Alterations in Cardiac Function in Response to Epinephrine in Rats with Hereditary Hypertension (An ECG Study)

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A comparative electrocardiographic evaluation of changes in cardiac function in rats with hereditary arterial hypertension (NISAG strain) and normotensive (Wistar) rats in response to a single epinephrine injection revealed much more pronounced changes in NISAG rats, including an unfavorable time course of electrocardiographic waves (left ventricle overload) and impaired conduction (blockade) and excitability (extrasystoles). The results indicate that the myocardium of NISAG rats is much more responsive to the acute stimulation of adrenergic receptors by epinephrine than is the myocardium of normotensive rats.

Key Words: *hereditary arterial hypertension; heart; epinephrine; electrocardiography*

The strong reaction of the cardiovascular system to hormones, including epinephrine, that are secreted during stress is held to be one of the important mechanisms responsible for the development of arterial hypertension and associated complications such as myocardial infarction and stroke [1,6]. For this reason, adrenergic receptor blockers are used as agents to lower arterial pressure and protect the heart [8].

A hypertensive rat strain, NISAG, was recently developed at the Institute of Cytology and Genetics of the Siberian Division of the Russian Academy of Sciences. The hypertensive status of these rats and the condition of their cardiovascular system can be judged by evaluating their responsiveness to epinephrine. Such an evaluation is of particular interest because arterial hypertension in this strain is established as a stress-dependent phenomenon [3, 4]. In the present electrocardiographic study we compared changes in cardiac function brought about by a single epinephrine injection in hypertensive NISAG rats and their normotensive Wistar counterparts.

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MATERIALS AND METHODS

Six-month-old male Wistar and NISAG rats were used, 60 animals of each population. For the recording of the electrocardiogram (ECG), they were anesthetized with ether (etherrausch) and placed supine in a screened box. Needle electrodes were inserted under the skin of all four limbs and also in the chest region in three positions: one electrode along the midsternal line at the level of the apex beat and the other two 1 cm to the left and 1 cm to the right of this line, which corresponds to the standard positions of the chest leads V_1, V_2, and V_3. The ECG was thus recorded in 3 standard leads, 3 augmented limb leads, and 3 unipolar chest leads. The recording was done on a Mingograph 34 cardiograph at a paper speed of 100 mm/sec and a channel sensitivity of 20 mm/mV. After the background ECG was recorded, each rat received a subcutaneous injection of epinephrine in a dose of 0.2 mg/100 g body weight. A second ECG was recorded ten minutes postinjection. The data were evaluated

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statistically by the t test and paired comparisons of conjugated variates [2].

RESULTS

Analysis of the background ECGs indicated an altered state of the cardiovascular system in NISAG rats: there were signs of left ventricle hypertrophy and relative coronary insufficiency, probably associated with the development of arterial hypertension.

The rapidly developing reaction to epinephrine, which was recorded 10 min after its subcutaneous injection, was manifested in ECG signs suggestive of increased load on the myocardium. These signs were all more conspicuous in NISAG rats. Statistically significant changes in the total value of *QRS* complex waves after epinephrine injection were found only in these rats, so that the electrical axis of the heart had shifted still more to the left and the α angle became negative as a result (Fig. 1 and Tables 1 and 2). NISAG rats also had a decreased normal inversion of the *QRS* complex in aVR. In aVF, this complex acquired a negative value whereas the total value of its waves in the chest leads was increased. This pattern is most likely an indication that the functional load falls predominantly on the left ventricle in NISAG rats. These hypertensive rats also had exaggerated atrial function, given that the *P* wave amplitude was significantly increased in the chest leads. A similar, though smaller, increase in the *P* wave was noted in Wistar rats. The *T* wave amplitude in the chest leads was increased in both strains, but the abnormal inversion of the *T* wave in aVR seen in NISAG rats pointed to an unfavorable time course of this wave in the latter. Wistar rats showed elevated *R* and *P* wave amplitudes in the chest leads, but this was paralleled by an increase in the *S* wave, indicating that the increased load was more evenly distributed between the right and left ventricles than in NISAG rats.

The prolongation of ECG waves and intervals following epinephrine injection (Tables 1 and 2) went along with a rise of the stroke volume index, which may be taken as evidence of a reduced functional capacity of the heart in comparison with the baseline in the rats of both strains.

