The Effect of Antiorthostatic Hypokinesia Training on Central Hemodynamics in Rats

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Antiorthostatic training increased stroke and minute blood volumes, and decreased heart rate and peripheral vascular resistance. In test and control rats these parameters changed individually during antiorthostatic hypokinesia. After returning to horizontal position, rats (control) exhibited the signs of orthostatic instability. Preliminary training raised the tolerance of the central hemodynamics to antiorthostatic hypokinesia and to the horizontal position recovery.

Key words: *cardiovascular system; antiorthostatic hypokinesia; training*

Considerable changes in central and peripheral hemodynamics during space flight relate mainly to blood redistribution in the cardiovascular system. These alterations are most pronounced during functional loading and after landing.

The recordings of hemodynamic parameters in rats in the standard conditions by invasive methods during antiorthostatic (AO) hypokinesia [2,11] provide a convenient experimental model for investigation of the cardiovascular system.

The shifts in central and peripheral circulation under AO hypokinesia have been extensively investigated [1,10,12,13].

However, there is little evidence on the hemodynamic response to the horizontal position recovery after AO hypokinesia [6]. Nothing is known to what extent a preliminary AO hypokinesia training modulates the dynamics of circulatory changes occurring in the system after the recovery of horizontal position.

Our aim was to study the effect of preliminary AO training on cardiovascular hemodynamic shifts in rats subjected to a 24-h AO hypokinesia.

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MATERIALS AND METHODS

Male Wistar rats weighing 200-400 g were put in the AO position (tilted at 30 degrees to the horizon) by hanging their tails up with an originally designed clamp which did not impede movements along the chamber and free access to food and water. The rats were trained for two weeks for 2 h every day.

In order to measure arterial pressure (AP), a polyethylene catheter was inserted via the femoral artery into the abdominal aorta under Nembutal anesthesia (40 mg/kg, intraperitoneally). The distal end of the catheter was fixed subcutaneausey in the interscapula area.

Cardiac output was determined with an intravascular ultrasonic flowmeter transducer [3]. The transducer consisted of a polyethylene catheter 0.6 mm in diameter and a miniature ultrasonic piezocrystal attached to its end that emitted 27 mHz waves. The detector was inserted via the right common carotid artery under Nembutal anesthesia under constant control of the signal shape. The outlets of the wires from the flowmeter laid subcutaneously were fixed on the scapulas with a plaster.

The cardiac output (CO) and AP signals were fed into an analogminicomputer to record SV, MBV, peripheral vascular bed resistance (PVR), CO acce-

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leration, HR, and cardiac power (a product of CO and AP signals [4]) in the real time.

Experiments with rat AO positioning were started 2 days after the surgery. At the end of experiments the animals were killed by intra-arterial injection of Nembutal overdose.

Supercalc-4 and Solo software was used for statistical analysis of the results by non-parametric Wilcoxon (for intragroup) and Mann-Whitney test (for intergroup differences).

RESULTS

Daily two-hour tilting of the rat for 2 weeks resulted in considerable changes in the studied hemodynamic parameters (Fig. 1.) followed by relative bradycardia; HR decreased by 11% and was 343±15 beats/min compared with 385±13 beats in the control group, and SV increased by 38% and MBV by 23% regardless to the bradycardia.

At the same time, AP did not change (111.75± 4.34 mm Hg in control rats and 113.78±6.88 mm Hg in trained rats).

The cardiac power in trained rats exceeded that in control rats by 18%. After AO training, PVR was lower by 24% than in control rats.

Rats from the two groups responded differently to the AO-tilt. In the control group, SV and MBV increased within the first 5 min by 7% and 6.5%, respectively. In the trained rats, both parameters did not change (Fig. 2, *a*, *b*).

Further exposing to AO position had no effect on HR and AP in the control rats, while in the trained rats HR raised by 11% and AP by 15.2% by the end of the first day ($p<0.05$, Fig. 3, *a*, *b*).

