>MAP, mmHg</td>
<td>86.5 ± 3.2</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>72.7 ± 2.9</td>
</tr>
<tr>
<td>BRS, ms/mmHg</td>
<td>14.6 ± 3.2</td>
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</table>

Values are means ± SE. Values are presented as means ± SE. MAP, mean arterial pressure; HR, heart rate; BRS, baroreflex sensitivity. *P < 0.05 vs. rest.

Table 2. Respiratory and gas-exchange responses to leg and forearm static exercise

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise</th>
<th>PECO</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>V̇E, l/min</td>
<td>7.9 ± 0.7</td>
<td>18.2 ± 1.1*</td>
<td>10.8 ± 0.6*</td>
<td>8.5 ± 0.6</td>
</tr>
<tr>
<td>V̇O₂, ml/min</td>
<td>277.3 ± 13.8</td>
<td>550.6 ± 39.5*</td>
<td>320.4 ± 15.4</td>
<td>282.9 ± 17.2</td>
</tr>
<tr>
<td>V̇CO₂, ml/min</td>
<td>233.8 ± 17.0</td>
<td>518.2 ± 42.4*</td>
<td>322.9 ± 15.0*</td>
<td>285.6 ± 21.3</td>
</tr>
<tr>
<td>SHG-30</td>
<td>SLE-15</td>
<td>SHG-30</td>
<td></td>
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<tr>
<td>V̇E, l/min</td>
<td>8.6 ± 0.7</td>
<td>13.4 ± 0.6*</td>
<td>9.9 ± 0.7</td>
<td>8.4 ± 0.8</td>
</tr>
<tr>
<td>V̇O₂, ml/min</td>
<td>297.3 ± 19.8</td>
<td>447.1 ± 29.6*</td>
<td>325.2 ± 20.4</td>
<td>296.6 ± 25.2</td>
</tr>
<tr>
<td>V̇CO₂, ml/min</td>
<td>241.1 ± 12.4</td>
<td>375.6 ± 20.1*</td>
<td>270.1 ± 21.3</td>
<td>245.7 ± 16.5</td>
</tr>
<tr>
<td>SLE-30</td>
<td>SLE-30</td>
<td>SHG-30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V̇E, l/min</td>
<td>8.2 ± 0.6</td>
<td>12.8 ± 1.4*</td>
<td>8.9 ± 0.9</td>
<td>8.6 ± 1.0</td>
</tr>
<tr>
<td>V̇O₂, ml/min</td>
<td>271.1 ± 21.4</td>
<td>398.4 ± 21.1*</td>
<td>267.8 ± 24.4</td>
<td>265.9 ± 17.7</td>
</tr>
<tr>
<td>V̇CO₂, ml/min</td>
<td>242.2 ± 14.4</td>
<td>377.0 ± 21.8*</td>
<td>268.1 ± 17.6</td>
<td>247.4 ± 16.6</td>
</tr>
</tbody>
</table>

Values are means ± SE. V̇E, minute ventilation; V̇O₂, oxygen uptake; V̇CO₂, carbon dioxide production. All variables are calculated from 10 subjects, except for respiratory responses to SHG-30, in which entries are from 9 subjects.

Spontaneous baroreflex analysis (Table 1). Resting baroreflex sensitivity (BRS) values did not significantly differ among the three exercise trials. There were no significant changes in BRS, as estimated by the mean slope of spontaneous SAP/PI relationship, among rest, exercise, and PECO in SLE-15 and SHG-30 trials. That is, SLE-15 and SHG-30 trials resulted in a maintained baroreflex gain. On the contrary, SLE-30 resulted in a significant decrease in BRS. No significant differences in BRS were found between +PI/+ SAP and −PI− SAP sequences during the exercise as well as at rest. The mean slope of +PI/+ SAP and −PI− SAP sequences was 14.1 ± 2.5 vs. 13.6 ± 2.5 and 8.2 ± 1.4 vs. 7.8 ± 1.5 ms/mmHg during rest and PECO, respectively. The extent of resulted BRS decrease significantly related to the extent of PI decrease (r = 0.70, P = 0.02). There was no correlation between SAP values attained during SLE-30 trial and the corresponding baroreflex response slopes (r = 0.23, P = 0.53). During PECO, BRS recovered, and its value did not differ significantly from rest.

