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Characterization of Cardiac Function in Hypertensive Rats of the NISAG Strain (an ECG Study)

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Analysis of ECGs recorded in 3 standard leads, 3 augmented limb leads, and 3 chest leads revealed typical signs of left ventricular hypertrophy with a relative deterioration of coronary blood supply in NISAG rats, a new strain with hereditary arterial hypertension. These signs are considered to be characteristic of an established arterial hypertension and may be taken as evidence that the NISAG strain can serve as an adequate animal model of human hypertensive disease.

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

A new rat strain (NISAG), which is an animal model of stress-sensitive arterial hypertension, has been developed by selective breeding at the Institute of Cytology and Genetics in the Siberian Division of the Russian Academy of Sciences [3,5]. Behavioral characteristics [4] and functions of the neurochemical [1,2,6] and neuroendocrine [8] regulatory systems in this strain have now been examined.

The purpose of the present work was to evaluate cardiac function in the NISAG strain through a detailed ECG study, which is necessary for characterizing the hypertensive status of the new strain.

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MATERIALS AND METHODS

Six-month-old male rats of two strains were used: 60 NISAG (hypertensive) rats and 60 Wistar (normotensive) rats. Cardiac function in these strains was evaluated electrocardiographically. For this, the animals were anesthetized with ether (etherrausch), placed into a screened box in the supine position, and connected to a Mingograf-34 cardiograph (Sweden) by means of thin needle electrodes. These were placed subcutaneously in all four limbs and in the chest at the level of the

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TABLE 1. Amplitudes of ECG Waves (mm) in Wistar and NISAG Rats

ECG lead	Rats	Wave amplitude				
		P	R	QRS	S	T
I	Wistar	0.9±0.1	11.7±0.6	9.4±0.7	2.1±0.3	−0.7±0.2
	NISAG	1.4±0.1**	9.0±0.6**	5.5±0.8**	2.5±0.4	−0.8±0.2
II	Wistar	1.5±0.1	12.7±0.5	9.9±0.6	2.7±0.3	0.9±0.2
	NISAG	1.5±0.1	8.5±0.4**	3.2±0.7**	5.4±0.5**	0.1±0.2*
III	Wistar	0.9±0.1	5.9±0.4	1.9±0.7	3.9±0.5	1.3±0.1
	NISAG	0.5±0.1*	5.2±0.4	−2.0±0.9**	7.6±0.7**	1.1±0.1
aVR	Wistar	−1.0±0.1	2.1±0.3	−6.9±1.0	0.7±0.4	0.1±0.2
	NISAG	−0.6±0.2*	3.0±0.4*	−4.6±0.7	2.6±0.7*	1.4±0.2**
aVL	Wistar	0.2±0.1	6.9±0.4	3.9±0.6	2.2±0.3	−1.1±0.1
	NISAG	0.7±0.1**	7.4±0.6	3.9±0.8	1.8±0.4	−0.5±0.2*
aVF	Wistar	1.0±0.1	8.4±0.3	5.8±0.5	2.5±0.3	1.1±0.1
	NISAG	0.9±0.1	6.1±0.3**	0.8±0.7**	5.5±0.6**	0.6±0.1**
V_1	Wistar	0.6±0.1	4.5±0.4	−5.1±0.7	9.7±0.6	3.1±0.2
	NISAG	0.7±0.1	5.2±0.5	−0.8±0.8**	6.6±1.0**	2.8±0.2
V_3	Wistar	1.6±0.1	13.4±0.7	2.3±1.2	10.8±0.8	4.6±0.2
	NISAG	2.3±0.1**	12.2±0.8	4.5±1.2	7.5±0.8**	4.0±0.2
V_5	Wistar	1.2±0.1	12.2±0.8	8.4±0.9	3.9±0.4	1.9±0.2
	NISAG	1.9±0.1**	10.2±0.8	5.6±1.1*	5.9±1.3	1.5±0.2

Note. Here and in Table 2, the asterisks denote significant differences between these two strains: *$p<0.05$, **$p<0.01$.

apex beat in three positions: along the chest midline and 1 cm to the right and to the left of the midline electrode, which corresponded approximately to the standard positions V_1, V_3, and V_5 of the chest electrode. The ECG was recorded in 3 standard leads, 3 augmented limb leads, and 3 chest leads, at a paper speed of 100 mm/sec and a channel sensitivity of 20 mm/mV. Student's *t* test was used for statistical estimation of interstrain differences.

