ever, we believe that these receptors already function at birth, since our previous experiments [6] showed that injection of MT into newborn rats modulates the response of the thyroid gland to thyrotropic hormone in 1-month-old rat pups.

Thus, our findings suggest that the effect of MT on thyrocytes is realized through a transmembrane pathway. This effect is most probably associated with the light/dark cycle and represents an adaptive phenomenon.

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Ontogenetic Dynamics of Arterial Pressure and ECG in NISAG Rats

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Ontogenetic changes in cardiac function, relative heart mass, and arterial pressure occurring in rats with genetically determined arterial hypertension (NISAG) are compared with those occurring in normotensive rats (Wistar). In NISAG rats hypertension is accompanied by shift of electrical axis of the heart to the left, increased heart rate, cardiac conductance disturbances, and relative coronary insufficiency. It is suggested that in NISAG rats changes in ECG are secondary to arterial hypertension.

Key Words: *genetically-determined arterial hypertension; heart; electrocardiography; ontogenesis*

NISAG rats with stress-sensitive arterial hypertension were bred by selection at the Institute of Cytology and Genetics (Siberian Division of the Russian Academy of Sciences) [11]. Previously, it was shown that adult NISAG rats with high arterial pressure (AP) develop typical changes in the cardiovascular system. These changes are hypertrophy of left heart [3], ECG deviations typical of relative coronary insufficiency, proneness to arrhythmias, and formation of necrotic foci in the myocardium in response to epinephrine [4].

In this study we examined ontogenetic changes in AP and cardiac function in NISAG rats.

MATERIALS AND METHODS

Male NISAG (hypertensive) and Wistar (normotensive) rats aging 1, 2, 3, and 6 months were used. Arterial pressure was measured sphygmographically on the tail [6]. Electrocardiogram was recorded with a Mingograph-34 cardiograph using needle electrodes. The electrodes were inserted subcutaneously

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in four limbs, and ECG was recorded in 3 standard and 3 enhanced leads at paper speed 100 mm/sec and channel sensitivity 20 mm/mV. The amplitude and duration of the *P*, *R*, *S*, and *T* waves, *QRS* complex, and *PQ*, *QRST*, and *RR* intervals were measured. The relative mass of the heart was determined in NISAG and Wistar rats in each age group. Statistical analysis of results was performed using Student's *t* test.

RESULTS

The ECG of rats differs from that of humans by higher heart rate, absence of the *Q* wave, and poorly expressed *ST* segment [1]. The *QRS* complex and the *P* and *T* waves have no common isoelectrical line. Our analysis of ECG showed that the development of arterial hypertension NISAG rats is accompanied by changes in cardiac function in comparison with Wistar rats.

The vertical position of the heart is characteristic of 1-month-old NISAG rats, which is determined by negative sum of the amplitude of the *QRS* complex in aVL lead and positive sum in aVF lead (Fig. 1). Accordingly, the electrical axis of heart in NISAG rats is shifted to the right, which was observed in spontaneously hypertensive rats (SHR) [2]. An intermediate electrical position of the heart with normal position of electrical axis has been preserved in Wistar rats of all studied ages (Fig. 1, Table 1). In normotensive rats, the mean α angle is 47° [8]. In 2-month-old NISAG rats this parameter is 47.2° and in 3-month-old rats it is 48.0°, while in Wistar rats it is 31.8° and 36.0°, respectively (Table 1).

As in normotensive Wistar rats, in adult NISAG rats an intermediate position of the heart has been