Respiratory responses to exercise and PECO (Table 2 and Fig. 1). All three exercise trials induced significant in-
Increases in ventilation, oxygen consumption (VO₂) and carbon dioxide excretion (VCO₂). The increase in VE induced by SLE-30 (10.3 ± 1.4 l/min) was significantly greater (P < 0.05) than that induced by both SLE-15 and SHG-30 trials (4.8 ± 0.8 and 4.6 ± 1.0 l/min, respectively), whereas VE response did not differ between SLE-15 and SHG-30 trials. A similar response pattern was observed for VO₂ and VCO₂. VO₂ increased by 273.3 ± 41.0, 149.8 ± 29.2, and 123.3 ± 12.0 ml/min during SLE-30, SLE-15, and SHG-30 trials, respectively [P < 0.05 for SLE-30 vs. both SLE-15 and SHG-30; P = not significant (NS) between SLE-15 and SHG-30]. Increases in VCO₂ in response to SLE-30, SLE-15, and SHG-30 trials were 46.7, 134.5, and 123.3 ml/min, respectively [P < 0.05 vs. rest]. The part of the pressor response that was maintained by PECO (i.e., by muscle metaboreflex) after SLE-30 and SHG-30 trials accounted for 88.3 ± 10.6 vs. 67.8 ± 12.7% (P < 0.02) of the overall MAP response (i.e., change from rest) attained during the respective exercise periods. No significant differences were found in the pressor responses between SHG-30 and SLE-15 trials, either during contraction or during the maintained muscle metaboreflex activation by PECO. Overall, these findings suggest that the pressor response elicited through the muscle metaboreflex is influenced by both the strength of contraction and the mass of active muscles. Because the muscle receptors are sensitive to the metabolic changes related to the muscle activity being performed, it can be hypothesized that during static contractions of higher intensity and larger muscle masses the amount of metabolites production is greater, with a consequent greater activation of the muscle metaboreflex. This suggestion is supported by the observation that TTI was significantly greater during SLE-30 than during both SLE-15 and SHG-30 trials and also by the significant linear relationship between TTI and MAP responses, as would be expected from a response determined by the metabolic demands of the active muscles (23), since tension is a result of metabolic processes.

Our findings and interpretation of a link between the size of muscle mass, a greater activation of muscle metaboreflex, and the magnitude of the exercise pressor response are in line with those of Seals (27, 28) of a greater increase in muscle sympathetic nerve activity (MSNA) during two- vs. one-arm SGH at 30% of MVC, with the difference being maintained during PECO. Gandevia and Hobbs (6), on the other hand, observed
that the pressor responses to posthandgrip circulatory occlusion increased in parallel with the intensity of contraction. Thus our results and those of others (6, 27, 28) support the concept that the relative contribution of muscle metaboreflex to the pressor response to static contractions is greater when larger muscle masses and higher intensities are involved in the exercise.

Other studies failed to show a mass dependency of the blood pressure response to static exercise (4, 15). These discrepancies may perhaps be explained by the different experimental protocols used in the above studies, which employed high-intensity, very brief contractions of one vs. both forearms (4) or rather small range of muscle masses (15), possibly minimizing the differences in muscle mass than anticipated. Williams (30) recently reported no significant difference in the pressor responses to high-intensity static exercises sustained to exhaustion between forearm and quadriceps muscles. However, in Williams’ study, the responses to forearm and leg exercises have been contrasted by comparing the absolute peak AP values attained during contractions. When looking at Table 1 of her paper, it appears that, if the pressor responses had been evaluated as changes from resting levels, a clear trend would have emerged for the pressor responses to be greater during leg than forearm exercise, with differences in MAP responses to leg vs. forearm exercises even greater than 20 mmHg.

We considered the possibility that our results could have been influenced by different degree of cardiopulmonary receptors stimulation during leg as opposed to forearm exercise. Ray et al. (25) reported in fact that, while SHG evoked an increase in MSNA, SLE performed at the same intensity in the sitting posture did not increase MSNA, possibly as a consequence of an increase in venous return induced by quadriceps (but not forearm) contraction that would result in a sympathoinhibitory effect from cardiopulmonary receptors. In the present study, regional sympathetic outflow and central venous pressure were not measured; however, leg exercise should have induced an increase in the overall sympathetic response for the pressor response to be greater during leg than forearm exercise, likely as a result of an overriding effect of the muscle metaboreflex on other inhibitory influences. The maintenance of a significant difference in the leg vs. forearm response during PECO supports this suggestion.

