Human carotid baroreflex during isometric lower arm contraction and ischemia

Spaak, Jonas, Patrik Sundblad, and Dag Linnarsson. Human carotid baroreflex during isometric lower arm contraction and ischemia. Am. J. Physiol. 275 (Heart Circ. Physiol. 44): H940–H945, 1998.—Our aim was to determine the roles of somatomotor activation and muscle ischemia for the tachycardia and hypertension of isometric arm contraction. Carotid-cardiac and carotid-mean arterial pressure (MAP) baroreflex response curves were determined in 10 men during rest, during isometric arm contraction at 30% of maximum, and during postcontraction ischemia. Carotid distending pressure (CDP) was changed by applying pressure and suction in a neck chamber. Pressures ranged from +40 to −80 mmHg and were applied repeatedly for 15 s during the three conditions. Maximum slopes and ranges of the response curves did not differ among conditions. The heart rate (HR) curve was shifted to a 14 ± 1.8 (mean ± SE) beats/min higher HR and a 9 ± 5.7 mmHg higher CDP during contraction and to a 14 ± 5.9 mmHg higher CDP during postcontraction ischemia with no change of HR compared with rest. The MAP curve was shifted to a 20 ± 2.8 mmHg higher MAP and to a 18 ± 5.4 mmHg higher CDP during contraction, and the same shifts were recorded during postcontraction ischemia. We conclude that neither somatomotor activation nor muscle ischemia changes the sensitivity of arterial baroreflexes. The upward shift of the MAP response curve, with no shift of the HR response curve during postexercise ischemia, supports the notion of parallel pathways for MAP and HR regulation in which HR responses are entirely caused by somatomotor activation and the pressor response is mainly caused by muscle ischemia.

MATERIALS AND METHODS

Subjects. Ten healthy men, with an average age of 24 (range 22–25) yr, weight 73.5 (60–96) kg, and height 1.79 (1.69–1.90) m volunteered for the study. All were nonsmokers, and none was currently taking any medication. They all had normal findings in a physical examination, normal resting electrocardiograms (ECG), and normal blood pressure. The experiments were performed either in the morning, 2 h after a light caffeine-free breakfast, or in the afternoon, 2 h after a light caffeine-free lunch. Ambient temperature ranged from 22 to 24°C, adjusted to the comfort of each subject. The subjects had given their informed consent for the protocol, and the experimental procedures had been approved by the Ethical Committee of Karolinska Institutet.

Carotid stimulation. Changes in the carotid sinus distending pressure (CDP) were generated by the application of positive or negative pressure in a lead neck chamber. The chamber encosed both sides and the front of the neck from the mandibular level to the sternum and clavicles (5). Each stimulation consisted of a 15-s period of constant (nonpulsatile) pressure or suction. Two levels of neck pressure (NP) (+20 and +40 mmHg) and four levels of neck suction (NS) (−20, −40, −60, and −80 mmHg) were applied. Pressures were generated by two vacuum cleaners, with one blowing and the other sucking air through a series of adjustable resistances. The pump system was installed in an adjacent room to eliminate acoustic noise. Carotid stimulations were controlled with the use of an R wave triggered circuit operating a large-bore three-way solenoid valve (type 323, 0363-6135/98 $5.00 Copyright © 1998 the American Physiological Society...
were ensemble averaged by using the instant of the onset of Linnarsson (32). Briefly, recordings from identical NS levels NP/NS stimulus was analyzed as described by Sundblad and the neck chamber pressure from MAP at the hydrostatic level fourth intercostal space. CDP was obtained by subtracting cuff and a point at the midaxillary line at the level of the section for the hydrostatic pressure difference between the finger section of MAP at the level of the heart. This included compensa-
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Cardiovascular measurements. An ECG was acquired from chest electrodes and a combined amplifier and beat-to-beat tachometer (Biotach ECG, model 20-4615-65, Gould, Valley View, OH). A continuous beat-to-beat recording of arterial blood pressure in the left-hand middle finger was obtained by using a photoplethysmographic device (Finapres 2300, Ohmeda, Englewood, CO). The Finapres provides continuous recordings of mean arterial blood pressure (MAP) in close agreement with concomitant invasive recordings (12).

Procedure. Each subject was seated comfortably in an armchair in a semireclining position, with the back of the seat tilted 10° backward. The experiment operator and the equipment were outside the view of the subject. The subject held a hand dynamometer (Vigorimeter, Martin, Tutlingen, Germany) in his lap in the right, dominant hand. Immediately upon the subject's arrival, the maximal contraction force was determined from three 2-s-long maximal voluntary contractions. A contraction force of 30% of maximum was used during subsequent tests.