TABLE 1. The ECG Parameters (msec) and α Angle in Wistar and NISAG Rats

Parameter ECG	Age, months	Wistar	NISAG
P	1	18.2±0.6 (16)***	23.7±0.7 (20)
	2	17.2±0.6 (13)**	21.8±1.2 (19)
	3	18.0±0.7 (13)***	24.8±0.8 (19)+
	6	19.0±1.0 (58)*	22.0±1.0 (63)+
PQ	1	49.1±1.7 (16)**	54.1±1.0 (20)
	2	48.2±0.9 (13)*	54.1±2.1 (19)
	3	51.0±1.0 (13)****	60.5±1.7 (19)+
	6	58.0±1.0 (58)*****	62.0±1.0 (63)
QRS	1	13.9±0.6 (16)*	16.7±0.9 (20)
	2	16.5±0.8 (13)+	17.5±0.8 (19)
	3	17.8±0.6 (13)**	20.3±0.6 (19)++
	6	19.0±0.0 (58)**	24.0±1.0 (63)+++
QRST	1	55.3±1.1 (16)	52.8±0.9 (20)
	2	59.6±1.3 (13)+	60.6±2.4 (19)++
	3	60.1±1.2 (13)***	69.8±2.8 (19)+
	6	67.0±2.0 (58)*****	53.0±1.0 (63)+++
RR	1	159.5±3.6 (16)	165.6±2.7 (20)
	2	146.6±3.3 (13)+	156.9±4.7 (19)
	3	156.3±3.9 (13)	166.1±3.9 (19)
	6	182.0±2.0 (58)*****	153.0±2.0 (63)++
Systolic parameter	1	34.6±0.8 (16)*	32.1±0.8 (20)
	2	40.7±0.7 (13)***	38.7±1.0 (19)+++
	3	38.6±0.7 (13)*	42.0±1.3 (19)
	6	36.8±1.5 (58)	34.6±1.0 (63)++
α angle	1	35.5±7.4 (16)***	69.9±5.4 (20)
	2	31.8±6.5 (13)	47.2±10.1 (19)
	3	36.0±7.9 (13)	48.0±12.3 (19)
	6	37.4±3.7 (53)**	0.2±6.2 (63)+++

Note. *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with Wistar rats, +$p< 0.05$, ++$p<0.010$, +++$p<0.001$ compared with previous age. Number of rats is given in parentheses.