RESULTS

Analysis of the ECGs revealed significant differences between the hypertensive NISAG rats and the Wistar rats. First, as was to be expected, the arterial hypertension resulted in a considerable deviation of the cardiac electrical axis to the left, which was determined by a positive total value of the QRS complex waves in standard lead I and their negative total value in standard lead III (Table 1). The ECGs of Wistar rats were of a "normal" type, and this was confirmed by calculation of the α angle. In the NISAG rats, this angle had virtually a zero value, which attested to a horizontal position of the cardiac electrical axis (Table 2). In the Wistar rats, the value of the α angle corresponded to an intermediate position of the cardiac electrical axis between the normal and vertical positions, which appears to be a characteristic feature of rat ECGs [7]. This gives good grounds for suggesting the presence of left ventricular hypertrophy in NISAG rats.

TABLE 2. Lengths of ECG Intervals (msec) and Values of the α Angle in Wistar and NISAG Rats

ECG parameter	Rats	
	Wistar	NISAG
R−R	182.0±2.0	153.0±2.0**
P	19.0±1.0	22.0±1.0**
P−Q	58.0±1.0	62.0±1.0**
QRS	19.0±0.1	24.0±1.0**
QRST	67.0±2.0	53.0±1.0**
Systolic index, %	36.8±1.5	34.6±1.0
α angle, degrees	37.4±3.7	0.2±6.2**

This assumption is borne out by the pattern of the QRS complex in the augmented limb leads (Table 1). In the NISAG rats the total amplitude of the QRS complex waves in lead aVL was significantly higher than in aVF, whereas the reverse was true in Wistar rats. In the chest leads, the transitional zone between the right and left ventricles of NISAG rats was patently shifted to the right as compared to Wistar rats, indicating that the projection of the left ventricle on the anterior chest wall predominated in the former rats. Left ventricular hypertrophy in the NISAG rats was also manifested in a significant widening of the

QRS complex, despite their relative (as compared to Wistar rats) tachycardia, as was evidenced by the shortened the R-R interval (Table 2). The tachycardia could be a consequence of increased sympathetic tonus in the hypertensive rats, and this could in turn be one of the causes of elevated arterial pressure in them. That sympathetic tonus is enhanced in NISAG rats is also indicated by the results of our previous study [9].

In addition to left ventricular hypertrophy, NISAG rats appear to develop a relative deficit of coronary blood supply to the myocardium of increased mass. This is indicated by the size of the T wave and its relation to the QRS complex. First, NISAG rats had a lower T-wave amplitude in standard lead II and in leads aVL and aVF than Wistar rats (Table 1). Second, the hypertensive rats had a very abnormal inversion of the T wave in aVR, which resulted in discordance of the QRS complex and T wave in this lead. Mention may also be made of a discordance of the QRS complex and T wave in standard lead III. Nevertheless, the functional capacity of the heart in NISAG rats did not appear to have changed much, as could be judged by the relative length of the electrical systole (the QRST complex), i.e., by the values of the systolic index which were virtually the same in both strains (Table 2). The hypertrophied left ventricle of six-month-old hypertensive NISAG rats is therefore well adapted to work against the elevated arterial pressure and can cope successfully with overloads under ordinary circumstances.

Changes in the left ventricle of NISAG rats were also accompanied by some hypertrophy of the left atrium, as was indicated by increased P-wave amplitudes in standard lead I and in the aVL and left chest leads (Table 1). Moreover, a significant prolongation of the P wave and an increased atrioventricular delay (the P-Q interval) were noted in these rats (Table 2).

Thus, as can be seen from the results presented above, the NISAG strain provides an adequate model of human hypertensive disease in terms of ECG characteristics.

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