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*Short communication*

# Systemic Arterial Blood Pressure Responses of Stroke-prone Spontaneously Hypertensive Rats to Treadmill Exercise

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## Abstract

**The present study was undertaken to compare the systemic blood pressure responses during graded acute exercise of stroke-prone spontaneously hypertensive rats (SHRSP) and normotensive Wistar-Kyoto rats (WKY). Systemic blood pressure was measured by left carotid artery catheter during exercise. Systolic blood pressure increments with running exercises at 10, 15, and 20 m/min were significantly greater in SHRSP than in WKY. Diastolic blood pressure increments with exercise were singnificantly greater only at 20 m/min in SHRSP compared to WKY. This study suggests that the blood pressure response to exercise is accentuated in SHRSP.**

**Key words:** Hypertension, Exercise, SHRSP

## Introduction

According to clinical, epidemiological, and pathological studies, physical activity appears to play an important role in the treatment and prevention of several cardiovascular diseases[1-4]. Therefore, it is believed that appropriate physical activity may be a valuable tool in the therapeutic regiments for the control and amelioration of cardiovascular disease, though the underlying mechanisms of this "exercise hypothesis" are still under investigation[3]. The inherent experimental limitations of studies on human subjects have led to extensive studies on spontaneously hypertensive rats (SHR). The hemodynamics during acute exercise have not been investigated in unanesthetized hypertensive rats, even though previous studies indicate that repeated exercise may cause lower systemic blood pressure in SHR. We wanted to determine whether the systemic artery would have different responses to exercise in SHRSP. Therefore, the present study was undertaken to compare the systemic blood pressure responses during graded acute exercise in stroke-prone spontaneously hypertensive rats (SHRSP) and normotensive rats.

## Methods

Eight male SHRSP and eight male Wistar-Kyoto control (WKY) rats,12 weeks of age, were used in this experiment. SHRSP were obtained from the colony of Dr.Yukio Yamori (Kyoto University). Following anesthesia with ketamine hydrochloride (10 mg/100g body weigh, i.p.), a catheter (PE-50, internal diameter 0.58mm) was implanted into the left carotid artery to the level of the aortic arch.

The cannula was tunneled beneath the skin and exited from the back of the neck. The procedures have been previously described in detail[5]. The catheter was connected to a pressure transducer system (TP-300T, Nihon Koden, Japan). Heart rate (HR) was counted with the pulse wave. About eight hours after catheter placement the experiment was carried out on the conscious rats[5]. After measurement of blood pressure at rest for 10 min, these rats progressively ran on a small animal treadmill (KN-73, Natsume, Japan) at 10, 15 and 20 m/min, for 3 min at each speed. The running intensities were approximately 50-65% of their maximal exercise capacity in WKY[6]. Blood pressure measurements were taken after the animals had run for 2 min at each speed, and resting measurements were taken after 20 min of rest. Before the experiment, all rats had been handled daily and been familiarized with running on a treadmill. The familiarization runing time was 5 min/day for 3 days, and the running intensity was 15 m/min. The rats had their left ventricular walls and the septum (LV+S) removed after being anesthetized with pentobarbital (5 mg/100g body weight, ip) and weighed.[7]. Two-way analysis of variance was used to determine differences between various time points within each group. The post hoc Scheffe's test was used to determine significant differences between individual means. $P<0.05$ was selected to denote statistical significance. The values given in this paper are mean ± standard deviation.

The present study was approved by our institutional Animal

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## Results

There was no significant difference in body weight (BW) between the SHRSP (219.2 ± 5.3g) and WKY (234.0 ± 8.8g) groups. The LV+S weight-to-body weight ratio in WKY (0.22 ± 0.03mg/100g BW) was significantly less than in SHRSP (0.33 ± 0.01mg/100g BW), indicating that the latter had left ventricular hypertrophy. As presented in Table 1, both systolic and diastolic blood pressures were significantly elevated above the resting levels throughout the run for all grades of exercise in the WKY and SHRSP groups. Pulse pressure was significantly increased by the three running speeds only in the SHRSP group. Systolic, diastolic and pulse pressures in the SHRSP group were significantly higher than in the WKY group both at rest and during exercise. Heart rate rose during exercise in both groups, but there was no significant difference in heart rate between the SHRSP group and the WKY group at rest or during exercise. The systolic blood pressure increment with exercise was significantly higher in the SHRSP group than in the WKY group. Moreover, in both groups, the systolic and diastolic blood pressure levels were not significantly different between 1 min and 2 min at each running speed. After the first running speed, the systolic blood pressure increment with progressive work load did not change in either group. The diastolic pressure increment with exercise was significantly higher in the SHRSP group than in the WKY group only after 3 min of running at 20 m/min.

## Discussion

Human hypertensive diseases, as well as most of experimental hypertension models such as SHR and SHRSP, are characterized by elevated systemic blood pressure.

In this study, there appeared to be increased left ventricular wall thickness in SHRSP. This might have been related to active systemic hypertension, indicating an increased left ventricular workload in SHRSP.