In the control group, after 24 h SV increased by 16.5% and MBV by 15.4% compared with the initial values. In the trained rats, these parameters decreased by 16.3% ($p<0.05$) and by 6.1%, respectively (Fig. 3, *c*, *d*).

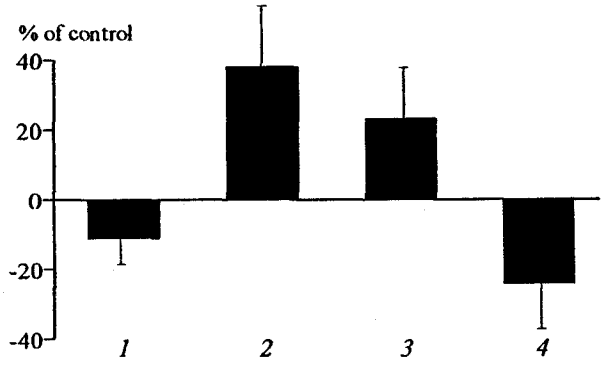

Fig. 1. The effect of preliminary antiorthostatic training on hemodynamic parameters. The columns are: heart rate (*1*); stroke (2) and (3) minute blood volumes; peripheral vascular bed resistance (*4*).

PVR exceeded the initial values by 7.5% in the trained rats and by 27.1% in control rats ($p<0.05$).

The CO acceleration, which reflects the contractility of the myocardium, did not vary significantly during AO tilting in both groups.

AO training produced the strongest effect on hemodynamics after returning to horizontal position. HR increased to a greater extent in the trained animals (by 12.6%) than in the control (by 4.8%) as compared with the values observed after 24 h of AO tilting (Fig. 3). AP showed a tendency to increase with time in the trained rats and to decrease in the control. SV decreased in both groups, however, to a greater extent in the control rats (by 19.4%, $p<0.05$ compared with the 24-h value) *vs.* 7.6% in the trained rats (Fig. 3). In the view of the reverse character of HR and SV shifts, MBV was reduced only in the control group (by 12.1%), while in the trained animals it slightly increased (by 2.5%). PVR exceeded the basal level by 23.1% ($p<0.05$) in the trained rats, and was by 9.5% below it in control rats.

Thirty minutes after the horizontal position recovery, the dynamics of changes of the tested parameters was similar. There was a tendency to a greater reduction in MBV because HR was virtually normalized. PVR continued to grow in the trained rats (by 32.5%, $p<0.05$), while in the control rats it remained lower (by 2.5 %) than in the basal level.

Reduced cardiac diastolic and stroke volumes and inability to compensate this by raising HR are the main factors responsible for orthostatic nonstability [5]. These data indicate that the signs of orthostatic nonstability appear in the nontrained rats after returning to horizontal position. These rats exhibited a tendency toward a decrease in AP, which was absent in the trained rats.

The time course of changes in central hemodynamics in the two groups of rats resembles that in humans with or without postural syncope after AO tilt resting in the bed. Thus, the subjects with a syncope syndrome were unable to adequately raise HR in spite of considerable drop in AP associated with weak baroreflex reactions [7].

In the literature there is some uncertainty about the interpretation of hemodynamic changes associated with baroreflexes in rats [8,9]. There is evidence that in rats the baroreflex sensitivity in rats deteriorates after AO tilting [6,9,14]. It is likely that preliminary AO training leads to persistence of the baroreflex regulation after recovery of horizontal position.

Thus, AO tilting of rats for 24 h is sufficient to impair the cardiac pumping function and, probably, the regulatory mechanism (baroreflex control of

