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COMPARISON OF THE SYSTEMIC HEMODYNAMICS IN NORMOTENSIVE AND HYPERTENSIVE RATS

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Spontaneously hypertensive rats of the Wistar-Kyoto line (SHR) and rats with renovascular hypertension (RVHR) are regarded as experimental models of essential and symptomatic hypertension in man and are widely used in medical and biological research [1, 6, 7, 9]. Many studies of hypertension have been carried out by the use mainly of only one of these models of hypertension.

The aim of the present investigation was accordingly to study and compare the basic parameters of the systemic hemodynamics and function of the baroreceptor reflex (the cardiac component) in normotensive rats (NR) and in animals with the two different models of hypertension: SHR and RVHR.

EXPERIMENTAL METHOD

Male rats weighing 250-300 g were divided into three groups (15 rats in each group): 1) control, noninbred NR, 2) SHR, 3) RVHR.

The last group consisted of noninbred rats in which a coil with internal diameter of 0.35 mm had been wound around the left renal artery and the right kidney completely removed 28-30 days before the experiment.

All the rats were anesthetized with a mixture of urethane (600 mg/kg) and chloralose (40 mg/kg). The blood pressure was measured by an EMT-34 electromanometer in the femoral artery. Momentary values of the heart rate were determined by a digital pulsotachometer, triggered by the arterial pressure pulse wave. All parameters of the hemodynamics measured were recorded in analog form on a Mingograph-81 apparatus and numerical values of the arterial pressure and pulse rate were recorded on a digital printer. The cardiac output was determined by the tetrapolar rheography method on an RPG2-02 instrument [3]. The formula used for the calculation was:

$$\Delta V = Kp\frac{L2}{Z2}AdT_{ej},$$

where ΔV is the stroke volume of the heart (in cm^3); K a coefficient, with the value 0.7; p the specific resistance of rat blood, which is 165 Ω/cm; L the distance between the chest

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TABLE 1. Hemodynamic Parameters in NR, SHR, and RVHR

Group of rats	SP	DP	MAP	HR	SV
NR	121,33±2,22	72,00±2,11	97,00±1,67	**420,06±4,04**	0,157±0,0076
SHR	188,00±2,96*	119,09±0,85*	153,33±1,57*	**424,33±3,69**	0,144±0,0059
RVHR	185,00±3,70*	121,00±1,39*	152,46±2,37*	**425,20±5,30**	0,148±0,0064

Group of rats	CO	TPR	PR	RH	BR
NR	66,21±2,79	1,50±0,09	44,66±1,14	**37,13±1,67**	0,451±0,033
SHR	61,32±2,53	2,56±0,02†	75,66±1,76†	**53,53±2,31†**	0,056±0,0006*
RVHR	63,01±2,93	2,48±0,09‡	76,41±1,49*	**50,66±1,68***	0,049±0,0006*

Legend. SP) Systolic pressure (in mm Hg), DP) diastolic pressure (in mm Hg), MAP) mean arterial pressure (in mm Hg), HR) heart rate (beats/min), SV) stroke volume (in ml), CO) cardiac output (in ml/min), TPR) total peripheral resistance (in mm Hg/ml/min), PR) pressor response (in mm Hg), RH) reactive hyperemia (in mm Hg), BR) baroreflex (in mm Hg). *$P < 0.001$, †$P < 0.01$, ‡$P < 0.05$ (significance of differences between values for NR and SHR in all cases).

