Role of arterial baroreceptor function on cardiovascular adjustments to acute and chronic dynamic exercise

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Our series of experiments in rats, and other data of the literature, indicate that the arterial baroreceptors are actively involved in the reflex control of circulation during acute and chronic exercise. Although heart rate increases simultaneously with arterial blood pressure during an acute bout of dynamic exercise, the gain of the baroreflex bradycardia remains unchanged. Moreover, the more pronounced increase in mean arterial pressure during all exercise period observed in sino-aortic denervated rats, compared to sham-operated rats, suggests that the arterial baroreflex restrains the increase in blood pressure during dynamic exercise. However, the arterial baroreflex seems to have no influence on the development of exercise tachycardia. Exercise training can affect baroreflex bradycardia and tachycardia in the opposite direction, since decreased baroreflex bradycardia is observed despite increased baroreflex tachycardia. Since the increased baroreflex tachycardia may be attributed to an increased sensitivity of the afferent pathway of the baroreceptors, the attenuation of the baroreflex bradycardia is probably due to an impairment of the efferent pathway of the reflex. Finally, the decreased tonic sympathetic nerve activity produced by exercise training can be considered as one of the mechanisms involved in the attenuation of hypertension induced by exercise training.

Key terms: *arterial pressure, baroreceptor, baroreflex, cardiovascular adjustments, circulatory reflexes, dynamic exercise, heart rate*

INTRODUCTION

Dynamic exercise requires substantial cardiovascular adjustments to maintain optimal oxygen delivery to exercising muscle. The cardiovascular response to exercise is characterized by an increase in arterial blood pressure (BP), which is very important to maintain blood flow to critical areas such as the heart and brain, as well to satisfy the requirements of the working muscles and skin. There is a large fall in peripheral resistance due to metabolic vasodilatation in active muscle, but BP is increased due to the large increase in cardiac output and also the vasoconstriction in nonworking tissues (6, 18). To achieve all these responses, BP needs to be

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continuously regulated by the central control of the cardiovascular areas, through a complex interaction between signals arising from chemosensitive and mechanosensitive afferent nerve fibers in the active muscle and arterial baroreceptors, and also from central areas of the brain (central command).

This review deals specifically with the role of arterial baroreceptor function on cardiovascular adjustments to acute and chronic dynamic exercise. In the first part, the role of the arterial baroreflex during an acute bout of exercise will be discussed in terms of: *i*- sensitivity of arterial baroreflex during such exercise, and *ii*- arterial baroreflex contribution to the cardiovascular response to exercise. In the second part of this review, the effect of exercise training on the sensitivity control of arterial baroreflex of heart and sympathetic nerve activity will be analyzed.

ARTERIAL BAROREFLEX FUNCTION DURING AN ACUTE BOUT OF DYNAMIC EXERCISE

The arterial baroreflex, the major controller of BP, has a high gain and responds rapidly to perturbation in BP (16). Under normal conditions, the baroreflex is effective in minimizing fluctuations of the mean arterial pressure (MAP) around its operating point. Although this function of the reflex has been widely studied under different physiological conditions, the role of arterial baroreflex during an acute bout of exercise is not yet well established. Two major questions need to be addressed: 1) Does the baroreflex buffer BP fluctuations as effectively during exercise as at rest; 2) Does the arterial baroreflex contribute to the cardiovascular response during exercise?

Baroreflex sensitivity during dynamic exercise.

The elevation in BP observed during exercise is accompanied by increased heart rate (HR), and not by bradycardia. This has been used as evidence to support the concept that the arterial baroreflex is

"turned off" during exercise. Although some investigators still report that the reflex influences of arterial baroreceptors are abolished or blunted at the onset of exercise (5, 21, 28), more recent data support the contention that they are actively involved in the reflex control of circulation during exercise (20, 27, 30).