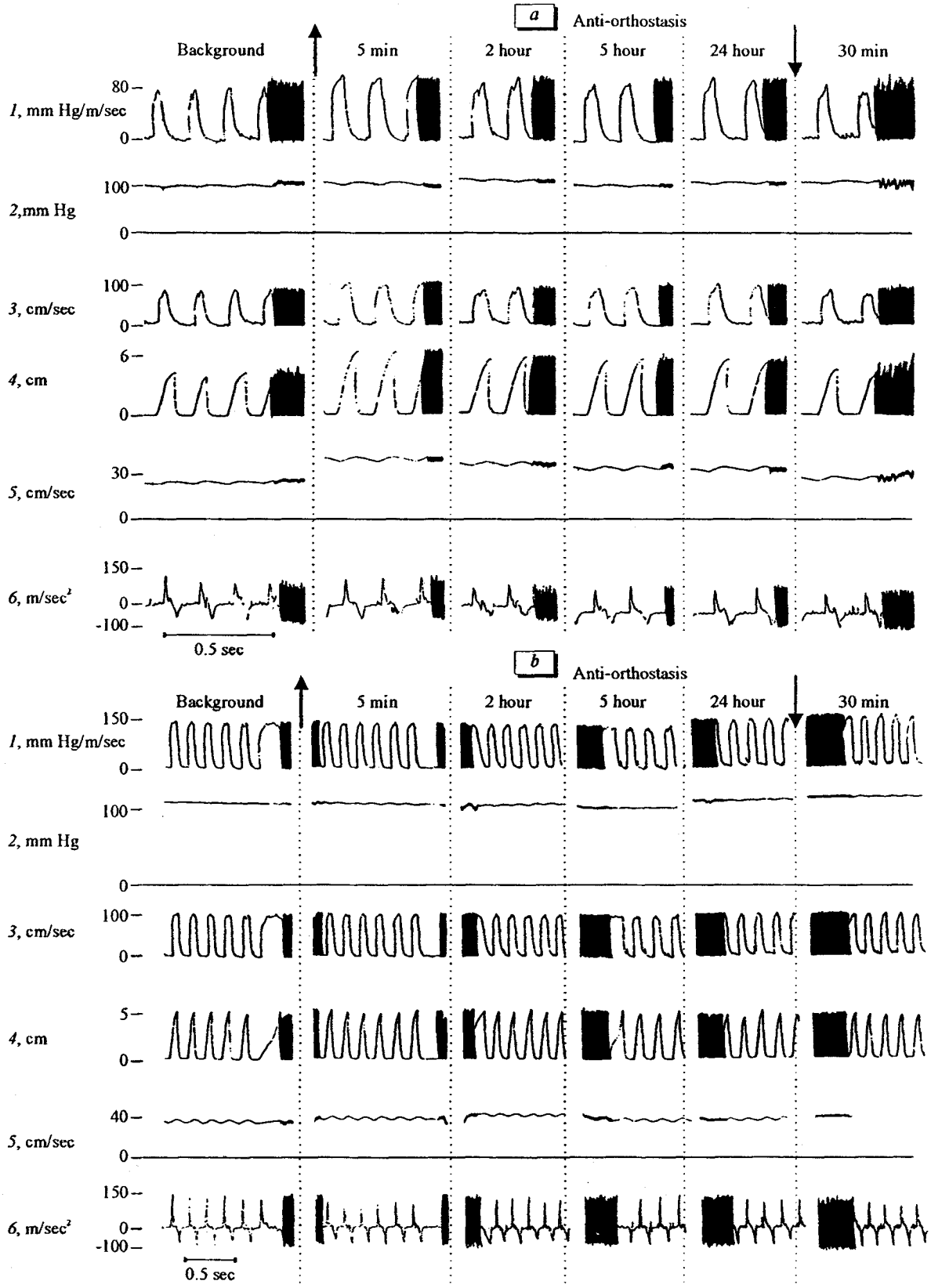

Fig. 2. The main hemodynamic parameters in control rats (*a*) and in rats trained to antiorthostatic position (*b*). The following parameters are shown: power (*1*); arterial pressure (*2*); linear flow rate (*3*); stroke (*4*) and (*5*) minute blood volumes; acceleration (*6*).