Each subject performed six experimental sequences. There were 15-min resting periods between sequences. Each sequence included 3.5 min of rest, 2.5 min of isometric lower arm contraction, and 3 min of arterial arm occlusion with relaxed muscles (postcontraction ischemia). Each of the six sequences included eight NP/NS stimulations, with at least 60 s between stimulations: three baseline stimulations before the start of contraction, two NP/NS stimulations 45 and 105 s after the onset of contraction, and three NP/NS stimulations 30, 105, and 165 s after the onset of arterial occlusion. Occlusion was obtained by inflating a cuff around the upper arm, and when the cuff pressure reached 200 mmHg, the subject was instructed to relax his arm. Levels of NP/NS were varied in a pseudorandom mode so that, for each subject, each of the NP/NS levels was applied three times during precontraction and two times during contraction, and three times during postcontraction ischemia. The subjects reported a somewhat increased difficulty in maintaining the determined contraction force during the later sequences, but no subject failed to maintain the contraction throughout the contraction periods.

Data acquisition and analysis. Beat-to-beat heart rate (HR), continuous arterial blood pressure, and neck chamber pressure were recorded with a personal computer-based data collection system (Biopac Systems, Goleta, CA). The calibrated data were recorded at 100 Hz per channel and subsequently stored and analyzed with an AcqKnowledge 3.1 software package (Biopac Systems). Data were stored starting 10 s before and until 15 s after the end of each NS or NP stimulus.

Off-line computations included the beat-to-beat computation of MAP at the level of the heart. This included compensation for the hydrostatic pressure difference between the finger cuff and a point at the midaxillary line at the level of the fourth intercostal space. CDP was obtained by subtracting the neck chamber pressure from MAP at the hydrostatic level of the carotid sinus.

Each 40-s recording period before, during, and after a NP/NS stimulus was analyzed as described by Sundblad and Linnarsson (32). Briefly, recordings from identical NS levels were ensemble averaged by using the instant of the onset of the NP/NS stimulus for time alignment. Prestimulus control levels were determined as the average HR, MAP, or CDP levels during the 10 s before the stimulus. The peak or nadir of HR and MAP responses during each NP/NS period was determined from individual average time courses.

Baroreflex response curves for HR and for MAP were synthesized as follows. First, grand mean prestimulus baseline (prevailing) levels for HR, MAP, and CDP (21) were computed from all NS/NS sequences during each of the two conditions, rest and occlusion. During contraction, prevailing levels were based on conditions before the last NS/NS after 105 s of contraction. For each NP/NS level, peak or nadir changes of HR and MAP were added to or subtracted from the prevailing levels and plotted as a function of CDP.

Two types of baroreflex response curves were synthesized: 1) six-segment curves were obtained by interpolation between the NS/NP levels (Fig. 1) and 2) fitted logistic functions (Fig. 2) were determined as described by Kent et al. (13) using commercial software (Enzfitter 1.02, Elsevier-Biosoft, Cambridge, UK).

From the six-segment curves, the range, maximum slope, and optimum point were determined for each subject. Maxi-

![Fig. 1. Six-segment carotid baroreflex response curves. A: curves are linear interpolations between group mean values for mean arterial pressure (MAP, at level of the heart) responses to changes in carotid distending pressure (CDP) elicited by application of pressures of +40, +20, −20, −40, −60, and −80 mmHg in a neck chamber during rest, isometric lower arm contraction, and postcontraction ischemia (occlusion). Third data point from left for each curve represents prevailing MAP and CDP; i.e., with no external neck pressure. Open symbols represent estimated optimum points at which a given absolute CDP change will result in equal responses in both directions. Data are means ± SE; n = 10 subjects. B: responses of heart rate (HR) during same conditions as in A.](http://ajpheart.physiology.org/)
maximum slope was taken from the steepest segment in each curve, and the optimum point was estimated as a point on the interpolated curve halfway between minimum and maximum HR or MAP responses. The optimum point is defined by Sagawa (29) as the point of maximum slope, which also is the point at which a given absolute CDP change would result in equal HR or MAP responses in both directions. The present terminology has been adopted to avoid confusion between the terms optimum point (29) (also called operation point or center point) and prevailing point (21) (also called operational point).

The procedure used to fit logistic functions to individual baroreflex response curves did not result in convergence into unique, best-fit sets of fitting parameters for all subjects and conditions. Thus group mean curve parameters obtained from the interpolated curves were utilized to synthesize logistic curves roughly characterizing carotid-cardiac and carotid-MAP responses for the group. CDP values corresponding to threshold and saturation of the curves were computed as described by Chen et al. (3).