We evaluated the sensitivity of the baroreflex bradycardia at rest and during two different exercise intensities in normotensive rats (25). The sensitivity of baroreflex bradycardia was studied by measuring the changes in HR in response to transient drug-induced increases in BP. On the first day of the experiment, increasing doses of phenylephrine (iv) were injected at rest. One day later, a single dose of phenylephrine was injected during exercise performed at 0.5 and 0.8 miles·h⁻¹. To compare the sensitivity of baroreflex bradycardia during exercise with that at rest, we used a similar increase in MAP in both situations. The baroreflex index was calculated using the average values of all ratios of changes in HR and MAP (ΔHR/ΔMAP). The calculated baroreflex indexes at 0.5 and 0.8 miles·h⁻¹ were similar to those observed at rest (-1.45 ± 0.3 and -1.48 ± 0.3 *vs* -1.41 ± 0.1 beats·min⁻¹·mmHg⁻¹, respectively) (Fig 1). These data indicate that the arterial baroreflex is equally effective during rest and exercise.

In the above context, Melcher and Donald (20) have studied carotid sinus stimulus-response curves relating BP to
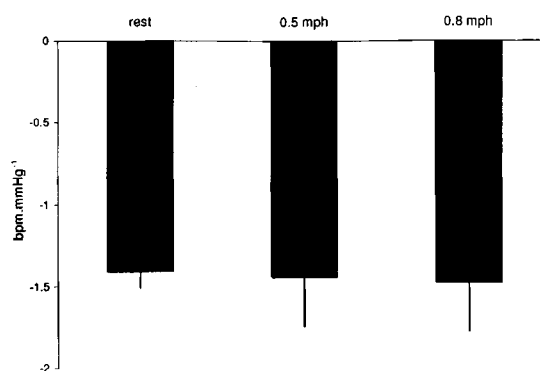
Fig 1. Baroreflex bradycardia analyzed by the relationship HR/MAP at rest and during exercise (0.5 and 0.8 miles·h⁻¹) in normotensive Wistar rats (n = 10). Data presented as means ± SEMs. One way ANOVA.

carotid sinus pressure (CSP) generated by controlling pressure within surgically isolated sinuses, in resting and exercising dogs. Exercise caused no alteration in the shape (slope or gain) of stimulus-response curves. The entire curve was simply shifted vertically so that BP was higher at any given CSP. This finding suggested that the operating point of the baroreflex was increased during exercise. In a more recent study, Papelier et al (27) reported the responses of HR and BP to changes in CSP in human beings at rest and during exercise at increasing intensities. The results showed no effect of exercise on the slope of relationships HR-CSP or MAP-CSP. However, exercise did cause a progressive shift of the relationship, where each increment in exercise intensity shifted upward the linear curves relating HR and BP to CSP, suggesting an increased operating point of the reflex. In conclusion, our observations and those obtained in these two studies (20, 27) provide clear evidence that the baroreflex gain is maintained during exercise, simultaneously with a shift in the set point of the baroreflex.

Arterial baroreflex contribution to the cardiovascular response to dynamic exercise.

One way to examine whether the arterial baroreflex contributes to the cardiovascular response to exercise is to compare cardiovascular responses during dynamic exercise before and after baroreceptor deafferentation. Therefore, these studies have been performed only in experimental animals, in which the arterial baroreflex can be surgically interrupted by denervation of the baroreceptor areas (sino-aortic denervation).

In our laboratory, we have studied BP and HR responses to dynamic exercise in sham-operated and sino-aortic denervated (SAD) rats (7). At rest, MAP and HR values were not different between both groups studied one week after surgery (120 ± 15 vs 119 ± 8 mmHg and 332 ± 6 vs 335 ± 18 beats·min⁻¹, respectively). However, SAD rats exhibited the characteristic increased BP variability (18 ± 5 vs 6 ± 1

