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Effect of Adaptation to Stress-Inducing Electrical Stimulation on the Reactivity of the Isolated Resistive Artery

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Recent studies have shown that adaptation to repeated moderate stress induces the activation of the so-called stress-limiting systems [1] and simultaneously improves the organism's resistance to stress-induced [1] and ischemic [2,5] damage, and global hypoxia [3]. It is now proven that these protective effects of adaptation may be achieved through course of mild transauricular electrostimulation (ES), which during its first presentation induces a stress reaction, but then suppresses it while at the same time activating the stress-limiting systems [4]. The cardioprotective effects of a course of EC have now been studied in detail, yet there are still no data on the effect of a course of ES on the tonus or adreno- and cholinoreactivity of blood vessels.

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The aim of the present study was to investigate the effect of adaptation to stress on the constrictive and dilatory responses mediated through α- and β-adrenoreceptors, and endothelium-dependent relaxation of the isolated rat caudal artery.

MATERIALS AND METHODS

Experiments were carried out on female Wistar rats weighing 350-400 g. The animals were divided into 2 groups: the first were intact controls and th4e second comprised rats which underwent a course of ES. Transauricular electrostimulation was performed with a Lasper CS-504 electrostimulator (Japan), originally designed for electropuncture in humans. The stimulation was carried out with single sharp pulses of 1.5-2 mA amplitude and 1.5 msec duration. Needle electrodes were inserted into both auricles near the external auditory meatus. The frequensy of stimulation was 200 pulses per minute. The course of stimulation consisted of 10 sessions, the first of which lasted 10 min and all subsequent ones 20 min. It was shown that, apart from reflex effects, the mehanism of action of the course of ES also involved the passage of a weak electrical current through the brain and adaptation to stress accompanying the procedure [5].

An 8-mm-long segment of artery taken from the proximal part of the rat caudal artery was cannulated at both ends and placed in an incubation chamber. The segment was perfused with Krebs-Henseleit solution by means of a Mikrostal'tik roll pump (Russia) under a constant flow rate (2 ml/min) [1]. The vessel was also washed on the outside with physiological saline, the temperature of which was maintained at 37°C. The reaction of the perfused vessel was estimated according to the changes in perfusion pressure detected with a Statham pressure transducer (USA) and recorded with a KSP-4 voltage meter.

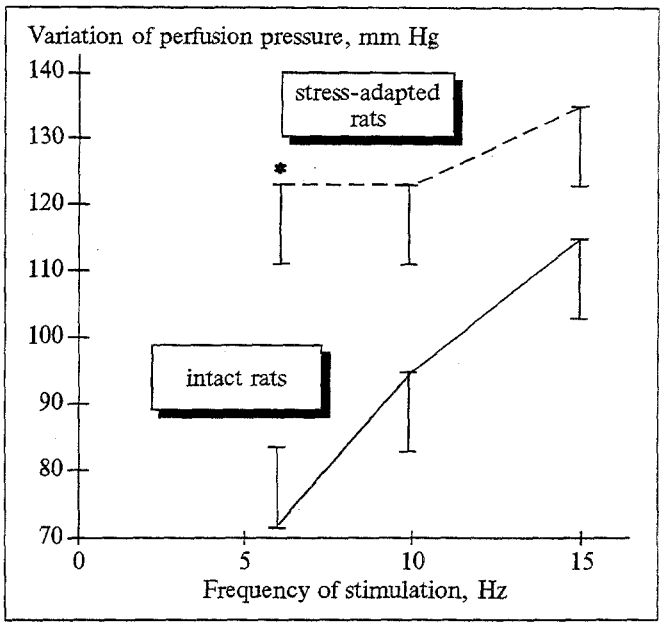
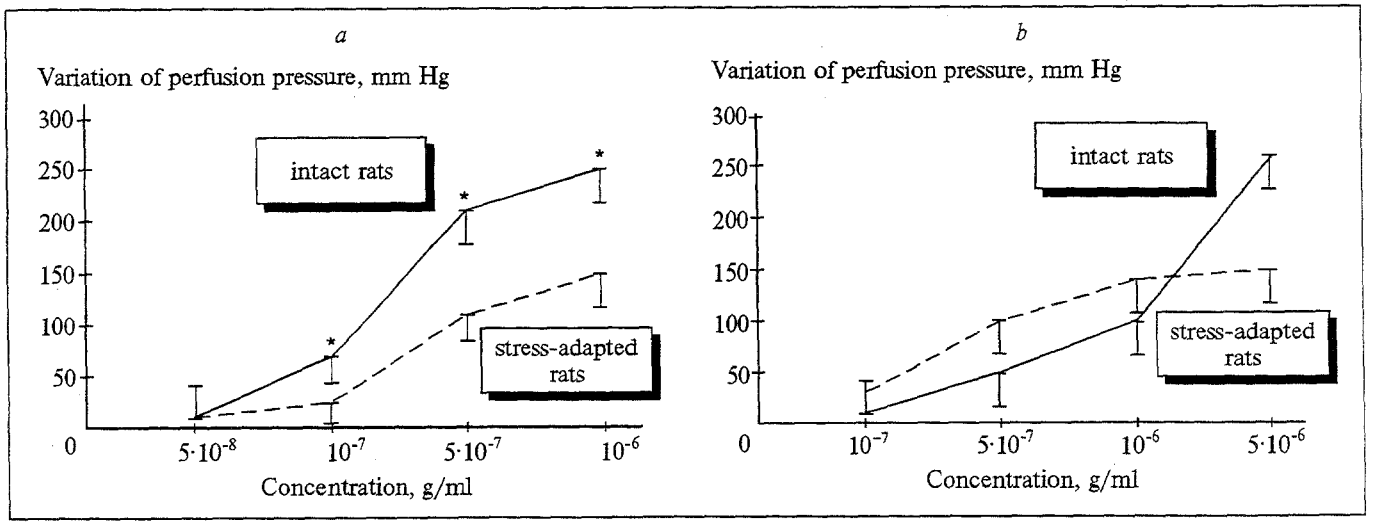


