Thermoregulatory Reactions to Cooling in Rats with Hereditary Arterial Hypertension

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Experiments on rats with hereditary stress-induced arterial hypertension showed that hypertension shortened the latency and increased the amplitude of constrictive reaction of skin blood vessels to rapid cooling characterized by more rapid and considerable increase in blood norepinephrine content compared to slow cooling. Decreased thermal threshold of metabolic reaction suggests that arterial hypertension is accompanied by changes in both the vascular walls and tissues involved in metabolic reaction to cooling.

Key Words: *arterial hypertension; cooling; thermoregulatory reactions*

Circulation plays an important role in thermal exchange with the environment. Constrictive reaction of skin blood vessels limiting heat exchange between the body and environment is an important reaction to cooling in homoiothermic vertebrates. Modulation of peripheral circulation can modify organism's response to cold. Strengthening of constrictor properties of blood vessels in subjects with cardiovascular diseases, for example arterial hypertension, can modulate the formation of thermoprotective reactions during cold exposure. It is also interesting to evaluate the contribution of vascular reaction to the maintenance of thermal homeostasis during developing hypertension and to elucidate whether it is associated with changes in the metabolic component of organism's reaction to cold.

Here we studied the effect of arterial hypertension on the threshold and amplitude of thermoregulatory reactions during cooling.

MATERIALS AND METHODS

Experiments were carried out on male NISAG rats, a biological model of hereditary stress-induced arterial hypertension (mean systolic arterial pressure 172.0± 2.2 mm Hg) [9]. Wistar rats (mean systolic pressure 109.0±5.6 mm Hg) served as controls. The animals were kept at 21-24°C. Cooling was carried out under Nembutal narcosis (40 mg/kg) to exclude the effect of emotional stress. Shaven abdominal surface (25 cm^2) was cooled with a thermode at a rate of 0.08°C/sec (rapid cooling) or 0.008°C/sec (slow cooling). These regimens of cooling ensured the presence of dynamic activity of skin cold receptors during rapid cooling and absence of this activity during slow cooling [2]. Cooling was stopped after a 3°C decrease in rectal temperature.

The temperature on ear skin, intracutaneous temperature of cooled abdominal surface, rectal temperature, total O_2 consumption, and electrical activity of cervical muscles (EACM) were recorded throughout the experiment by the methods described previously [2]. Intracutaneous and rectal temperature were measured by copper constant thermocouples (0.01°C sensitivity). The velocity and intensity of cold exposure was evaluated by changes in abdominal skin temperature, shifts in core body temperature were evaluated by rectal temperature, and the beginning, velocity, and intensity of vascular reaction were evaluated by ear skin temperature. The metabolic reaction was monitored by changes in total O_2 consumption and contractile thermogenesis was evaluated by EACM. Change of O_2 consumption by 1 ml/min/kg was taken for the start of metabolic reaction, increase or decrease by 0.1°C was taken for the threshold value for skin and

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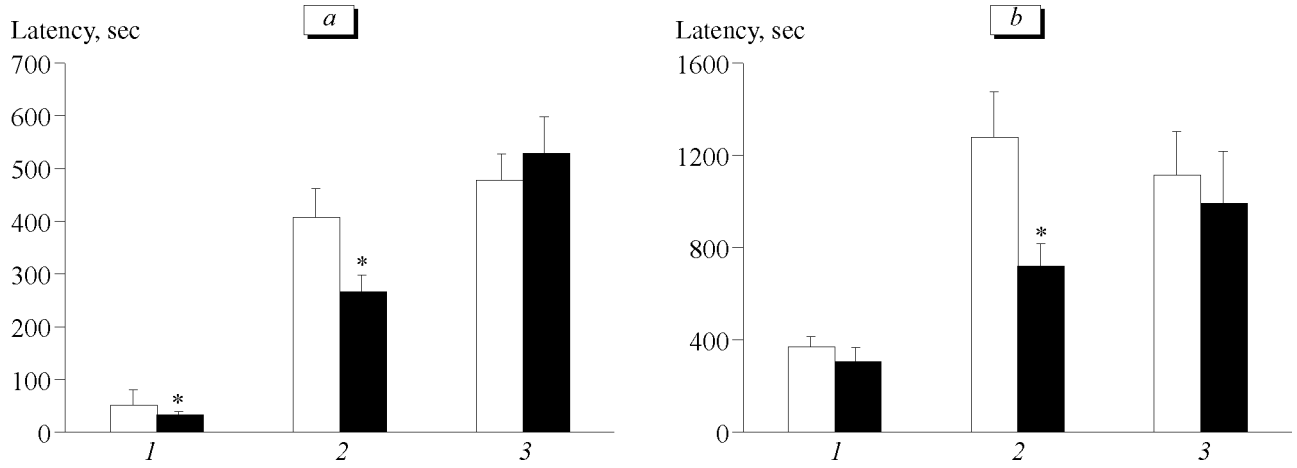


Fig. 1. Latencies of vascular (*1*) and metabolic reactions (*2*) and appearance of electrical activity of muscles in Wistar and NISAG rats during rapid (*a*) and slow (*b*) cooling. Here and in Figs. 2 and 3: light bars: Wistar rats; dark bars: NISAG rats. *$p<0.05$ compared to Wistar rats.

rectal temperatures, and a shift by 1 μV was taken for threshold muscular activity.