mmHg). At the onset of exercise (20 s), SAD rats had a more pronounced increased in MAP as compared with sham-operated rats (Fig 2A). In contrast, the tachycardiac response at the onset of exercise was not significantly different between both groups (Fig 2B). The increased BP response in SAD rats was maintained during steady state exercise (2 min at 0.5 miles·h⁻¹) (30 ± 6 vs 13 ± 3 mmHg), suggesting that the influence of the arterial baroreflex control of BP persisted during all the exercise period. However, no significant difference was observed in HR increases between SAD and sham-operated rats (85 ± 15 vs 79 ± 9 beats·min⁻¹, respectively). These data suggested that the arterial baroreflex restrains the increase of BP during dynamic
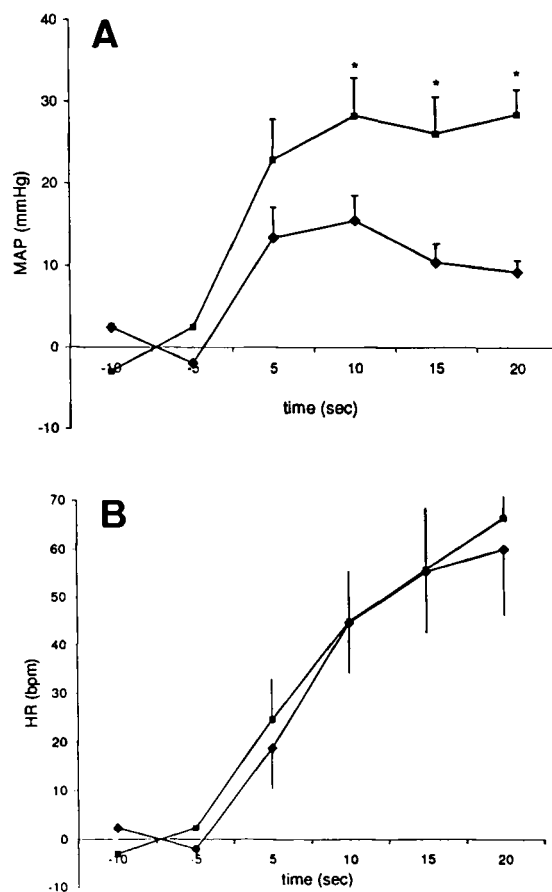

Fig 2. Mean arterial pressure (MAP; panel A) and heart rate (HR; panel B) increases at onset of exercise in sham-operated (diamonds; n = 7) and sino-aortic denervated (squares; n = 7) Wistar rats. Data presented as means ± SEMs. Asterisks, significant differences between both groups (p < 0.05). Student's t test.

exercise in rats. Moreover, the baroreflex modulation of the cardiovascular system during exercise seems to be selective, since the exercise-tachycardiac response was not affected by baroreceptors denervation.

In contrast to our results, other studies (1, 17, 21) using the sino-aortic denervation technique concluded that the arterial baroreflex had little or no effect on the cardiovascular response to exercise. Arterial blood pressure was not different during steady state exercise in control and SAD dogs. Moreover, a transient decrease in BP has been observed at the onset of exercise in dogs (1, 17, 21). It seems that the role of the arterial baroreflex during exercise is different among species. In fact, the mechanisms matching the exercising muscle blood flow and metabolic requirements are species dependent. In dogs, the increased blood supply to the exercising muscles is obtained without vasoconstriction in nonworking beds (1). In contrast, in rats (26) and humans (9), the cardiac output is diverted to exercising muscle by a vasoconstriction in visceral beds

EFFECT OF EXERCISE TRAINING ON ARTERIAL BAROREFLEX

Exercise training induces cardiovascular adaptations, such as decreased HR and increased stroke volume (4, 13, 22, 23), both at rest and during submaximal exercise, which are generally viewed as beneficial to the cardiovascular system. Although these cardiovascular responses to exercise training have been extensively studied, the influence exerted by exercise training on the baroreflex control of the cardiovascular system has not been clarified yet.

Effect of exercise training on baroreflex control of heart rate.

Several investigators have reported increased baroreflex sensitivity in exercise-trained humans (2, 19, 31). In contrast, studies performed in exercise-trained animals showed an attenuation of baroreflex bradycardia at rest (23).