In SHR, three different causes have been proposed to explain the development of hypertension. The first one is active vasoconstriction of the arteriolar resistance vessels, which may be due to increased sympathetic nerve activity or increased sensitivity to vasoactive agents[8]. The second is that exaggerated responses in heart rate and blood pressure lead to hypertrophy of the vascular smooth muscle, which encroaches upon the vessel lumen and reduces the internal radius of the arterioles[9]. The third is that there are fewer parallel conductance channels due to rarefaction of arterioles or capillary density[10]. Plasma levels of neuropeptides are increased with acute exercise[11] and repeated exposures to increased catecholamine levels during repeated exercise[12] may alter the responses of the vascular wall to thouse neurotransmitters. In the present study, the cardiac output was not measured, but it is knouwn to always increase with exercise[13]. In SHRSP, these greater blood pressure responses with acute exercise may be due to morphological and physiological vascular variety. Acute exercise has been reported to increase systolic blood pressure and blood flow, and reduce vascular resistance in the skeletal muscle bed in both SHR and WKY[14]. However, this exercise-induced skeletal muscle vasodilator response was inhibited in the SHRSP group, perhaps due to higher elevated systemic blood pressure. There might also be a significantly greater blood pressure response, that is, enhanced sympathetic nerve activity, with exercise in the SHRSP group than in the WKY group[8].

Forced treadmill exercise, regardless of the experimental design or the manner in which it is evaluated, involves the threat of electrical stimulation[15]. Heavy exercise is also associated with

**Table 1 Comparison of blood pressure and heart rate during rest and exercise between the SHRSP and the WKY groups**

| | SHRSP (n=8) | | | | WKY (n=8) | | | |
|---|---|---|---|---|---|---|---|---|
| | | Running speed (m/min) | | | | Running speed (m/min) | | |
| | Rest | 10 | 15 | 20 | Rest | 10 | 15 | 20 |
| Systolic pressure (mmHg) | 211.3† ±11.3 | 230.0†* ±7.5 | 225.0†* ±6.0 | 230.0†* ±7.5 | 135.8 ±4.2 | 140.0* ±3.5 | 139.1* ±7.2 | 141.7* ±6.6 |
| Diastolic pressure (mmHg) | 153.8† ±1.3 | 162.5†* ±4.0 | 160.0†* ±3.5 | 167.5†* ±4.0 | 113.3 ±3.1 | 117.5* ±2.0 | 118.3* ±1.2 | 117.5* ±2.0 |
| Pulse pressure (mmHg) | 57.5† ±4.0 | 67.5†* ±4.0 | 65.0†* ±4.2 | 62.5†* ±5.5 | 22.5 ±3.1 | 22.5 ±2.0 | 20.8 ±6.2 | 24.2 ±6.5 |
| Heart rate (beats/min) | 459.0 ±9.0 | 510.0* ±12.0 | 530.0* ±16.0 | 570.0* ±17.0 | 447.3 ±19.1 | 501.0* ±16.4 | 520.7* ±13.7 | 560.0* ±8.2 |
| SP increment (mmHg) | | 18.7† ±3.0 | 13.7† ±2.0 | 18.7† ±4.3 | | 4.2 ±3.1 | 3.3 ±3.1 | 5.8 ±2.3 |
| DP increment (mmHg) | | 8.7 ±4.0 | 6.2 ±3.0 | 13.7† ±4.0 | | 5.6 ±2.7 | 6.4 ±1.5 | 5.7 ±2.7 |

Rats ran for 3 min at each running speed.
SP: Systolic blood pressure, DP: Diastolic blood pressure
increment: Blood pressure increments with exercise
Values are mean ± s.d.
† indicates significant differences between SHRSP and WKY under comparable conditions ($p<0.05$).
* indicates significant differences from resting values within each group ($p<0.05$).

higher resting pressures in trained rats, but moderate exercise is associated with a significantly lower resting blood pressure[15]. We speculate that SHRSP are hypertensive and hyperresponsive to a variety of external and exogenous stimuli. The possibility always exists that the exercise being prescribed is too strenuous for these populations. In the present study all rats were handled daily and ware familiarized with running on a treadmill. Therefore, they were unlikely to be influenced by the use or threat of forced treadmill exercise.

In SHRSP, the systemic blood pressure increment was not increased in proportion to the intensity of exercise. Systolic blood pressure increased rapidly in response to light exercise, then the pressure remained constant over the exercise time with the higher exercise intensities. The results of our study may indicate that systolic blood pressure does not change with increased work load owing to some shift of blood volume from the central shunt circuit, such as regional vascular resistance in the skeletal muscle bed. It is speculated that 2 min is not long enough for steady-state blood pressure levels to be attained at each running speed. Future studies are needed to understand the mechanism responsible for greater blood pressure responses with acute exercise in SHRSP than in WKY. This study may provide an important base for future studies investigating the mechanisms to explain why regular exercise is beneficial to human health, and which kind of exercise may induce lower blood pressure.

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