Effects of Isometric Exercise on the Carotid Baroreflex in Hypertensive Subjects

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SUMMARY Previous studies indicate that arterial baroreceptor modulation of heart rate is drastically reduced during static or dynamic exercise. We have investigated whether this reduction also occurs with regard to blood pressure modulation by the baroreflex. The study was performed in 19 subjects with uncomplicated untreated essential hypertension in whom blood pressure was measured intraarterially, and R-R interval was obtained by an electrocardiogram. The carotid baroreceptors were stimulated by neck suction of 30 seconds' duration, and equal stimuli were applied at rest and during hand-grip exercise performed at 40% of the subjects' maximal strength. Baroreceptor stimulation at rest increased R-R interval and reduced blood pressure. During hand-grip, the R-R interval responses to the baroreceptor stimulus were diminished by 61%. In contrast, the blood pressure responses were not significantly altered. Similar results were obtained when two subgroups of subjects with a lesser or greater degree of hypertension were separately considered. Thus, the carotid baroreceptor influence on blood pressure is largely preserved during exercise in contrast to the carotid baroreceptor influence on the sinus node, which is markedly impaired. (Hypertension 4: 245-250, 1982)

KEY WORDS • blood pressure • carotid sinus reflex • isometric exercise • essential hypertension • heart rate

SEVERAL studies in normotensive humans have shown that the reflex effects of arterial baroreceptor stimulation upon heart rate are drastically reduced and even abolished during dynamic or isometric exercise,1-5 thus suggesting that the arterial baroreflex is impaired under these circumstances. This suggestion has not been supported by other studies, however. Bevegard and Shepherd6 have observed that in normotensive subjects the hypotension induced by carotid baroreceptor stimulation is the same before and during dynamic exercise, and Ludbrook et al.7 have also reported this in normotensive subjects during isometric exercise, although the heart rate response is simultaneously markedly reduced.

There are two important implications in the studies above. First, the hemodynamic influences of arterial baroreceptors are modified in a complex fashion during exercise, those on the heart rate being impaired and those on the blood pressure being left unchanged. Second, since conditions may exist that affect baroreceptor influences on heart rate though not on blood pressure, measurements that are limited to heart rate responses to arterial baroreceptor manipulations may not be able to define under all circumstances the most important function of the baroreflex, i.e., blood pressure control. This is of practical interest as observation of heart rate changes in response to alterations in baroreceptor activity is the most widely used method for studying the arterial baroreflex in man.

So far there is no evidence on the comparative effect of isometric exercise on the arterial baroreceptor influence on blood pressure and heart rate in essential hypertension, a condition in which the baroreceptor control of both these variables is known to be markedly modified.5,10-14 We have investigated this point in the present study. Furthermore, we have extended the investigation to include the reverse condition, i.e., the influence of baroreceptor stimulation on the hemodynamic responses to exercise.
Methods

Our study was performed on 19 hospital inpatients, 12 men and seven women who ranged in age from 26 to 67 years. All patients had uncomplicated essential hypertension. None had been treated with cardiovascular drugs during the 3 weeks preceding the study. Each patient freely consented to the procedure after having had its nature and purpose explained.

Measurements

Pulsatile arterial blood pressure was measured by a catheter introduced percutaneously into a femoral artery (previous local anesthesia with 2\% procaine) and connected to a strain-gauge transducer (Statham P23 DC). Mean arterial pressure was obtained from the pulsatile signal both by electronic damping and by continuous integration of the tracing over consecutive periods of 10 seconds. A cardiotachometer was triggered by the R wave of an electrocardiogram. The tachometer display was calibrated as heart rate, and from the heart rate readings the heart interval (R-R interval) was recalculated in milliseconds. Reasons for choosing R-R interval as the most suitable index of chronotropic neural influences have been discussed by others.1