The baseline values for all parameters under thermoneutral conditions were taken for the initial values. All parameters were in-put into a PC using Term software developed in our laboratory. Twenty hypertensive and 26 control rats were used.

The data were processed statistically using Student's *t* test.

RESULTS

Under thermoneutral conditions the studied parameters did not differ in NISAG and Wistar rats (Table 1). Cooling was associated with thermoprotective reactions (decreased heat emission and increased heat production).

Constrictor reaction of ear skin vessels in narcotized animals preceded the changes in total O_2 consumption and EACM in both control and NISAG rats during both rapid and slow cooling. Vascular reaction appeared before attaining the threshold rectal temperature.

During rapid cooling vascular reaction in NISAG rats developed earlier (Fig. 1) and at higher abdominal skin temperatures (Fig. 2) than in controls. Vascular reaction of NISAG rats during rapid cooling was more pronounced: the maximum decrease of ear skin temperature was 3.40±0.34°C *vs.* 2.60±0.18°C in the control ($p<0.05$).

During slow cooling the latency, threshold temperatures, and intensity of vascular reaction in hypertensive rats did not differ from those in the control (Figs. 1, 2).

The metabolic reaction in NISAG rats during both rapid and slow cooling developed earlier (Fig. 1) and at higher skin and rectal temperatures in comparison with the control (Fig. 3, *a*, *b*). The maximum increase in O_2 consumption during cooling was virtually the same in both groups (Fig. 3, *c*).

EACM of NISAG and Wistar rats during both rapid and slow cooling were similar. In both groups EACM appeared earlier during rapid cooling compared to slow cooling (Fig. 1). The threshold decease of abdominal skin temperature during slow cooling (7.50±0.89°C in NISAG and 7.30±0.93°C in Wistar rats) was significantly lower than during rapid cooling (10.50±0.65°C in NISAG and 10.20±0.76°C in Wistar rats), while the threshold decrease of rectal temperature (1.5±0.3°C) and the maximum EACM (15.0±3.8 μV) were similar.

Published reports indicate that the sympathetic nervous system acting through α-adrenoreceptors in the vascular wall plays an important role in the development of hypertensive conditions [5-7]. It was shown that NISAG rats are characterized by higher activity of the sympathetic system [8,9] and higher sensitivity of arteries to norepinephrine [1]. On the other hand, cooling is accompanied by activation of the peripheral sympathetic nervous system (SNS) and increase in blood catecholamine concentration [4]. Moreover, activation of SNS and increase in blood norepinephrine concentration during rapid cooling occur more rapidly than during slow cooling [3].

TABLE 1. Parameters Recorded under Thermoneutral Conditions in Wistar and NISAG Rats (*M*±*m*)

Parameter	NISAG	Wistar
Total oxygen consumption, ml/min	15.50±0.69	17.06±0.81
Temperature, °C		
ear skin	30.20±0.29	30.46±0.21
abdominal intracutaneous	37.10±0.18	37.42±0.12
rectal	36.53±0.11	36.85±0.13
EACM, μV	2.60±0.23	2.59±0.20