Apart from the changes in the overall ECG picture, the acute stimulation of cardiac adrenoceptors led to marked disturbances of myocardial conduction and excitability in some animals. Such disturbances were recorded much more frequently among NISAG than among Wistar rats (12 cases *vs.* 2). Other findings in hypertensive rats were episodes of atrioventricular block and of bundle-branch block, ventricular and atrioventricular extrasystoles, and, frequently, gross alternation of the *QRS* complex. Among Wistar rats, a transient atrioventricular block was noted in one animal and atrial migration of the pacemaker in another.

Epinephrine administration was thus followed by overt signs of impaired cardiac activity in the NISAG rats. A factor apparently contributing to this is that, because of the changes already present in it,

TABLE 1. Amplitudes of ECG Waves (in mm) in Wistar and NISAG Rats after Epinephrine Injection ($M \pm m$)

Lead	Genotype	ECG waves				
		P	*R*	*S*	*QRS*	*T*
I	Wistar	0.0±0.05	0.1±0.15	0.6±0.20*	−0.8±0.42	0.0±0.15
	NISAG	−0.1±0.07	−0.5±0.20*	0.3±0.20	−1.1±0.40**	−0.3±0.20
II	Wistar	0.0±0.06	0.1±0.15	0.3±0.10	−0.3±0.20	0.4±0.25
	NISAG	−0.2±0.10	−1.3±0.20**	1.1±0.20**	−2.4±0.40	0.4±0.25
III	Wistar	0.1±0.06	0.8±0.20**	−0.1±0.20	0.6±0.35	0.2±0.20
	NISAG	−0.3±0.10*	0.2±0.15	1.0±0.20**	−1.5±0.40**	0.0±0.10
aVR	Wistar	−0.1±0.06	0.3±0.20	0.4±0.25	1.7±0.85	−0.2±0.10
	NISAG	−0.2±0.10	1.0±0.20**	0.2±0.10	2.0±0.40**	0.4±0.10
aVL	Wistar	−0.1±0.07	0.4±0.20	0.6±0.20*	0.2±0.15	0.0±0.10
	NISAG	−0.1±0.07	0.4±0.20	1.8±0.95	−0.5±0.30	0.1±0.20
aVF	Wistar	0.2±0.10	0.2±0.10	0.3±0.10*	−0.2±0.10	0.1±0.10
	NISAG	−0.1±0.07	−0.6±0.20**	1.0±0.20**	−1.5±0.40**	−0.2±0.10
V_1	Wistar	0.2±0.10	1.5±0.30**	1.0±0.35*	0.9±0.50	0.0±0.20
	NISAG	0.4±0.10**	1.7±0.30**	−1.4±0.80	1.8±0.40**	0.4±0.20*
V_3	Wistar	0.4±0.10**	2.1±0.40**	1.4±0.50*	1.0±0.55	0.3±0.15*
	NISAG	0.6±0.10**	2.1±0.35**	−0.3±0.20	2.5±0.50**	0.4±0.20*
V_5	Wistar	0.2±0.05**	0.8±0.30*	0.3±0.20	0.5±0.30	0.4±0.20*
	NISAG	0.6±0.15**	0.8±0.45	−0.5±0.30	0.4±0.40	0.4±0.25

Note. *$p<0.05$, **$p<0.01$.