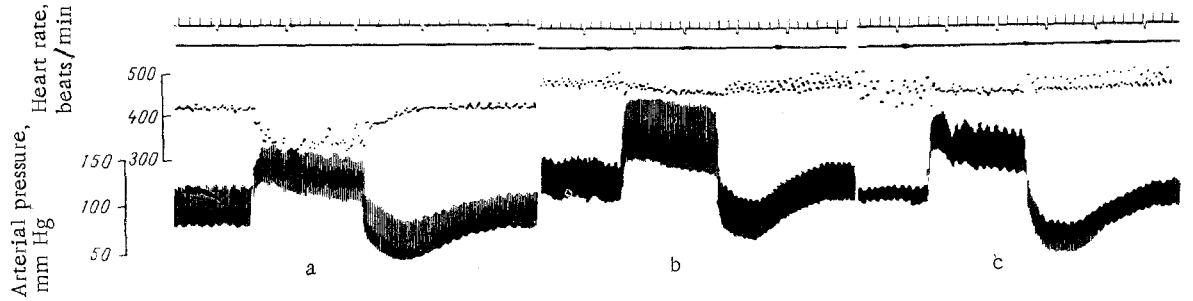

Fig. 1. Changes in heart rate and arterial pressure in NR (a), SHR (b), and RVHR (c) in response to brief (msec) occlusion of abdominal aorta.

electrodes, 3 cm; Z the basic impedance, determined from the rheograph scale (in Ω); Ad the amplitude of the differential rheogram (in Ω/sec); T_{ej} the time of ejection of blood by the heart, determined from the arterial pressure curve or the rheogram.

The cardiac component of the baroreceptor reflex was tested by compressing the aorta (in the region where it emerges from beneath the diaphragm) briefly (for 10 sec). The pressor response was measured from the increase in systolic pressure, postocclusion reactive hyperemia was determined from the fall in diastolic pressure, and the sensitivity of the baroreflex was determined from the change in the intersystolic interval (in msec) in response to a rise of arterial pressure of 1 mm Hg.

The experimental rexults were subjected to statistical analysis by the variance method and by Student's t test on the gE-115/3 computer (France).

EXPERIMENTAL RESULTS

As Table 1 shows, the mean arterial pressure in rats with both types of hypertension was 57% higher than in NR. Meanwhile no significant difference in the pulse rate was found in the rats of the three groups. The stroke volume and cardiac output of the hypertensive rats showed a tendency to fall. It can thus be concluded that the high blood pressure in the rats of both hypertensive groups was due entirely to the high total peripheral resistance.

Although a higher pressor response to brief occlusion of the abdominal aorta was observed in SHR and RVHR, nevertheless, when expressed as percentages (the rise in systolic pressure relative to its initial value) these parameters became almost equal (36.8% in NR, 40.2% in SHR, 41.3% in RVHR) and differences between them were not significant.

Reactive hyperemia (the ratio between the postocclusion fall of diastolic pressure and its initial level) differed statistically significantly only between NR and RVHR (53.00 ± 2.52% in NR, 50.66 ± 1.68% in SHR, 41.95 ± 2.04% in RVHR).

As was shown previously [5], an essential role in the mechanism of postocclusion reactive hyperemia is played by tissue depressor prostaglandins. It is evidently this fact which determines the reduced postocclusion reactive hyperemia in RVHR, for definite inhibition of biosynthesis of depressor prostaglandins is found in these animals [2]. Meanwhile increased activity of the renin–angiotensin system is known to be present in RVHR [4], and the high angiotensin II concentration in the circulating blood maintains the increased tone of the arteries and arterioles. Consequently, the fall in postocclusion reactive hyperemia in RVHR is evidently associated both with reduced biosynthesis of depressor prostaglandins by the vascular tissues and with a high blood level of angiotensin II.

In response to brief compression of the aorta bradycardia developed to a lesser degree in the hypertensive rats than in NR, depsite the higher pressor response. This indicates considerable inhibition of the baroreceptor reflex. The sensitivity of the baroreceptor reflex in SHR was reduced by 88% and in RVHR by 89% compared with NR (Table 1, Fig. 1). Comparison of the two groups of hypertensive animals showed that the sensitivity of the baroreceptor reflex was 11% lower in RVHR than in SHR.

It is well known that the development of any form of arterial hypertension is accompanied by a lowering of sensitivity of the baroreflex system both in man and in experimental animals. Stronger inhibition of the baroreceptor reflex in RVHR than in SHR was evidently due to the higher blood concentration of angiotensin II, which inhibits the cardiac component of the baroreceptor reflex [8].

Despite the similar picture of the systemic hemodynamics in the two groups of hypertensive rats, the RVHR were distinguished by their reduced ability to develop reactive hyperemia and the more marked inhibition of the cardiac component of their baroreceptor reflex.

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