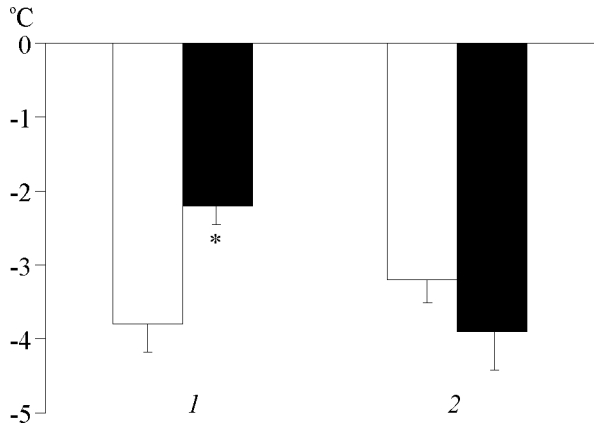
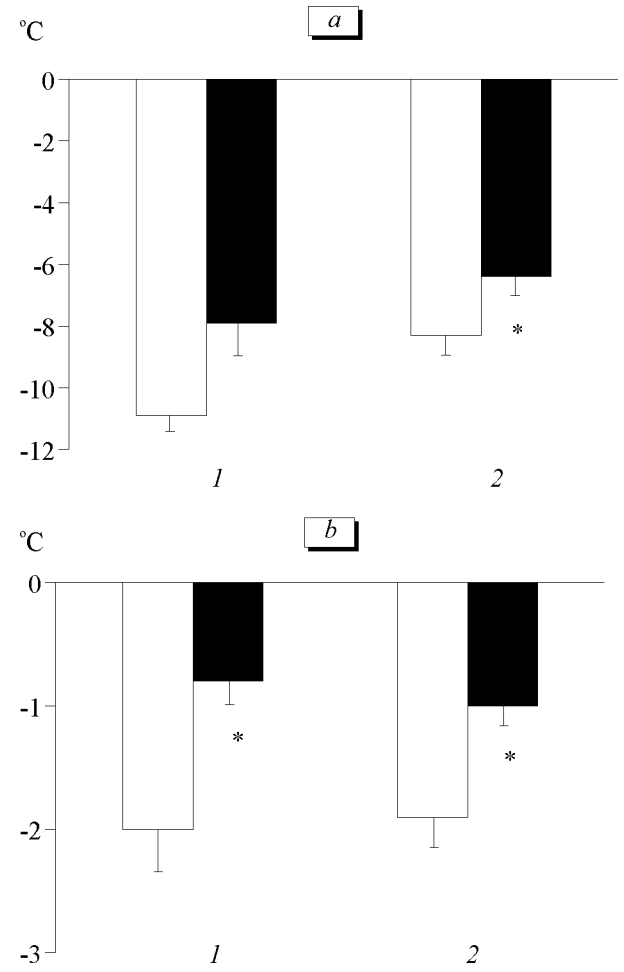


Fig. 2. Threshold decrease of skin temperature for vascular reaction during rapid (*1*) and slow (*2*) cooling in NISAG and Wistar rats.

It can be hypothesized that different effects of these two modes of cooling on the thresholds and amplitudes of vascular response to cooling are determined by different activity of skin cold receptors. Since more rapid vascular reaction of hypertensive rats was observed only during rapid cooling characterized by the presence of the dynamic component of thermoregulatory activity, we believe that the shorter latency and the higher amplitude of constrictive reactions in hypertensive rats were determined by additional activation of SNS during rapid cooling. In our experiments the metabolic reaction during both rapid and slow cooling in hypertensive animals was observed earlier than in controls. The metabolic reaction included intensification of the metabolic processes in the viscera, particularly in brown adipose tissue (noncontractile thermogenesis), and increase of electrical activity of skeletal muscles (contractile thermogenesis). It is noteworthy that in hypertensive animals the metabolic reaction to cooling (judging from total O_2 consumption) appeared earlier than shivering (Fig. 1), which attests to higher contribution of noncontractile thermogenesis into organism's response to cold exposure in NISAG rats. In controls, the increase in total oxygen consumption and change in EACM appeared simultaneously and, therefore, the increase in oxygen consumption in these animals is determined primarily by contractile thermogenesis. Presumably, increased sympathetic activity in hypertensive animals is responsible for activation of noncontractile thermogenesis which, according to published reports, is mediated by β-adrenergic structures.



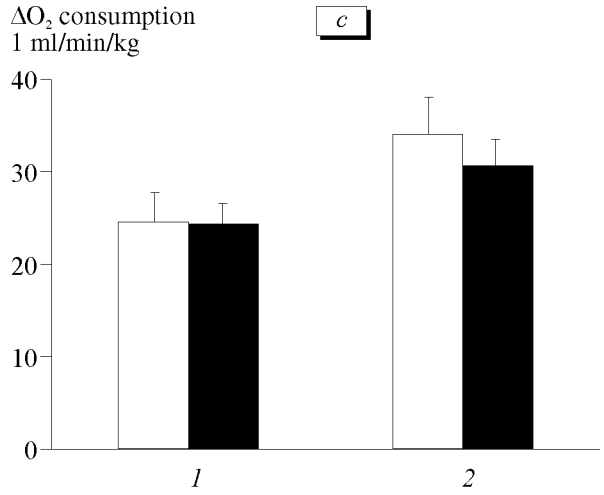


Fig. 3. Threshold decrease of skin temperature (*a*) and rectal temperature (*b*) for vascular reaction and increase of O_2 consumption (*c*) during rapid (*1*) and slow (*2*) cooling in Wistar and NISAG rats.

Thus, our findings suggest that hypertension decreases the latency and increases the amplitude of constrictor reaction of skin blood vessels during rapid cooling, characterized by the presence of dynamic activity of cold receptors and more drastic increase in blood norepinephrine content in comparison with slow cooling. Decreased thermal thresholds of metabolic reaction during slow and rapid cooling suggest that hereditary stress-induced arterial hypertension modulates functional characteristics of not only vascular wall, but also tissues involved in the metabolic reaction to cold.

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