EXPERIMENTAL BIOLOGY

Effect of Cold Stress in Early Postnatal Ontogeny on Blood Pressure and Heart Activity in Normo- and Hypertensive Rats

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Cold stress in the early postnatal ontogeny caused permanent functional changes in the cardiovascular system, which were different in hypertensive NISAG and normotensive WAG rats. Stress led to elevation of blood pressure and overload on the left heart chambers in adult WAG rats postnatally exposed to cold. At the same time, postnatal exposure to cold stress attenuated functional disturbances typical of hypertensive NISAG rats.

Key Words: *early treatments; cold stress; electrocardiography; arterial hypertension*

Acute cooling stress activates the sympathetic nervous system in warm-blooded animals [8]. On the other hand, the sympathetic tone is high in NISAG rats with stress-sensitive arterial hypertension [9]. Medicinal treatments changing the central mechanisms of sympathetic tone regulation in the early postnatal ontogeny can lead to a permanent decrease in blood pressure (BP) in NISAG rats. These data confirm an important role of sympathetic activity in the pathogenesis of stress-sensitive arterial hypertension [11]. We assumed that short-term cold stress in the early postnatal ontogeny would lead to permanent changes in the cardiovascular system and sympathetic activity in adult rats. These imprinting-like changes producing tolerance to various stimuli during the early postnatal ontogeny were discussed previously [4].

Here we studied the effects of cold stress during the early postnatal ontogeny on BP and heart activity (parameters of electrocardiogram, ECG) in adult hypertensive NISAG and normotensive WAG rats.

MATERIALS AND METHODS

Pregnant NISAG and WAG rats were kept in individual cages. Group 1 newborn rat pups (days 1-12 after birth) were daily exposed to cold stress at 5°C for 15 min. Group 2 rat pups served as the control. On day 30 after birth, the pups were isolated from dams; males and females were kept in cages to the age of 6 months. Adult male rats were placed in individual cages 3-4 days before the experiment. Basal BP was measured, and ECG was recorded. After 4-5 days, the rats were exposed to immobilization stress, and BP was measured. Body weights and weights of the heart, kidneys, and adrenal glands were estimated after decapitation.

BP in the caudal artery was measured by sphygmography. Basal BP and ECG were recorded under ether anesthesia. The rats in the prone position were placed in a shielded chamber. Needle limb electrodes were fixed subcutaneously and connected to a Mingograph-34 cardiograph. ECG was recorded in 3 standard

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and 3 augmented limb leads (tape speed 100 mm/sec, sensitivity 20 mm/mW). We measured the width and amplitude of *QRS* complex and *P*, *R*, *S*, and *T* waves and the duration of *PQ*, *QRST*, and *RR* intervals. During stress, BP was measured in non-narcotized animals. Stress was induced by 30-min immobilization in a wire cylindrical tube. The results were analyzed by Student's *t* test.

RESULTS

Basal and stress BP, ECG parameters, and absolute and relative weights of organs differed between control NISAG and WAG rats. Adult NISAG rats had higher basal and stress BP than WAG rats. The increase in basal BP caused by immobilization stress was more pronounced in NISAG rats than in WAG rats (Table 1). In hypertensive NISAG rats, high stress-reactivity was accompanied by adrenal gland hypertrophy. Our previous studies showed that the development of hypertension in NISAG rats is accompanied by functional changes in the cardiovascular system [3]: hypertrophy of the myocardium in the left heart chambers and walls of small arteries [2], increased sensitivity to norepinephrine [1], ECG changes typical of arterial hypertension, relative cardiac insufficiency, and predisposition to epinephrine-induced arrhythmias and myocardial necroses [10]. The present study confirmed these data. Hypertrophy of the left heart chambers in NISAG rats was manifested in left axis deviation (α=-30°), high amplitudes of the *P* wave and *QRS* complex in leads I and aVL, wide *QRS* complex, and increased absolute and relative weights of the heart compared to that in WAG rats (Tables 1 and 2, Fig. 1). Signs of relative cardiac insufficiency were also noted: discordance of the *QRS* complex and *T* wave in all leads and *T* wave inversion in lead aVR (Fig. 1). Conduction disturbances in NISAG rats were manifested in lengthening of the *PQ* and *QRS* intervals and increased *S* wave amplitude in leads II, III, and aVF (Table 2, Fig. 1). Despite these changes, cardiac conduction in NISAG rats under rest conditions was not impaired: the systolic index in these animals did not differ from that in normotensive rats (Table 2).