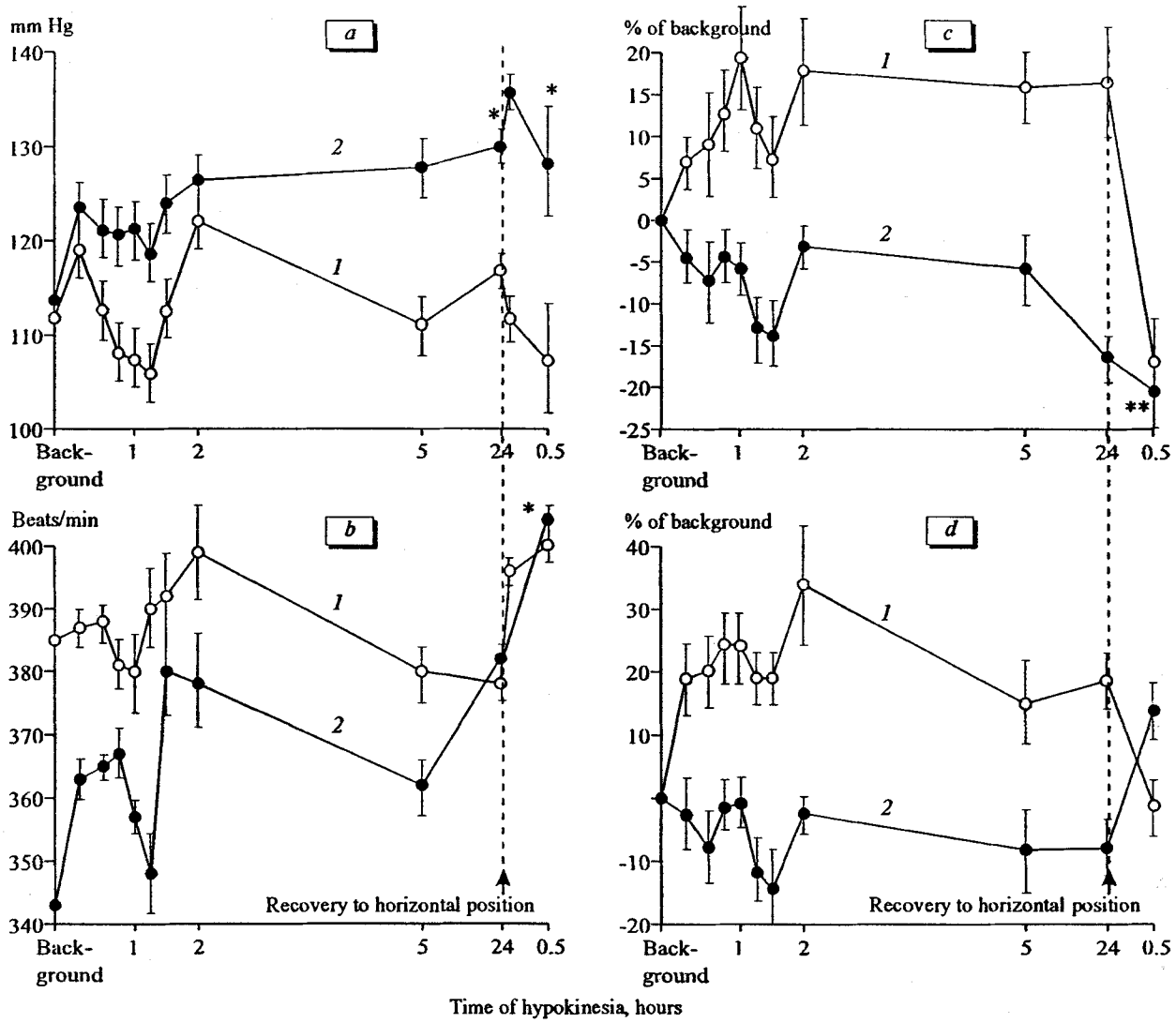

Fig. 3. Changes in the main systemic parameters in conscious rats during a 24-h antiorthostasis. In the plots: control rats (*1*) and trained rats (*2*); parameters — arterial pressure (*a*); heart rate (*b*); stroke (*c*) and (*d*) minute blood volumes. $p<0.05$ *compared with background, **compared with parameters after 24-hour AO-hypokinesia.

HR). These singes are clearly manifested after returning to horizontal position. Preliminary training makes hemodynamic parameters more stable during AO tilt and after recovery of horizontal position.

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