Effect of exercise on gain of the carotid-sinus reflex in rabbits

I. B. FARIS, G. G. JAMIESON AND J. LUDBROOK

Department of Surgery, University of Adelaide, Adelaide, South Australia, Australia

(Received 16 December 1981; accepted 24 March 1982)

Summary

1. Blood pressure, heart rate and cardiac output were measured in six rabbits before, during and immediately after treadmill exercise. During the same periods the dynamic gain of the carotid-sinus baroreceptor reflex was estimated by creating a sinusoidal oscillation of carotid-distending pressure.

2. The average blood pressure did not change significantly during or after exercise, but heart rate and cardiac output rose markedly and there was a concomitant fall in systemic vascular resistance.

3. The reflex gain for blood pressure decreased by one-fifth during exercise, and the gains for heart rate and vascular resistance by two-fifths. Immediately after exercise the gains for all three variables decreased further, to between one-half and one-third of the resting values.

4. Our results indicate that during and after dynamic exercise the correction of a potential disturbance of blood pressure by the carotid-sinus baroreceptor reflex is decreased in magnitude or in speed.

Key words: baroreflex, blood pressure, carotid, exercise, heart rate, sine wave, rabbit, vascular resistance.

Introduction

The question whether control of the circulation by the arterial baroreceptors is impaired during exercise has not been fully answered, partly because it is so difficult to study the performance of the arterial baroreceptor reflex in the conscious state. One approach has been to test reflex control of heart rate by measuring the bradycardia that occurs when blood pressure is transiently elevated by the injection of vasopressor drugs. This baroreceptor–heart-rate reflex is reported to be depressed in dogs when they are running [1], and in man when he performs isometric exercise or stationary bicycling [2]. Another approach has been to use a variable-pressure neck chamber in man to load or unload the carotid baroreceptors. Using this technique we confirmed that isometric handgrip markedly decreased the bradycardic response to loading the baroreceptors, but found that the opposite, tachycardic, response to carotid baroreceptor unloading was unaffected [3]. It has been suggested that these effects of exercise on the reflex control of heart rate are caused, at least in part, by interaction between the exercise stimulus and the central-nervous pathway of the baroreceptor reflex [1, 2, 3].

However, the control of blood pressure during exercise is of greater interest than that of heart rate. The variable-pressure neck chamber has also been used to study this. Bevegard & Shepherd [4] reported that supine bicycling exercise did not diminish the fall in blood pressure caused by carotid baroreceptor loading. We later found that isometric handgrip did not affect the responses of blood pressure either to loading or unloading the carotid baroreceptors [5]. However, these observations do not permit the general conclusion that reflex control of blood pressure is unimpaired by exercise. A defect of the neck-chamber method is that the carotid-sinus reflex may be buffered by the aortic baroreceptors. In the case of dynamic exercise, only the capacity of the reflex to resist a rise of blood pressure has been examined [4]. Single submaximal alterations in carotid-distending pres-
sure do not examine the full range of the sigmoidal stimulus–response relationship [6].

In the present study we have made use of a method for eliciting the carotid-sinus reflex in conscious rabbits [7] to examine the effects of dynamic exercise on reflex control of blood pressure, heart rate and peripheral resistance. The method allows the reflex to be examined over a wide range of carotid-distending pressures, and without there being a buffer effect from other arterial baroreceptors. In order to obtain maximum information about the reflex under the difficult experimental conditions of exercise, we have studied its dynamic [8], rather than its steady-state, characteristics.

Methods

Six New Zealand White rabbits were used in these experiments, aged 17–25 weeks and each weighing 2.5–3.0 kg. A fluid-filled capsule [7], within which the pressure could be altered so as to produce bidirectional and quantifiable changes in carotid sinus transmural pressure, had been implanted around one carotid bifurcation 4–6 weeks earlier. At the same time the opposite carotid sinus was denervated and both aortic nerves were divided. An electromagnetic flow probe (Biotronex 5050) had been placed around the ascending aorta 2–3 weeks earlier. The operations were performed under halothane anaesthesia, after induction with intravenous propranidid and endotracheal intubation. At the time of the experiment all rabbits were gaining weight. Their median haematocrit was 32.4% (range 31.1–33.8%).

On the day of the experiment a catheter was inserted into the central artery of the ear on the side opposite to the capsule, to measure blood pressure. A needle was inserted through the skin into the carotid capsule and anchored there by means of a suture. These procedures were performed under local analgesia (1% lignocaine hydrochloride). The intracapsular needle was connected through a pressure transducer to a reservoir of sterile 0.9% NaCl within which the pressure could be varied by means of a sine-wave generating pump. In two rabbits right-atrial pressure was measured by way of a catheter inserted through the external jugular vein [9]. All pressure measurements were made with strain-gauge transducers (Statham P23DC), the zero levels being 50 mm above the surface on which the rabbit stood.