**Table 1. Baroreflex curve parameters**

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Contraction</th>
<th>Occlusion</th>
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<tbody>
<tr>
<td>HR prevailing, beats/min</td>
<td>73.1 ± 1.3†</td>
<td>85.6 ± 1.6‡</td>
<td>70.5 ± 1.4†</td>
</tr>
<tr>
<td>HR range, beats/min</td>
<td>17.6 ± 1.8</td>
<td>19.5 ± 1.9</td>
<td>22.4 ± 2.6</td>
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<tr>
<td>Max HR slope, beats·min⁻¹·mmHg⁻¹</td>
<td>−0.36 ± 0.04</td>
<td>−0.46 ± 0.04</td>
<td>−0.44 ± 0.05</td>
</tr>
<tr>
<td>CDP at optimum point, mmHg</td>
<td>72.7 ± 3.0‡</td>
<td>81.8 ± 4.4</td>
<td>87.1 ± 4.2*</td>
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<tr>
<td>HR at optimum point, beats/min</td>
<td>72.1 ± 3.1†</td>
<td>86.0 ± 3.9‡</td>
<td>70.9 ± 3.5*</td>
</tr>
<tr>
<td>CDP prevailing, mmHg</td>
<td>69.2 ± 1.0‡</td>
<td>89.5 ± 1.4‡</td>
<td>84.8 ± 1.0†</td>
</tr>
<tr>
<td>MAP prevailing, mmHg</td>
<td>81.6 ± 1.0‡</td>
<td>102.6 ± 1.4‡</td>
<td>97.2 ± 1.0†</td>
</tr>
<tr>
<td>MAP range, mmHg</td>
<td>17.5 ± 1.5</td>
<td>19.1 ± 1.5</td>
<td>17.0 ± 1.3</td>
</tr>
<tr>
<td>Max MAP slope, mmHg/mmHg</td>
<td>−0.39 ± 0.04</td>
<td>−0.47 ± 0.04</td>
<td>−0.36 ± 0.03</td>
</tr>
<tr>
<td>CDP at optimum point, mmHg</td>
<td>68.6 ± 5.7†</td>
<td>86.9 ± 3.4*</td>
<td>78.6 ± 3.2</td>
</tr>
<tr>
<td>MAP at optimum point, mmHg</td>
<td>82.5 ± 1.6‡</td>
<td>102.1 ± 2.6*</td>
<td>99.5 ± 2.2*</td>
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</tbody>
</table>

Data are means ± SE; n = 10 subjects. HR, heart rate; CDP, carotid distending pressure; MAP, mean arterial pressure; prevailing, pre-stimulus mean level; max slope, slope of steepest segment; optimum point, point of symmetry; contraction, lower arm contraction; occlusion, postcontraction ischemia. †Significantly different from rest; ‡Significantly different from contraction; *Significantly different from occlusion.
During occlusion, the carotid-cardiac response curve was displaced vertically compared with that during contraction, i.e., to the same HR level as during rest but to a 14-mmHg higher CDP level than during rest. At the same time, the carotid-MAP response curve was displaced horizontally to 8-mmHg lower CDP values compared with those during contraction.

**DISCUSSION**

The distinctive feature of this study was the definition of complete sets of curve parameters for arterial baroreflex response curves during both isometric arm contraction and postcontraction ischemia in humans. The changes of the hemodynamics induced by isometric arm contraction have been defined (for reviews see Refs. 6, 14, 26, and 28). Our contribution has been to define the optimum points of the arterial baroreflex response curves for HR and MAP, thereby enabling us to determine to what extent arterial baroreflex curves are shifted to the right along the CDP axis and upward in terms of HR and MAP responses and to determine that the maximum slopes were not changed. We also showed that the prevailing points were at or slightly below the optimum points and that arterial baroreflex sensitivity as defined by the maximum slope at the optimum points of HR and MAP was not altered compared with that during rest.

Limitations of study. Most of our subjects reported that they found it more difficult to maintain the required force during the final experimental sequences than during the first, and it is likely that the level of central command was increased accordingly. With the present randomization of the order of the neck chamber pressures, we assume that this effect of repetition had little or no effect on our results.