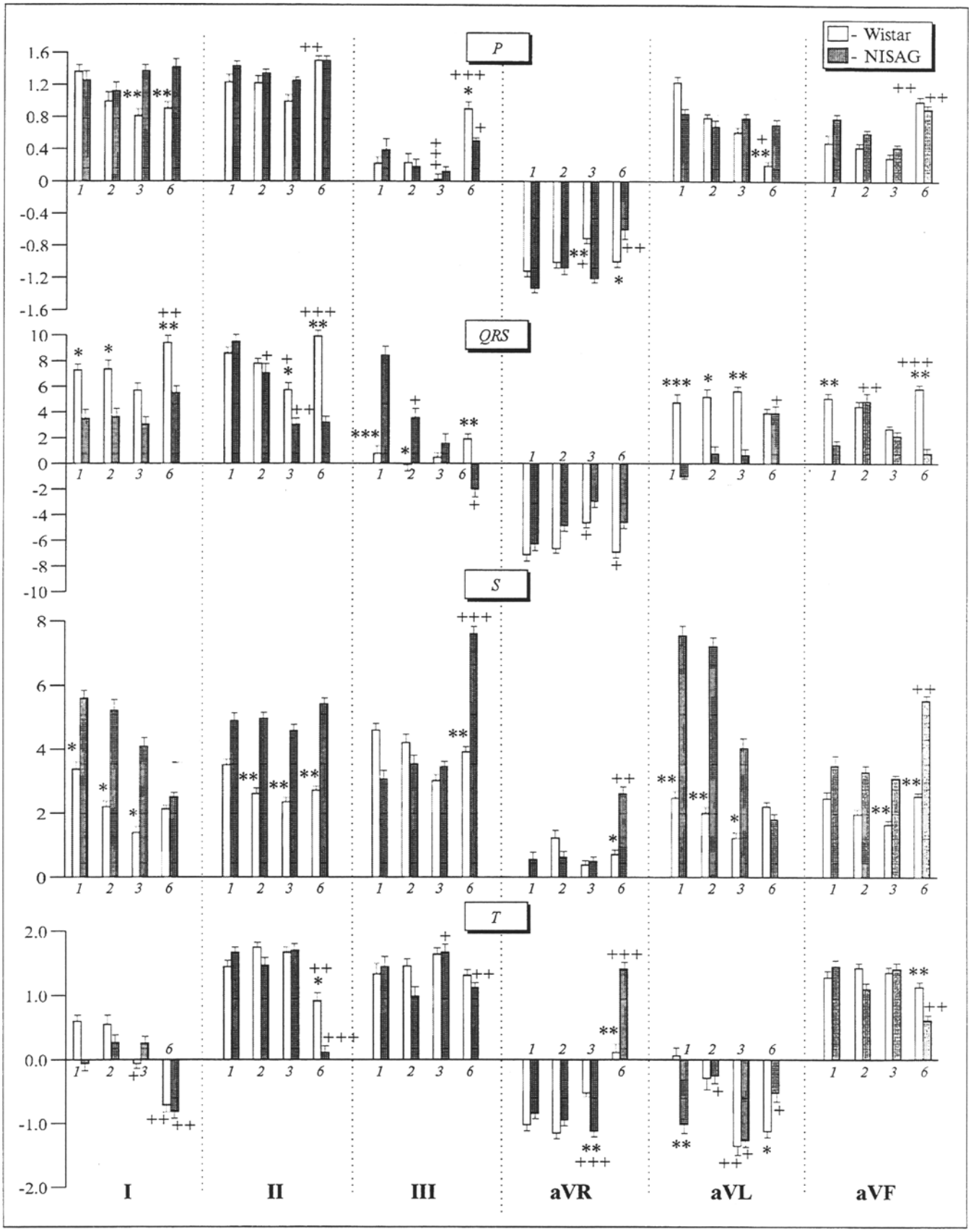

Fig. 1. Amplitude of ECG waves (mm) in NISAG and Wistar rats during ontogeny. Abscissa: age, months. *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with NISAG rats, *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with previous age.

observed, but electrical axis of the heart was shifted to the left, which is determined by a positive *QRS* complex in standard lead I and negative in lead III (Fig. 1). Shift to the left is typical of SHR [2]. An increase in the *QRS* complex in aVL lead compared with that in aVF lead has been observed in NISAG rats, while in Wistar the *QRS* sum in aVF lead was higher than in aVL lead (Fig. 1). In NISAG rats the *QRS* complex was longer (Table 1), which was also observed in SHR [15].

Thus, according to the ECG, in NISAG rats, similar to SHR, the left ventricle is hypertrophied [12]. In addition, in 3- and 6-month-old NISAG rats the left atrium is hypertrophied, as evidenced by high amplitude of the *P* wave in I standard and aVL leads (Fig. 1) and significant increase in its duration (Table 1). At the same time, starting from the age of 2 months the relative mass of the heart significantly increased in comparison with that of Wistar rats (Fig. 2). From these findings it can be concluded that ECG does not provide sufficient information regarding the beginning of myocardial hypertrophy in NISAG rats, which also holds true for SHR [10].

With age the duration of the *QRS* complex increases both in Wistar and NISAG rats; however, in hypertensive rats, as well as in SHR [13], in the age of 3 and 6 months the duration of the *QRS* complex is >20 msec (Table 1), which probably reflects myocardial damage [5].

Presumably, together with hypertrophy of the left heart, adult NISAG rats develop relative insufficiency of coronary circulation, which is confirmed by morphological data [12]. In the ECG, this is reflected by the amplitude of the *T* wave and the ratio between the *T* wave and the *QRS* complex (Fig. 1): the inversion of the *T* wave is impaired in aVR lead, which results in discordance between the *QRS* complex and the *T* wave in this lead. The discordance between the *QRS* complex and the *T* wave was also observed in lead III. In NISAG rats the amplitude of the *T* wave in aVL and aVF leads is lower than that in Wistar rats (Fig. 1).