Ascending aortic flow was measured by connecting the flow probe to a meter (Biotronex BL-612). End-diastolic flow was taken as zero, and this baseline was monitored on an oscilloscope. Beat-to-beat heart rate was measured by connecting a tachometer to the ascending aortic flowmeter. The cardiovascular variables were displayed on a Grass model 7 polygraph, and 2 s mean values were obtained by integration. The 2 s means comprised heart rate (HR), blood pressure (BP), cardiac output (CO) and intracapsular pressure. Mean systemic vascular resistance (SVR) was calculated as \( \frac{BP}{CO} \), and carotid-sinus transmural pressure (CSTMP) as \( \frac{BP}{intracapsular pressure} \).

The carotid-sinus baroreceptor reflex was elicited by effecting sinusoidal pressure changes within the intracapsular fluid that were symmetrical with respect to zero, at a frequency of 0.02 Hz. These created sinusoidal changes in carotid-sinus transmural pressure of median amplitude 97 mmHg (range 77–113 mmHg) under resting conditions, from which dynamic gain (G) was calculated as \( \frac{output amplitude of the dependent variable}{input amplitude of CSTMP} \) [8]. A continuous check was made that the intracapsular needle was patent by displaying the pulsations transmitted from the carotid bifurcation on an oscilloscope. Carotid-body chemoreceptor stimulation can occur in the rabbit when carotid-body perfusion pressure falls below about 20 mmHg [7, 10]. The amplitudes of the driving sine waves were selected to avoid this. For all rabbits and all states the lowest carotid transmural pressure (and hence carotid-body perfusion pressure) reached was 25 mmHg.

The rabbit was placed on an endless-belt treadmill, within a restraining enclosure. The carotid-sinus reflex was first elicited at rest, and then the treadmill was run at 13 m min\(^{-1}\), which was the maximum speed at which we found the rabbit would run repeatedly. The sinusoidal pressure changes in intracapsular pressure were instituted while the rabbit was at rest. They were continued while the treadmill ran for 70–120 s and, except in one case, for 160–210 s after it was stopped. The calculations of dynamic gain were made by analysing full sine waves immediately before exercise, after 75 s (range 40–85 s) of exercise when the circulatory changes were maximal, and 80 s (range 70–90 s) after the exercise had finished. At these same times the values of the cardiovascular variables were averaged over a whole cycle, to indicate the effects of exercise itself on the circulation. A 5–10 min rest was allowed before the next period of exercise. The sequence was repeated until two satisfactory sets of results were obtained, which were averaged.

Distribution-free methods of data analysis
were used, because the sample size was small and the sample distribution was sometimes skewed. The central tendency of each set of measurements in the six rabbits is expressed as the median, calculated as the mid point between the third and fourth ranked values. The corresponding range is given in parenthesis. Comparisons between the resting, exercise and post-exercise recovery states were made by the Friedman two-way analysis of variance \((n = 3, 6)\), the one set of missing values in the post-exercise period being entered by interpolation. Associations were tested for by calculating the Spearman rank-order correlation coefficient \(r_s\).

**Results**

Blood pressure did not consistently change over the resting, exercise and post-exercise periods (Table 1 and Fig. 1), because, although there was a marked increase in cardiac output, this was matched by a fall in systemic vascular resistance. Heart rate was consistently elevated in the exercise and post-exercise recovery periods. In the two rabbits in which it was measured, right-atrial pressure rose sharply by 3–5 mmHg at the commencement of exercise, and returned rapidly to normal in the recovery period.

Over the resting, exercise and recovery periods (Fig. 2) there was a consistent and progressive fall of the dynamic gain for heart rate, blood pressure and systemic vascular resistance. The median percentage falls in \(G_{BP}\) during the exercise and recovery periods were respectively 22% and 50%. The corresponding falls in \(G_{SVR}\) were 41% and 53%, and in \(G_{HR}\) were 44% and 67%. When results for the exercise and recovery periods were pooled there was found to be a close association between the percentage change in \(G_{BP}\) and \(G_{SVR}\) \((r_s = 0.555, P > 0.05)\).

**Discussion**

The novel feature of these experiments is that the control of blood pressure and peripheral resistance by the carotid baroreceptor reflex was examined during dynamic exercise. Despite the difficulties of making rabbits run in a laboratory setting, and of making measurements that were relatively free from artifact, the findings were quite clear-cut. There was a modest decrease in gain of the carotid reflex with respect to blood pressure during exercise, which became more

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**TABLE 1.** Values for heart rate (HR), blood pressure (BP), systemic vascular resistance (SVR) and cardiac output (CO), at rest, after 75 s of exercise, and 80 s after the completion of exercise (recovery), obtained by averaging over a full sine-wave cycle