We recently studied the sensitivity of the baroreflex bradycardia and tachycardia at rest

in exercise-trained rats (8). Baroreflex sensitivity was evaluated by measuring changes in HR in response to transient drug-induced progressive increases and decreases in BP, induced by iv injections of phenylephrine and sodium nitroprusside, respectively. The baroreflex sensitivity was evaluated by calculating the ratio of the mean of all HR changes to the mean of all MAP increases or decreases ($\Delta HR/\Delta MAP$). When all values of $\Delta HR/\Delta MAP$ were used, the baroreflex bradycardia was significantly lower in exercise-trained rats compared to sedentary rats (Fig 3A). In contrast, the baroreflex tachycardia was significantly higher in exercise-trained rats (Fig 3B). These data indicated that exercise training affects baroreflex bradycardia and tachycardia in opposite directions. This difference could be explained by alteration in the reflex pathways. In another study (23), we also observed that the decreased baroreflex bradycardia recorded in exercise-trained rats was accompanied by decreased bradycardic
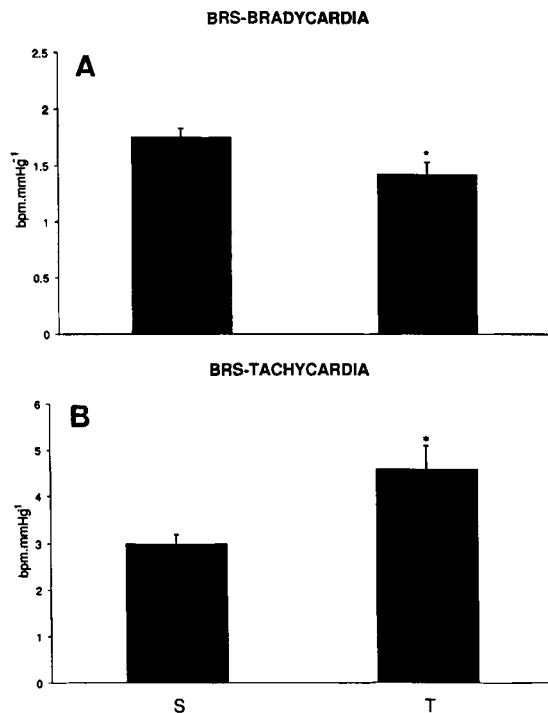

Fig 3. Baroreflex sensitivities (BRS) for bradycardia (panel A) and tachycardia (panel B), analyzed by index $\Delta HR/\Delta MAP$ obtained in sedentary (S; n = 12) and exercise-trained (T; n = 15) Wistar rats. Data presented as means ± SEMs. Asterisks, significant differences between both groups (p < 0.05). Student's t test.

responses to electrical vagal stimulation and methacholine injection, in exercise-trained rats. Therefore, the attenuated baroreflex bradycardia induced by exercise training could be explained by an impairment of the efferent pathway of the reflex. Conversely, the increased baroreflex tachycardia could be explained by an increased sensitivity of the afferent pathway of the baroreflex after exercise training, since the gain-sensitivity of the baroreceptor curve is increased by 44% in exercise-trained rats (8).

The difference between our results and those obtained in humans may be attributed to different methodological approaches and differences among species. The increased baroreflex sensitivity in exercise-trained subjects has been described by means of sigmoidal logistical function (19, 31). In contrast, the attenuation in baroreflex sensitivity has been described by means of the index of baroreflex bradycardia (23) or by regression analysis, fitting changes in mean arterial pressure to corresponding heart rates (3, 23). Unpublished data from our laboratory (Farah et al) show that the baroreflex sensitivity index obtained by sigmoidal logistical function in rats is quite similar to the baroreflex tachycardiac index, but approximately two-fold the baroreflex bradycardic index. As observed in this study, exercise training changes the baroreflex tachycardia and tachycardia in opposite directions. Therefore, the incremented baroreflex index obtained by sigmoidal logistical function may reflect mainly the changes in baroreflex tachycardia, but not the changes in baroreflex bradycardia, which could be actually depressed. Kingwell et al (15) observed no significant changes in the sensitivity of the baroreflex control of HR in exercise-trained humans, but an attenuation in the baroreflex sensitivity under cardiac sympathetic blockade with propranolol, suggesting a decrease in the sensitivity of the baroreflex bradycardia.