Fig. 1. Effect of adaptation to stress on constrictive and dilatory responses of isolated rat caudal artery, evoked by transmural electrical stimulation of nerve endings. Asterisk: $p<0.05$ in comparison with the control.

The electrical stimulation of nerve endings in the vessel wall was performed with a pair of electrodes. The first was a metal cannula inserted into the vessel, and the second electrode was led to the vessel from outside. The electrical stimulation was performed with square alternating pulses of the following parameters: duration 0.1 msec, voltage 50 V, and frequency 6, 10, and 15 Hz.

Vasoactive agents, norepinephrine (5×10^{-8}, 10^{-7}, 5×10^{-7}, 10^{-6} g/ml), phenylephrine (10^{-7}, 5×10^{-7}, 10^{-6}, 5×10^{-6} g/ml), isoproterenol (10^{-7} g/ml), and



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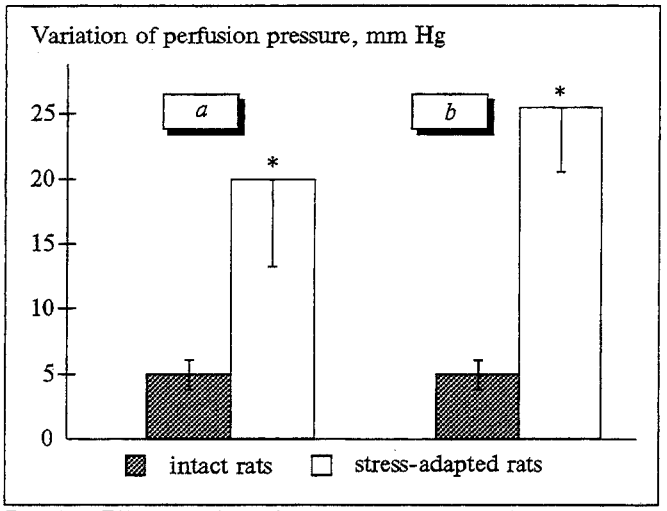

Fig. 3. Effect of adaptation to stress on constrictive response of isolated rat caudal artery. *a*) isoproterenol, *b*) acetylcholine.

acetylcholine (10^{-7} g/ml) were added to the physiological saline used for perfusion of the vessel segment. The vasodilatory responses were studied using a norepinephrine-precontracted vessel preparation. The norepinephrine concentration was so chosen as to induce a contraction of the isolated vessel approximately to 100 mm Hg.

The results were processed statistically using the Student *t* test.

RESULTS

The constrictive reactions of the isolated caudal arteries to transmural electrostimulation in rats having undergone the course of ES exceeded those in the controls approximately twofold (Fig. 1). Unlike in the controls, the caudal artery from adapted rats subjected to ES responded to a minimal stimulus with a submaximal contraction, which subsequently practically did not rise.

The constrictive reactions to norepinephrine were reliably lowered in rats subjected to ES (Fig. 2, *a*), whereas the reactions to phenylephrine did not differ reliably in the control and ES-subjected group (Fig. 2, *b*). These results suggest that transauricular ES does not change the sensitivity of α_1-adrenoreceptors. In this case, the increased amplitude of the constrictive responses of the caudal artery evoked by transmural electrical stimulation of the vascular wall occurs due to enhanced epinephrine release from presynaptic terminals. The reduced responses to norepinephrine are most probably related to increased dilatory reactions of the isolated vessel.

This assumption was confirmed during subsequent experiments aimed at the comparison of acetylcholine-induced endothelium-dependent relaxation and the reaction to the β-agonist isoproterenol of arteries from controls and rats subjected to a course of ES. The results of these experiments are presented in Fig. 3, *a* and *b*. Both the endothelium-dependent and β_2-adrenoreceptor-mediated dilatory reactions were considerably increased in rats which had undergone a course of ES.

Thus, the principal finding of the present study is that adaptation to repeated stress, which developed in the course of ES, resulted in stable changes in the reactivity of the isolated resistive artery obtained from adapted animals. These changes consist, first, in a decreased vasoconstrictive reaction to norepinephrine and, second, in a considerable enhancement of both, the acetylcholine-induced endothelium-dependent and β-agonist isoproterenol-induced vasodilatory reactions. In essence, this array of changes suggests that ES leaves a stuctural imprint in the organism, which profoundly alters the local regulation of the vascular tonus. The developed regulatory shift toward vasodilation in the resistive artery suggests the advisability of further investigating the effect of adaptation to stress on the state of the receptor apparatus of resistive arteries using labeled ligands. At the same time, this opens up prospects for studying the effect of a course of ES on arterial pressure in hypertension.

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