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise</th>
<th>Recovery</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats min(^{-1}))</td>
<td>267 (230–285)</td>
<td>296 (285–345)</td>
<td>292 (272–325)</td>
<td>0.0081</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>85 (78–98)</td>
<td>91 (85–111)</td>
<td>91 (81–114)</td>
<td>0.43</td>
</tr>
<tr>
<td>SVR (mmHg ml(^{-1})min(^{-1})kg(^{-1}))</td>
<td>0.48 (0.42–0.52)</td>
<td>0.33 (0.27–0.41)</td>
<td>0.39 (0.32–0.51)</td>
<td>0.0081</td>
</tr>
<tr>
<td>CO (ml min(^{-1})kg(^{-1}))</td>
<td>189 (163–210)</td>
<td>273 (250–298)</td>
<td>227 (222–259)</td>
<td>0.00013</td>
</tr>
</tbody>
</table>
apparent shortly after it ceased (Fig. 2). There was a closely associated loss of gain for systemic vascular resistance. This is in keeping with the observation that it is chiefly alterations in vascular resistance, rather than in cardiac output, that cause the changes in blood pressure that are evoked by the carotid-sinus reflex [11].

The changes in dynamic gain that we observed require further interpretation. First, in our measurements of gain the carotid baroreceptors were effectively disconnected from the rest of the circulation. However, gain for blood pressure measured under these artificial conditions does predict the capacity of the carotid-sinus reflex to prevent perturbations of blood pressure in the intact animal [12]. Secondly, a feature of causing carotid-sinus pressure to oscillate in a sinusoidal fashion is that the reflex responses are out of phase with the stimulus. At the sine-wave frequency used in the present experiments we have found [8] that heart rate follows the stimulus closely, but that blood pressure lags 4–5 s behind it. This inertia resides in the sympathetic vasoconstrictor component of the reflex arc [13]. Moreover, there is an inverse association between phase-lag and the magnitude of dynamic gain for blood pressure [8]. Therefore dynamic gain, as opposed to the more conventional steady-state gain, also provides an indication of how quickly a disturbance of blood pressure will be corrected. Thus our results indicate that during and after dynamic exercise a potential disturbance of blood pressure, such as may be caused by the exercise stimulus or its withdrawal, will be less completely or more slowly corrected.

Our conclusion that the control of blood pressure in the rabbit by the carotid baroreflex is impaired during dynamic exercise differs from that of Bevegård & Shepherd [4] in man. However, they studied only the steady-state responses of blood pressure to a step increase in carotid-distending pressure. Our measurement of dynamic gain involved both loading and unloading the carotid baroreceptors, and dynamic gain is dependent on both the magnitude and the speed of the blood-pressure response. It is therefore likely to be a more sensitive indicator of impairment of reflex control. Our present findings are also at variance with our earlier observations in man [5] that the control of blood pressure was unaffected by static handgrip. During isometric handgrip in normal subjects there is an increase in cardiac output, but only inconstant changes in systemic vascular resistance [14, 15, 16]. During and after treadmill exercise in the present experiments there was a marked fall in systemic vascular resistance (Table 1), consistent with metabolically induced vasodilatation in the exercising muscles. It has been shown that in an isolated preparation of skeletal muscle the action of the sympathetic nerves on resistance vessels is impaired by exercise [17]. Thus the depression of gain for vascular resistance, and hence blood pressure, that we observed in the present experiments is as likely to be due to a local effect at the level of the sympathetic neuro-effector apparatus as to an effect of the exercise stimulus on the baroreflex pathway within the central nervous system. Nevertheless, although carotid reflex control of blood pressure was impaired by treadmill exercise, it was far from completely lost. This supports the reports that sino-aortic denervation in dogs produces a recognizable disturbance of blood-pressure control during exercise [18, 19], rather than the conclusion that it does not [1].
We found a loss of carotid-reflex control of heart rate during exercise, just as has been observed for the baroreceptor—heart-rate reflex elicited by injecting vasopressor drugs [1, 2]. Although this phenomenon is consistent with the effect of volitional command on the control of heart rate by the baroreflex that we demonstrated during isometric handgrip [3], an alternative explanation is necessary to explain the persistence of the effect into the post-exercise recovery period. The pronounced tachycardia that occurs during and after exercise makes it observed for the baroreceptor-heart-rate reflex recovery period. The pronounced tachycardia native explanation is necessary to explain the response relationship.

The changes in gain for blood pressure and heart rate are depressed without there necessarily having been a genuine alteration in the overall stimulus—response relationship.

We observed only a weak association between the changes in gain for blood pressure and heart rate. This is not surprising, in view of the different sets of autonomic preganglionic neurons that are responsible for baroreceptor control of heart rate and blood pressure. In conscious man and animals carotid baroreceptor control of heart rate is effected chiefly by changes in vagal drive [20], whereas control of blood pressure is chiefly by changes in sympathetic constrictor drive to resistance vessels [11, 20]. Thus in exercise, as in other physiological and pathological states [21], it is unwise to suppose that alterations in baroreceptor control of heart rate reflect accurately alterations in control of blood pressure.

Acknowledgments

This work was supported by the National Health and Medical Research Council of Australia. We thank Mr John Iannos, B.Sc., and Miss Jennifer Ryan for their technical assistance.

References