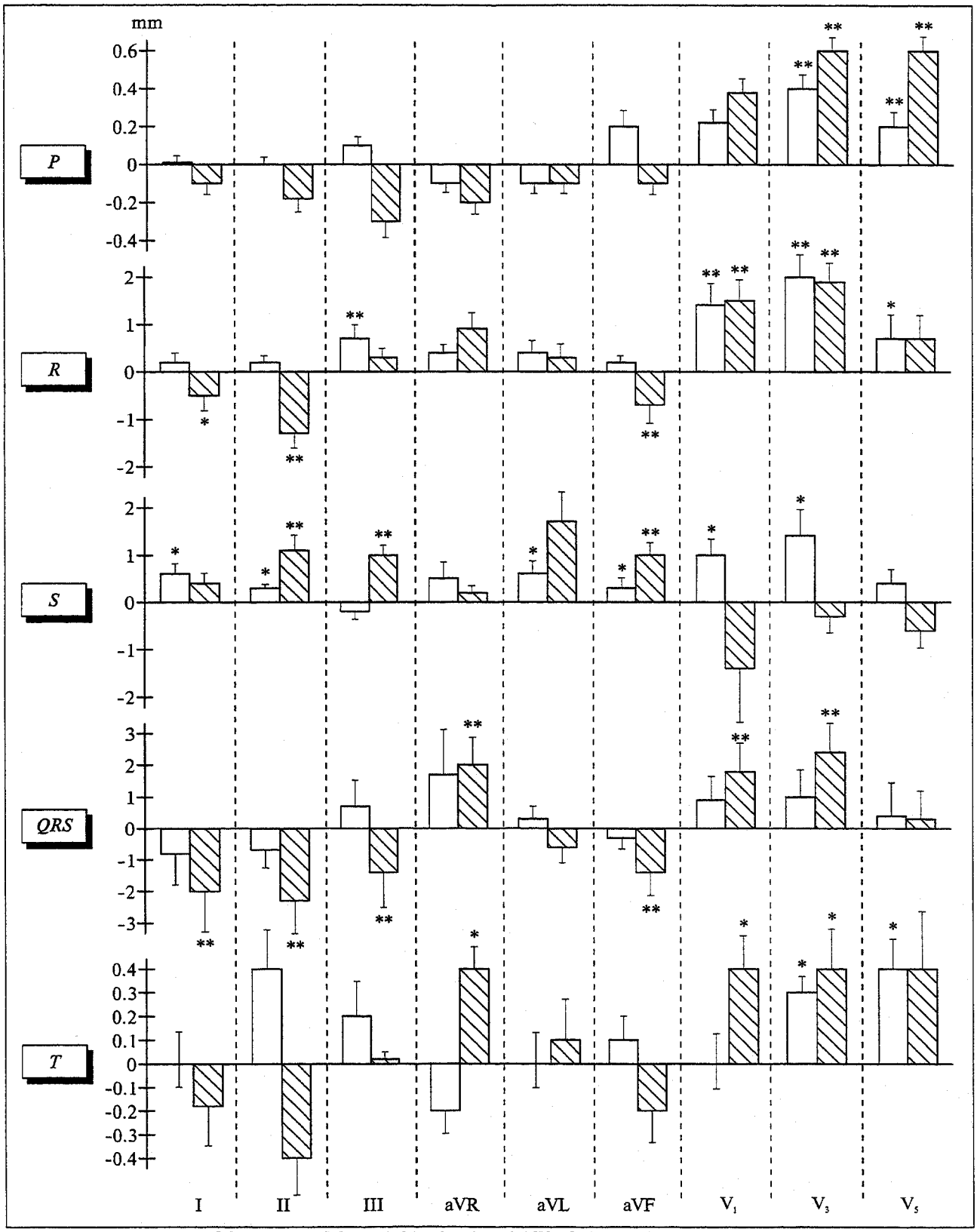

Fig. 1. Amplitudes of ECG waves in Wistar (white bars) and NISAG (hatched bars) rats 10 min after epinephrine injection. *$p<0.05$, **$p<0.01$ in comparison with the baseline.

the myocardium of NISAG rats is more susceptible to the damaging influences resulting from massive stimulation of the adrenoceptors. It is of course also possible that the adrenoceptor density is increased in

TABLE 2. ECG Intervals and Wave Widths (msec) and Angle α (Degrees) in Wistar and NISAG Rats ($M \pm m$)

ECG parameter	Group	Wistar (n=58)	NISAG (n=63)
R–R	Control	182.0±2.0	153.0±2.0*
	Epinephrine	186.0±4.0	153.0±2.0*
P	Control	19.0±1.0	22.0±1.0*
	Epinephrine	20.0±1.0	24.0±1.0*+
PQ	Control	58.0±1.0	62.0±1.0*
	Epinephrine	61.0±1.0++	65.0±1.0*++
QRS	Control	19.0±0.0	24.0±1.0*
	Epinephrine	21.0±0.0++	25.0±1.0*
QRST	Control	67.0±2.0	53.0±1.0*
	Epinephrine	75.0±2.0++	55.0±1.0*
Stroke volume index	Control	36.8±1.5	34.6±1.0
	Epinephrine	40.3±1.5++	36.0±1.0++
α Angle	Control	37.4±3.7	0.2±6.2*
	Epinephrine	31.0±4.9	−10.8±5.6*

Note. *$p<0.01$ in comparison with Wistar rats; +$p<0.05$, ++$p<0.01$ in comparison with the baseline.

the NISAG myocardium. Previously, we found altered densities of α- and β-adrenoceptors in the brain tissue of NISAG rats [5,7].

The enhanced sensitivity of NISAG rats to epinephrine is consistent with their high susceptibility to stress [9], primarily in relation to the cardiovascular system. This may have something to do with the hypertensive status of this strain.

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