In the present study, HR behavior during forearm and leg static exercises paralleled that observed for blood pressure. Thus also the HR response to static exercise appears to be dependent on the size of contracting muscles. However, our interpretation regarding the link between muscle metaboreflex engagement and the magnitude of pressor responses cannot be extended to HR response, inasmuch as during PECO HR fully recovered to the resting levels. Our results on arterial baroreflex control of sinus node may offer an additional clue of interpretation of HR regulation during static exercise and PECO. Indeed, this is the first study that directly addressed the influence of muscle mass on the arterial baroreflex control of sinus node during static contraction and postexercise muscle ischemia. We found that during SLE-15 and SHG-30 trials BRS was unchanged compared with rest, whereas during SLE-30 BRS was significantly reduced, meaning that any baroreflex opposition to an increase in HR would be lessened. The decrease in BRS observed during leg, but not forearm, exercise performed at the same contraction intensity could, therefore, have been involved in the greater HR response to SLE-30 vs. SHG-30, and this, in addition to a greater engagement of muscle metaboreflex, could have contributed to the augmented pressor response to the large- vs. small-mass static exercise. The significant relationship between the magnitude of PI response and the magnitude of BRS decrease during SLE-30 would support this suggestion.

It has been recently hypothesized the arterial baroreflex is “reset” to higher operating point by the action of central command on the central neuron pool receiving baroreceptor afferents, thus permitting concomitant increases in HR and AP (2, 9, 11, 26). In line with this view is the maintained BRS observed during SLE-15 and SHG-30 trials. However, the fact that in the SLE-30 trial BRS was reduced during contraction and then restored during PECO suggests that during static exercise central command may act also by decreasing the gain of the integrated baroreceptor-cardiac reflex, depending on the combined effects of the intensity of contraction and the size of active muscle mass. The restoration back to the level at rest of BRS during PECO after SLE-30, at the time when the pressor response was maintained, would explain the return of HR to resting levels through a baroreceptor-cardiac reflex mechanism.

Respiratory responses. The respiratory responses to isometric contractions showed a pattern very similar to the cardiovascular responses, in that increases in VE and V̇O2 were greater during SLE-30 than during both SHG-30 and SLE-15 and not different between the latter two. Thus, as for the blood pressure and HR, also the respiratory responses to static exercise appear to be dependent on the size of active muscle mass. In these studies, which employed high-intensity, very brief contractions of one vs. both forearms (4) or rather small range of muscle masses (15), the respiratory response to handgrip was remarkably enhanced in comparison to leg extension, being about twice as much for the smaller than the larger exercising muscle mass; MAP response was also greater in the former than in the latter exercise. These findings might be indicative of an involvement of accessory muscles to sustain a target force that could have been rather strenuous for the forearm muscles. Indeed, in the same study, a muscle-mass dependency of both VE and V̇O2 response was observed when contractions were performed at a lesser intensity (i.e., 20% of MVC). Regrettably, the force development by the forearm and the quadriceps contraction was not reported. In our study, the force development was greater during SLE-30 than during SHG-30 trials, and a close relationship was found between TTI and VE. The same relationship was also found for V̇O2.
as would be expected from a response that has to meet the metabolic requirements of exercising muscles.

Unlike the pressor response, the maintained muscle metaboreflex activation by circulatory occlusion did not prevent \( V_\text{E} \) from returning to resting levels after SLE-15 and SHG-30 trials. On the contrary, during circulatory occlusion following SLE-30, \( V_\text{E} \) remained significantly elevated above rest, an observation that is consistent with an important ventilatory drive from chemosensitive muscle afferents stimulation. These findings indicate that the muscle metaboreflex mechanism may contribute to the hyperpnea of the static muscular contractions, but its involvement depends on the combined effects of higher contraction intensities and larger active muscle masses, resulting in a greater amount of metabolite production.

During PECO following SLE-30, \( V_\text{CO}_2 \) was still slightly greater than at rest (on average 89 ml/min). This persistent, albeit small, \( V_\text{CO}_2 \) excretion measured in the expired air has already been observed during circulatory occlusion after dynamic handgrip (24), and it is likely the result of a maintained \( V_\text{CO}_2 \) "washout" as a consequence of the hyperpnea driven by the persistent muscle metaboreflex stimulation (24).

The possibility that our findings could have been substantially influenced by the possible discomfort related to the circulatory occlusion seems unlikely because no subject reported feeling pain. Moreover, within the framework of the present study, circulatory occlusion per se should have not influenced the observed differences between SLE-15 and SLE-30 trials, since the mass of muscles made ischemic was the same.

In conclusion, we investigated the effect of muscle mass and contraction intensity on the cardiovascular and respiratory adjustments to static exercise and their underlying neural regulatory mechanisms. Overall, the results stress the importance of both these factors in effecting the magnitude of cardiorespiratory responses and the relative contribution afforded by the muscle metaboreflex and arterial baroreflex mechanisms. We emphasize that our findings should be regarded as strictly pertinent to static exercise and should not be generalized to large muscle groups or whole body dynamic exercises, in which peripheral and central hemodynamics and, as a consequence, the attendant regulatory mechanisms, may be markedly different.

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