Cold stress during the early postnatal ontogeny caused different functional changes in the cardiovascular system in hypertensive NISAG and normotensive WAG rats (Fig. 1). In adult NISAG and WAG rats exposed to cold stress during the early postnatal ontogeny, the basal BP did not differ from the control. However, in adult WAG rats postnatally exposed to cold, immobilization stress caused BP rise (Table 1) and overload on the left heart chambers. This was manifested in increased amplitudes of the *P* (leads I and aVL) and *R* waves (lead I, Fig. 1). A decrease in heart rate (lengthening of the *RR* interval), widening of the *P* wave, and lengthening of the *PQ*, *QRS*, and *QRST* intervals were also found in WAG rats (Table 2).

In NISAG rats, cold stress reduced the severity of functional disturbances. The amplitude of the *S* (leads II and aVF) and *R* waves (lead aVL) decreased, while the amplitude of the *QRS* complex increased (leads II, III, and aVF), which indicated reduced overload on the left ventricle (Fig. 1). The systolic index decreased, which was probably related to enhanced heart activity (Table 2).

TABLE 1. Blood Pressure, Body Weights, and Weights of Organs in Adult Hypertensive NISAG and Normotensive WAG Rats (*M*±*m*)

Parameter	WAG		NISAG	
	control (*n*=13)	cold stress (*n*=11)	control (*n*=10)	cold stress (*n*=13)
Basal BP, mm Hg	136.58±1.75	137.73±3.12	164.00±3.32^{+}	159.23±1.78^{+}
Stress BP, mm Hg	139.58±1.89	147.55±2.58***	192.5±5.54^{+}	206.54±8.05^{+}
ΔBP, mm Hg	2.58±2.42	9.82±4.31	28.5±5.78^{+}	48.08±7.71^{+}
Body weight, g	246.83±9.77	263.64±6.47	257.30±15.18	263.85±7.89
Heart weight, g	0.87±0.04	0.92±0.01	1.03±0.05^{+++}	1.01±0.03^{+++}
mg/100 g body weight	355.27±14.00	352.66±9.45	404.90±10.34^{++}	385.10±5.82^{++}
Kidney weight, g	1.51±0.07	1.70±0.05***	1.80±0.06^{++}	1.68±0.08
mg/100 g body weight	613.80±18.93	648.15±22.60	709.78±21.61^{++}	634.11±17.90**
Adrenal weight, mg	31.83±0.64	32.00±0.90	43.20±2.18^{+}	46.38±1.19^{+}
mg/100 g body weight	13.15±0.67	12.18±0.35	16.89±0.40^{+}	17.66±0.37^{+}

Note. Here and in Table 2: *p<0.001, **p<0.01, and ***p<0.05 compared to the control; ^{+}p<0.001, ^{++}p<0.01, and ^{+++}p<0.05 compared to WAG rats.