During the first 3 months of life heart rate in NISAG rats is lower than in Wistar rats, while in adult NISAG rats it increases in comparison with that in Wistar rats, which is reflected by a shorter *RR* interval (Table 1). Tachycardia has been observed in SHR [14]. In adult NISAG rats, the duration of *P* wave, *QRS* complex, and *PQ* interval (Table 1) increased. The same increase was observed in younger NISAG rats. This probably points to a genetically determined decrease in the excitation velocity in the myocardium. The longer *S* wave almost in all leads testifies to alterations of ventricular conductance in

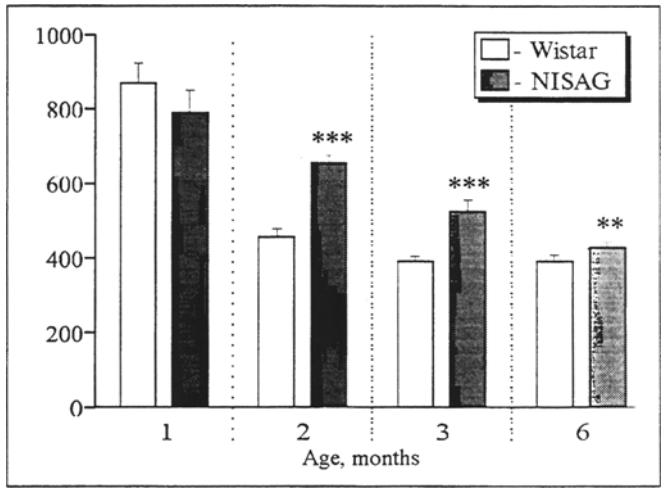

Fig. 2. Changes in the relative heart weight (mg/100 g body weight) of NISAG and Wistar rats during ontogeny. Here and in Fig. 3: *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with Wistar rats.

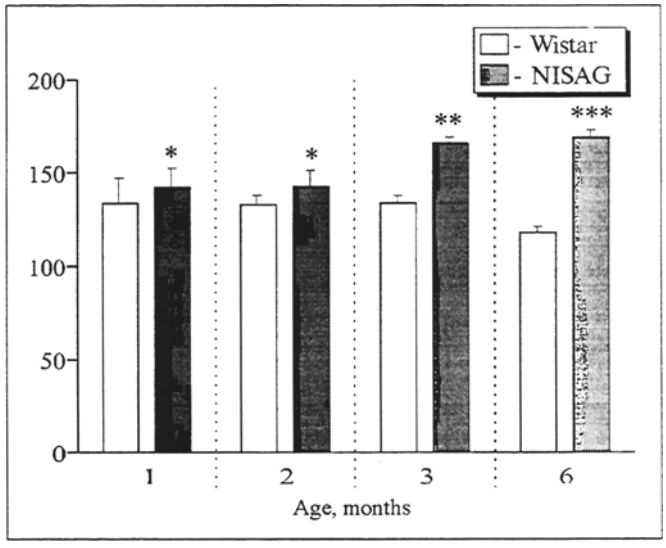

Fig. 3. Changes in arterial pressure (mm Hg) in NISAG and Wistar rats during ontogeny.

NISAG rats of all ages (analogy with S-type ventricular blockade in humans, Fig. 1).

With age the duration of electrical systole (the *QRST* interval) increases both in Wistar and NISAG rats, which was also observed SHR [10].

The relative length of electrical systole (Table 1) can be used as an indirect indicator of cardiac function. In NISAG rats it is shorter during the first months of life and becomes longer in 3-month-old rats. However, it does not differ in resting adult NISAG and Wistar rats, i.e., hypertrophied heart of NISAG rats is well adapted to higher AP. Contractile function of the heart SHR at the early stages of hypertension remains normal [9].

Arterial pressure is significantly higher in 1-month-old NISAG rats than in Wistar rats (Fig. 3). This difference becomes more pronounced with age,

reaching the "hypertensive level" (>150 mm Hg) in 3-month-old NISAG rats. However, at the age of 3 months there were no changes on the ECG typical of hypertension. It is reasonable to suggest that ECG changes, which reflect alterations of cardiac function in response to elevated AP, lag behind arterial hypertension.

Thus, we have demonstrated that myocardial hypertrophy and some ECG changes in NISAG rats are secondary relative to arterial hypertension.

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