Hemodynamic Tests

In each subject the circulatory responses to isometric exercise and to stimulation of the carotid sinus baroreceptors were studied. These stimuli were applied both separately and in combination, as specified by the description of the protocol. Isometric exercise consisted of steadily gripping a spring with the right hand for 90 seconds. The strength of gripping was measured by a dynamometer and was always maintained at 40\% of the subjects' maximal strength, which was determined by two brief handgrips performed at the beginning and end of the study. Stimulation of the carotid sinus baroreceptors was obtained by the neck chamber technique, which has been described in detail.10 In brief, negative pneumatic pressure was applied all around the subjects' neck by means of a plastic tight collar connected to a vacuum cleaner. This procedure allowed tissue pressure outside the carotid sinuses to be altered in a negative direction (in the amount of 64\% of the externally applied suction), with a resulting increase in carotid transmural pressure and stimulation of carotid sinus baroreceptors beyond the existing level. As in previous studies,10,11 the neck suction was applied rapidly (90\% of the pressure change accomplished in less than 1 second) and was maintained constant for the selected time (see protocol), to be reversed at a similarly rapid rate. The magnitude of the applied neck suction was similar in the various subjects and identical in each subject throughout the study (see protocol).

Protocol

The study was made with the subjects supine and began with the introduction of the arterial catheter and the fitting of the collar. To study the effect of isometric exercise on the carotid baroreflex, neck suction of 30-second duration was applied both at rest and during handgrip exercise. This duration was selected to encompass the maximal heart rate and blood pressure effects from the carotid baroreceptor stimulation, which occur with our neck chamber at 5 to 15 seconds after application of the stimulus.12,13 The two maneuvers were applied in a variable order in the different subjects and were separated by an interval of 10 minutes.

We also examined the effects of carotid baroreceptor stimulation on the hemodynamic response to isometric exercise. To this aim the preceding tests were followed by two further handgrip exercises, one applied alone and the other superimposed on the steady-state hemodynamic reflex changes induced by a prolonged (about 3 minutes) neck suction. Also, these maneuvers were randomly performed in the various subjects following 10 minutes interval.

Data Analysis

The hemodynamic effects of carotid baroreceptor stimulation were calculated by averaging R-R interval and mean arterial pressure during the 10 seconds immediately preceding neck suction and during 5 to 15 seconds of neck suction. These calculations were done for neck suction of 30-second duration performed both at rest and during handgrip.

The hemodynamic effects of isometric exercise were calculated by averaging R-R interval and mean arterial pressure during the 10 seconds immediately preceding handgrip and during the last 10 seconds of this stimulus. These calculations were done for the handgrip performed alone and for the handgrip superimposed upon the continuous baroreceptor stimulation.

Data from single subjects were summed to obtain means ± SE for the whole group. Furthermore, data were summed to obtain means ± SE for two subgroups with a lesser and greater severity of hypertension, the dividing line being arbitrarily taken as the baseline value of a mean arterial pressure of 130 mm Hg. Statistical analysis was performed by t test for paired observations, and a p value of at least 0.05 was taken as the minimal level of statistical significance.

Results

Isolated Stimuli

The hemodynamic effects of neck suction alone are shown in figure 1 (continuous line) and the hemodynamic effects of handgrip alone are shown in figure 2 (continuous line). These effects were those expected from the data available in the literature. Neck suction caused a reduction in mean arterial pressure and a lengthening of the R-R interval.13,16 whereas both these variables showed respectively a marked increase and a shortening during handgrip.16
EXERCISE AND BAROREFLEXES IN MAN/Mancia et al

FIGURE 1. Reduction in mean arterial pressure and increase in R-R interval induced by stimulating the carotid baroreceptors at rest and during handgrip. Data are shown as means ± se from 19 subjects with essential hypertension. The stimulus to the carotid baroreceptors was provided by a reduction in neck tissue pressure outside the carotid sinuses of 28.5 ± 1.6 mm Hg at rest and of 29.4 ± 1.9 mm Hg during handgrip. C = control, BS = during baroreceptor stimulation by neck suction.

Neck Suction Superimposed Upon Handgrip

When neck suction was applied while the patients were performing the handgrip exercise, the lengthening of the R-R interval was significantly and markedly reduced as compared to the response observed when neck suction was performed at rest (fig. 1 and 3). For the whole group of subjects the average lengthening in R-R interval induced by this maneuver was 59.9 ± 12 msec during handgrip as compared to 142 ± 29 msec at rest, which amounted to a 59% reduction of the response.

On the other hand, the fall in blood pressure induced by neck suction was largely preserved during handgrip. For the whole group of subjects the average fall induced by this maneuver during handgrip was 15.9 ± 2.3 mm Hg. This value was slightly but not significantly reduced from the average blood pressure fall of 18.7 ± 2.1 mm Hg that was observed by application of neck suction at rest.