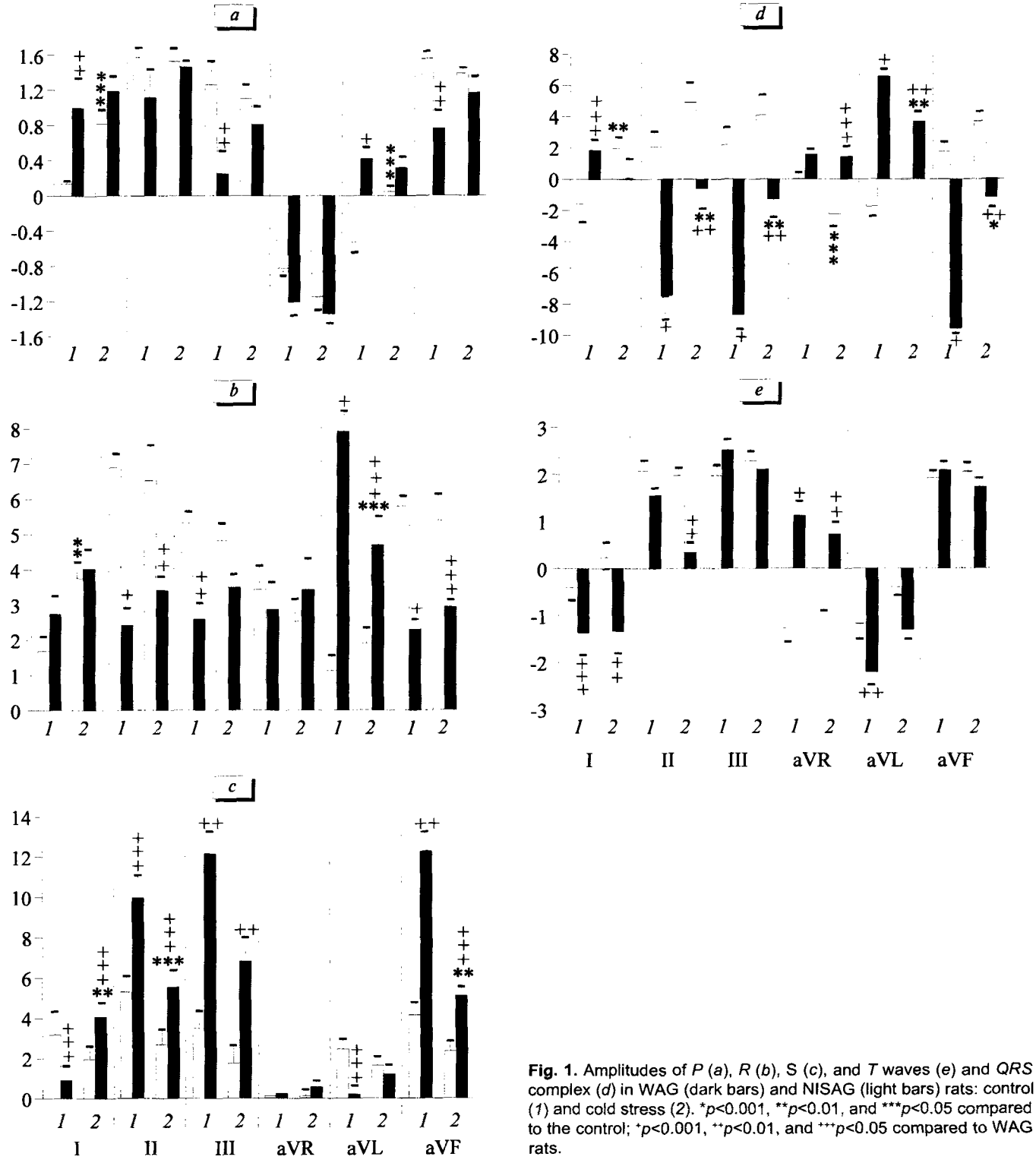

Fig. 1. Amplitudes of *P* (*a*), *R* (*b*), S (*c*), and *T* waves (*e*) and *QRS* complex (*d*) in WAG (dark bars) and NISAG (light bars) rats: control (*1*) and cold stress (*2*). $^{*}p<0.001$, $^{**}p<0.01$, and $^{***}p<0.05$ compared to the control; $^{+}p<0.001$, $^{++}p<0.01$, and $^{+++}p<0.05$ compared to WAG rats.

Thus, cold stress during the early postnatal ontogeny causes different functional changes in the cardiovascular system in NISAG and WAG rats. This procedure produces a positive effect in NISAG rats: their tolerance to emotional stress increases, which is manifested in adequate rather than attenuated reactions to 30-min immobilization (although stress-induced elevation of BP in these animals is more pronounced than in WAG rats). Postnatal exposure to cold stress attenuates functional disturbances in NISAG rats kept under standard vivarium conditions. At the same time, these rats retain the ability to react to immobilization

TABLE 2. ECG Intervals and Systolic Index in WAG and NISAG Rats (*M*±*m*)

Parameter	WAG		NISAG	
	control (*n*=11)	cold stress (*n*=11)	control (*n*=9)	cold stress (*n*=11)
ECG intervals, 10^{-2} sec				
P	2.17±0.03	2.64±0.14**	2.32±0.09	2.33±0.08
PQ	5.01±0.11	6.11±0.30**	5.81±0.15^{+}	6.04±0.08
QRS	2.31±0.06	2.95±0.10*	2.70±0.09^{++}	2.67±0.09^{+++}
QRST	7.26±0.27	8.67±0.59***	7.12±0.34	6.57±0.21^{++}
RR	14.00±0.36	17.95±0.79*	14.53±0.51	14.60±0.42^{++}
Systolic index, %	51.76±1.20	57.75±4.93	48.9±0.91	45.21±1.29***$^{+++}$

stress. These effects of stress in the early ontogeny on behavioral characteristics of adult rats were reported by V. H. Denenberg [5,6] and P. S. Goldman [7].

At the same time, immobilization stress causes BP elevation in adult WAG rats postnatally exposed to cold. In 4 of 11 WAG rats, BP was above the normal (150 mm Hg). This hypertensive reaction is not characteristic of control WAG rats. The relative weight of the kidneys in postnatally stressed WAG rats approached that in hypertensive rats. By contrast, this parameter in NISAG rats exposed to cold stress during the early ontogeny was normalized.

Thus, the genotype of rats determines delayed effects of short-term cold stress in the early ontogeny.

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