It is well established that isolated sinus preparations adapt more quickly to static than to pulsatile pressure changes (2). With the assumption that there was a similar difference between static and pulsatile NS/NP stimulations in humans, Papelier et al. (21) and Strange et al. (31) used pulsatile carotid sinus stimulations when studying responses to sustained stimulation. In the present study, however, we examined the initial, fast responses of HR and MAP, so the responses are not likely to be substantially reduced by the adaptation process. Also, the initial carotid sinus stimulation of the first stimulated systolic pulse wave will be the same for both modes of stimulation. This is probably why the HR response to nonpulsatile stimulations at a level of -60 mmHg (-7.1 ± 1.5 beats/min) did not differ significantly from the responses to a pulsatile stimulation with -50 mmHg under otherwise identical conditions (-9.1 ± 2.6 beats/min, unpaired t-test) in another group of subjects (32). In summary, therefore, we do not believe that our choice of nonpulsatile over pulsatile NS/NP critically influenced our results, especially because the same stimulation mode was used in the three conditions that were compared.

The neck chamber technique can only estimate open-loop relationships among CDP, HR, and MAP, whereas, at the same time, the system is closed-loop for aortic and cardiopulmonary baroreceptors. This is unavoidable in human research, but it is likely that the extracarotid baroreceptor contribution was similar during all three conditions, so we assume that this inherent limitation of the technique had little or no impact on our results.

Hemodynamic responses to isometric arm contraction and postcontraction ischemia. Hemodynamic responses to isometric arm contractions include concomitant tachycardia and elevated arterial blood pressure (1). There is an increase of muscle sympathetic nerve activity after the first minute (17, 30, 34) and a decreased radial artery diameter (20), suggesting vasoconstriction in important vascular beds. However, determinations of total peripheral resistance have shown no difference from resting control (23). This apparent paradox may be explained by passive widening of resistance vessels caused by the markedly elevated systemic arterial pressure as suggested by Eckberg et al. (5) and Olesen et al. (20). Thus one key component of the hemodynamic response to isometric arm contraction is an increase of cardiac output (23) equal in size to that of the MAP increase.

The rightward/upward shifts of the prevailing points for HR and MAP after >1 min of isometric arm contraction are in close agreement with the data from previous studies, in which experimental protocols have been similar. For example, the present responses of prevailing HR and estimated CDP are identical to those reported by Scherrer et al. (30) for both the contraction phase and the postcontraction ischemic phase. The same is true for the postcontraction ischemic phase of Pawelczyk et al. (23), whereas they reported less marked HR responses during the contraction phase, probably because they utilized a lower relative contraction force, 20% of maximum, than that used in the present study and by Scherrer et al. (30). One important commonality among these two cited studies and the present study is the finding of a combination of increased estimated CDP and a reduced HR during postcontraction ischemia compared with during rest.

An important underlying assumption for the present experimental design is that the occlusion of both arterial and venous circulation in one arm would not in itself cause a major shift in the dynamics of the systemic circulation but that the responses during that phase are secondary to an increased muscle chemoreflex compared with responses during rest or a maintained muscle chemoreflex stimulus compared with responses during isometric contraction. In the resting, euthermic man, <2% of cardiac output goes to one arm (26), and occlusion would not in itself cause any significant hemodynamic changes. During an isometric arm contraction at 30% of maximum force, muscle blood flow is arrested to such an extent that xenon-133 washout from a lower arm muscle does not differ from that under resting conditions (10). These observations are in support of the present experimental design, in which we consider data from postocclusion ischemia to represent the results of a muscle chemoreflex stimulus acting alone. It does not necessarily follow, however,
that the arithmetic difference between the responses to contraction and postcontraction ischemia is caused by the central command and/or mechanoreceptors in the contracting limb. Such a conclusion would only be justified if hemodynamic responses to muscle chemoreflex stimulation and somatomotor activation were additive, which cannot be assumed a priori. An analysis of the prevailing points for HR and MAP nevertheless supports the generally accepted notions (26) that somatomotor activation is the dominating factor behind the tachycardia and that muscle chemoreflex stimulation must be the dominant factor behind the hypertensive response during isometric arm contraction of the present intensity and duration.

Arterial baroreflex responses during isometric arm contraction and postcontraction ischemia. Although the most important stimuli behind the cardiovascular responses to muscle activity have been identified, the mechanisms by which central command, mechanoreflexes, and the muscle chemoreflex interact with other major afferent input such as arterial baroreceptor stimuli need to be elucidated. Ludbrook et al. (15) and Ebert (4) determined the slopes of both the hypotensive and hypertensive parts of the carotid-cardiac baroreflex response curve and found no differences between rest and isometric lower arm contraction. Other curve parameters were not analyzed, so it is not obvious from these studies whether the change toward higher HR and blood pressures represents an upward shift or a rightward shift, or both, of the arterial baroreflex response curves for HR and blood pressure. Also, it was not ascertained that the recorded slopes were the maximum slopes. To our knowledge, the full ranges of baroreflex response curves have not previously been characterized during both isometric lower arm contraction and postcontraction ischemia.