Table 1 shows the average effects of neck suction at rest and during handgrip separately calculated from the two subgroups of patients with hypertension of lesser or greater severity. The results in these subgroups reproduced what has been described for the whole group of subjects. That is, during handgrip the lengthening in R-R interval induced by neck suction was markedly and significantly reduced in the moderate and more severely hypertensive subjects,
Table 1. Hemodynamic Effects of Carotid Baroreceptor Stimulation Performed Alone and Superimposed Upon Handgrip in Moderate and More Severe Hypertension

<table>
<thead>
<tr>
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<th>Moderate hypertension (n = 10)</th>
<th>More severe hypertension (n = 9)</th>
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<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Change</td>
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<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No handgrip</td>
<td>110.5 ± 4.3</td>
<td>-16.7 ± 1.6</td>
</tr>
<tr>
<td>During handgrip</td>
<td>132.3 ± 6.3</td>
<td>-14.9 ± 1.6</td>
</tr>
<tr>
<td>R-R interval (msec)</td>
<td>700 ± 23</td>
<td>127 ± 28</td>
</tr>
<tr>
<td>No handgrip</td>
<td>539 ± 29</td>
<td>64 ± 21</td>
</tr>
<tr>
<td>During handgrip</td>
<td>688 ± 42</td>
<td>159 ± 55</td>
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</tbody>
</table>

Data are shown as means ± SE. The carotid baroreceptors were stimulated by reducing tissue pressure outside the carotid sinuses by 33.1 ± 2.1 mm Hg in the moderate and by 27.1 ± 2.4 mm Hg in the more severe hypertensive subjects.

whereas the blood pressure fall was not significantly affected in either case.

The results were further analyzed by separately considering two subgroups of subjects according to whether they were older or younger than 42 years (mean age of the two groups was 50.1 ± 2.4 and 34.0 ± 2.3 years). In the older group the reductions in mean arterial pressure induced by baroreceptor stimulation were 21.1 ± 3.6 mm Hg before and 19.4 ± 3.7 mm Hg during handgrip exercise whereas the respective increases in R-R interval were 159 ± 48 and 53 ± 6 msec. In the younger group, the baroreceptor-induced reductions in mean arterial pressure before and during handgrip were 16.3 ± 1.7 and 12.0 ± 2.0 mm Hg, whereas the increase in R-R interval under the two circumstances were 124 ± 33 and 9 ± 3 msec respectively. Thus, the alteration in the baroreflex responses induced by handgrip was similar in the older and the younger subjects.

Handgrip Superimposed Upon Neck Suction

As shown in figure 2, in the whole group of subjects the pressor responses to handgrip were not significantly different when this maneuver was performed in the absence of or during a continuous baroreceptor stimulation induced by neck suction. On the other hand, the handgrip induced shortening in R-R interval was significantly greater during baroreceptor stimulation than before.

Table 2 shows the average effects of handgrip before and during neck suction in the two subgroups of moderate and more severe hypertensive subjects; they were similar to those described for the whole group. The increase in blood pressure induced by handgrip was similar in the two conditions whereas the reduction in R-R interval was significantly greater when handgrip was performed during than in the absence of baroreceptor stimulation.

Table 2. Hemodynamic Effects of Handgrip Performed Alone and During Carotid Baroreceptor Stimulation in Moderate and More Severe Hypertension

<table>
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<tr>
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<th>Moderate hypertension (n = 10)</th>
<th>More severe hypertension (n = 9)</th>
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<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Change</td>
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<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No baroreceptor stimulation</td>
<td>108.8 ± 4.2</td>
<td>27.8 ± 3.4</td>
</tr>
<tr>
<td>During baroreceptor stimulation</td>
<td>93.4 ± 4.4</td>
<td>29.7 ± 2.9</td>
</tr>
<tr>
<td>R-R interval (msec)</td>
<td>696 ± 21</td>
<td>-157 ± 15</td>
</tr>
<tr>
<td>No baroreceptor stimulation</td>
<td>739 ± 38</td>
<td>-208 ± 32.6</td>
</tr>
<tr>
<td>During baroreceptor stimulation</td>
<td>0.05</td>
<td>0.05</td>
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</tbody>
</table>

Data are shown as means ± SE. The carotid baroreceptors were stimulated at rest by reducing tissue pressure outside the carotid sinuses by 30.6 ± 2.0 mm Hg in moderate and by 26.3 ± 2.3 mm Hg in more severe hypertensive subjects. The respective reductions in tissue pressure during handgrip were 32.0 ± 2.5 mm Hg and 26.4 ± 2.6 mm Hg.
Discussion