Effect of exercise training on baroreflex control of sympathetic nerve activity.

Catecholamines release is significantly diminished in exercise-trained humans at rest and during exercise performed at the

same workload (33). The mechanisms involved in the attenuation of the sympathetic nerve activity after exercise training are still unclear, but may be mediated by central depression of the sympathetic system and/or changes in sensitivity of peripheral reflexes that control circulation, including the arterial baroreflex.

The relationship between spontaneous changes in BP and averaged renal sympathetic nerve activity (RSNA) shows a "baroreceptor pattern" (29) represented by the negative correlation between RSNA and systolic arterial pressure. Di Carlo and Bishop (11) observed that exercise training in rabbits decreased the sensitivity of the baroreflex control of RSNA, which was attributed to a tonic inhibition of cardiopulmonary receptors. We have studied the effect of exercise training on tonic and reflex RSNA in conscious unrestrained rats by directly measuring neural activity through a platinum bipolar electrode implanted on a branch of the renal nerve (24). The RSNA was significantly lower in exercise-trained rats than in sedentary ones (Fig 4). Moreover, an impairment of baroreflex control of RSNA in response to AP decrease was observed (4.92 ± 0.89 vs 12.3 ± 1.2 bars·cycle^{-1}·mmHg^{-1}). Prolonged increases in BP during exercise may contribute to the reflex attenuation of RSNA. Some researchers have demonstrated that a
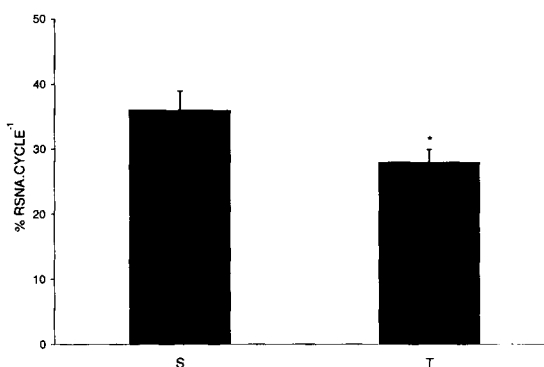

Fig 4. Renal sympathetic nerve activity (RSNA) expressed as percentage of maximal activity during 1,000 cardiac cycles in sedentary (S; n = 6) and exercise-trained (T; n = 6) Wistar rats. Data presented as means ± SEMs. Asterisks, significant differences between both groups (p < 0.05). Student's t test.

sustained increase in BP for 90 min (phenylephrine infusion) inhibited RSNA in rabbits, even after the infusion had been stopped and the BP had returned to baseline values (32). In addition, the increased sympathetic nerve activity observed during prolonged exercise may lead to a down-regulation of the sympathetic nervous system during the recovery period. In fact, after an acute bout of dynamic exercise, the sympathetic nerve activity is decreased in hypertensive subjects (12). Another possibility is that exercising muscle can stimulate the release of β-endorphin in the brain (10), causing inhibition of sympathetic activity. If this mechanism is elicited frequently, it could result in chronic sympathetic inhibition and decreased RSNA.

In humans, the study of the exercise training effect on the sympathetic nerve activity was substantially advanced by the microneurographic recording (percutaneous direct intraneural recordings) of multi-unitary postganglionic sympathetic nerve activity. Using this method, Grassi et al (14) studied the tonic and reflex control of muscular sympathetic nerve activity (MSNA) in humans beings, before and after a controlled program of exercise training. Similarly to our results, they observed a decrease in MSNA. However, they reported that the baroreflex control of MSNA was increased during rapid decrease in BP, whereas we observed a decrease under the same circumstances. Thus, exercise training seems to decrease tonic sympathetic nerve activity in both rats (24) and humans (14). However, the sensitivity of the baroreflex control of sympathetic nerve activity after exercise training can be species-dependent, or it can even be different in renal and muscular vascular beds.

ACKNOWLEDGEMENTS

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