Effects of dynamic exercise and postexercise ischemia on arterial baroreflexes have been studied by Papelier et al. (22), who demonstrated a marked resetting toward higher blood pressures due to the ischemic postexercise stimulus, with no changes in baroreflex sensitivity in the control of HR but an increased sensitivity of MAP responses to hypertensive stimuli. These results, however, cannot be directly translated to isometric arm contraction. In the present analysis, differences in baroreflex control of HR and arterial pressure between contraction and postcontraction ischemia would primarily reflect differences in central command and mechanoreflexes, whereas inputs from muscle chemoreflex afferents would be similar. The same assumption cannot be made when comparing dynamic exercise with postexercise ischemia, because it is not probable that there exists a qualitatively similar ischemic stimulus (22).

Using the full-range baroreflex response curves, we have been able not only to define the slopes and the ranges of these curves but also to compare how the optimum points of these curves became shifted by combined somatomotor activation (central command and mechanoreceptors) and muscle chemoreflex stimulation compared with muscle chemoreflex stimulation alone.

Our major findings are that carotid-MAP baroreflex response curves were shifted to operate at higher CDP during both contraction (approximately +20 mmHg) and postcontraction ischemia (approximately +15 mmHg), with no apparent change in range or sensitivity. Carotid-cardiac chronotropic responses, however, were shifted during contraction but not in postcontraction ischemia, in which an unchanged baroreflex function, compared with that during rest, regulated HR to a level significantly lower than that during rest as a result of an elevated CDP. Thus it appears that neither somatomotor activation nor muscle chemoreflex afferent inflow changes the range and sensitivity of arterial baroreflexes, in general, and that the baroreflex is fully functional, although around higher levels of HR and MAP. The findings of rightward- and upward-shifted arterial baroreflex response curves with unchanged sensitivity have been hypothesized to be the result of a combination of an upward shift of target value, e.g., of HR, caused by somatomotor activation, in combination with a parallel generalized increase of sympathetic output caused by muscle chemoreflex afferent inflow (27).

Positions of prevailing points on baroreflex response curves. In resting man the prevailing points of HR and MAP are at the optimum point of the arterial baroreflex response curves (6, 29). Thus hypotensive and hypertensive carotid stimuli elicit approximately equal responses. Dynamic exercise, however, results in a shift of the position of the prevailing point upward and to the left of the optimum point (8, 25). Such a shift would be associated with reduced responses to hypotensive stimuli and might suggest that the baroreflex control of HR during dynamic exercise would be operating primarily against hypertensive deviations of CDP. This shift of operational point has been identified in the study of vagally induced HR responses to relatively brief (5–10 s) CDP perturbations (8, 25, 32). However, responses to more extended (≥20 s) CDP perturbations (21), which include both vagally and sympathetically induced chronotropic responses (33), have not shown such a shift in the position of the operational point on the baroreflex response curves. We determined the initial vagally induced HR responses to sudden baroreceptor loading and unloading. Thus our HR results should be compared with those obtained by Potts et al. (25), Sundblad and Linnaars (32), and Eiken et al. (8) rather than with those of Rose’s group (21, 22). Thus our observations suggest that there is a significant reserve of potential vagal withdrawal after 2 min of isometric arm contraction and under the influence of combined somatomotor activation and muscle chemoreflex stimulation. There are observations in support of the notion that the tachycardic response to isometric contraction is not due entirely to vagal withdrawal but may also be the result of increased sympathetic output to the heart. Martin et al. (18) and Hume et al. (11) observed that parasympathetic blockade with atropine eliminated the initial, rapid but not the late, tachycardic response. Pawelczyk
et al. (23), while studying normal subjects performing isometric handgrip under partial neuromuscular blockade, found elevated plasma norepinephrine concentrations during the contraction phase, but not during postcontraction ischemia, and concluded that the somatomotor activation influence on cardiac output may be directed by way of the sympathetic nerve system.

In conclusion, neither somatomotor activation nor ischemic stimuli appears to alter the sensitivity of arterial baroreflexes during isometric arm contraction in humans. Chronotropic responses do not appear to be influenced by muscle ischemia other than indirectly through the pressor response and the arterial baroreflex.

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