In our essential hypertensive subjects the reflex lengthening of R-R interval that was induced by carotid baroreceptor stimulation was reduced by about two-thirds during isometric exercise whereas the simultaneous reflex fall in blood pressure was slightly but not significantly affected. This was the case when subjects with either moderate and more severe hypertension were considered. It was also the case when subjects of either younger or older age were separately analyzed. From these results we conclude that, in hypertensive as well as in normotensive subjects, isometric exercise can impair the arterial baroreflex but that this impairment is limited to the influence of baroreceptors on the sinus node and does not involve more than to a slight extent the influence these receptors exert on blood pressure.

It should be emphasized that this differential effect on the cardiac and blood pressure components of the baroreflex should favor a proper circulatory adjustment during exercise both by leaving the exertional tachycardia unopposed (thus unopposing the increase in cardiac output and the perfusion of working muscles) and by simultaneously counteracting a blood pressure rise.

The mechanisms by which isometric exercise impairs the baroreceptor influence on heart rate but not on blood pressure has not been clarified. However, data obtained not only in human but also in animal studies allow discussion of some hypotheses. It may be suggested that during exercise the increase in central venous pressure stimulates atrial receptors that are involved in the production of tachycardia (the so-called Bainbridge reflex) and that this stimulation selectively counteracts the inhibitory influence of the arterial baroreceptors on the sinoatrial node. This is an unlikely hypothesis, however, as in humans no reduction in the bradycardic response to arterial baroreceptor stimulation has been reported following increase in central venous pressure. Likewise, it is unlikely that baroreceptor modulation of the sinus node is reduced during exercise because of the counteracting influence of excitatory reflexes originating in active skeletal muscles. These reflexes are important for the induction of exercise tachycardia but their activation in animals has not been found to reduce the sensitivity of the arterial baroreflexes.

A third more likely hypothesis is that of a selective effect of central influences on the cardiac and blood pressure components of the baroreflex. This hypothesis is supported by both human and animal studies. Human studies have shown that a central command plays an important role in determining the cardiovascular pattern of isometric exercise and that this role includes reduction of baroreceptor influence on heart rate. Furthermore, studies in animals have shown that engagement of hypotalamic areas involved in the defense reaction (a behavior which in animals has a prominent exercise component) drastically reduces the baroreceptor control of heart rate while leaving the control of several systemic vascular areas unaffected.

Some of these studies have further shown that this may depend on the ability of these influences to affect the vagus centrally (on which heart rate control largely depends) while leaving the sympathetic neurons (in which blood pressure regulation depends) unaffected. It cannot be excluded, however, that preservation of baroreceptor effects on blood pressure during exercise is determined at the effector site. For, at the higher blood pressure level that characterizes this condition, an increased diameter makes the vessels capable of normally altering their resistance even in response to a reduced reflex modulation.

Two further comments can be added. The first comment is related to the results we have obtained when the order of the stimuli was reversed, that is, when carotid baroreceptor stimulation was applied first with the later superimposition of handgrip. It is well known that the type and the extent of the interaction between two sets of stimuli may be largely modified by the sequence of their application. For stimuli that affect the cardiovascular system, this is best exemplified by the different reflex effects that can be obtained by differently combining carotid baroreceptor and chemoreceptor stimuli, each being capable of prevailing upon the other when applied first. We found that the order of application did not seem to matter for the isometric exercise and the carotid baroreflex, however, as the cardiovascular effects of the former stimulus were unchanged or even augmented when applied on the background of a carotid baroreceptor activation. Thus isometric exercise appears capable of affecting the carotid baroreflex (as far as its heart rate component is concerned) with no reciprocal influence from the baroreflex itself.

The second comment refers to the question asked in the introduction, i.e., whether methods that only measure baroreceptor influences upon heart rate can be always used to define the sensitivity of the whole baroreceptor reflex and, most important, of its blood pressure control. The evidence presented in our study suggests that this question should receive a negative answer, as conditions exist in which baroreceptor control of heart rate and blood pressure do not undergo similar alterations. We have shown evidence that one of these conditions might be essential hypertension and it is interesting to speculate whether, as it seems to happen during exercise, central factors are involved.

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