ADAPTATION TO HYPOXIA AT AN ALTITUDE OF 2 km AS A FACTOR PREVENTING DISTURBANCE OF CARDIAC CONTRACTIONS DURING EMOTIONAL AND PAIN-INDUCED STRESS

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Adaptation of animals to high-altitude (2 km) hypoxia in the mountains prevented disturbance of cardiac contractions during emotional and pain-induced stress but did not prevent the development of gastric ulcers.

KEY WORDS: emotional stress; adaptation to hypoxia; contractile function of the heart.

After emotional and pain-induced stress (EPS) not only do gastric ulcers develop [7], but disturbances also arise in the heart. These include activation of peroxidation of lipids, labilization of the lysosomes, a reduction in the catecholamine reserves, disturbance of glycolysis and the tricarboxylic acid cycle, and simultaneous disturbances of the contractile function of the heart [2, 4]. These phenomena do not develop in animals previously adapted to periodic hypoxia in a pressure chamber [4] and, consequently, such adaptation is a factor which prevents the disturbance of metabolism and cardiac function in EPS.

The object of the present investigation was to study the effect of preliminary adaptation to hypoxia under natural conditions at moderate altitudes in the mountains on cardiac function after EPS.

EXPERIMENTAL METHOD

Four series of experiments were carried out on female Wistar rats: The rats in series I were controls and received no treatment, those of series II had EPS, series III were animals adapted to mountain conditions, and series IV rats subjected to EPS after a stay in the mountains. Each series consisted of seven to nine experiments. EPS was produced by the formation of an anxiety neurosis, the model used previously [7] to obtain gastric ulcers. The EPS thus produced led to the development of gastric ulcers in 90% of rats.

Adaptation to mountain conditions took place in the village of Terskol at the Medico-Biological Station of the Academy of Sciences of the Ukrainian SSR at an altitude of about 2 km. Experiments on these animals were carried out at the same station by the method described earlier [3]. After electromanometric recording of the intraventricular pressure in both ventricles the rate of rise and fall of pressure and the index of intensity of functioning of structures (IFS), i.e., the product of the pressure developed and the frequency of contractions, divided by the mass of the ventricle, were calculated. These indices were determined for animals at relative physiological rest and with two types of functional load on the heart: a gradual increase in heart rate as a result of electrical stimulation and temporary compression of the ascending aorta.

EXPERIMENTAL RESULTS

In a state of relative physiological rest the principal indices of contractile function of both ventricles in animals with EPS did not differ from the control, in agreement with results published previously [4]. However, the absolute values of the indices in this series of experiments were lower than the usual values [3], evidently on account of the lower resis-

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TABLE 1. Effect of EPS on Indices of Contractile Function of Left Ventricle in Control Animals with Different Functional Loads

Experimental conditions	Systolic pressure, mm Hg		IFS index, mm/min/mg	
	control	EPS	control	EPS
Relative physiological rest	66±8	57±4	42±9	33±4
Increased heart rate to 300 beats/min	51±10	24±6*	42±5	21±6†
Compression of aorta	117±11	65±19*	48±9	22±2†

*P < 0.05.
†P < 0.02.

TABLE 2. Effect of EPS on Indices of Contractile Function of Left Ventricle in Animals Adapted to Altitude with Different Functional Loads

Experimental conditions	Systolic pressure, mm Hg		IFS index	
	adaptation	adaptation+EPS	adaptation	adaptation+EPS
Relative physiological rest	67±7	61±7	38±5	37±5
Increased heart rate to 300 beats/min	75±8	55±9	55±7	40±6
Compression of aorta	120±9	97±16	49±8	36±9

tance of female Wistar rats to the acute experimental conditions, and also to introduction of the cannula into both ventricles, which upsets cardiac activity. Consequently, the indices of function of the left ventricle of the control animals were substantially reduced in the presence of the functional loads. Nevertheless, comparison of the data in Table 1 shows that after EPS even a comparatively small and brief increase in the frequency of contractions — from 250 to 300/min — led to a sharp decrease in the IFS index. As a result, just as during compression of the aorta, it was reduced to under half of the control level. The rate of contraction and relaxation was reduced by about the same degree.

Prolonged adaptation of the animals to mountains of medium altitude was followed by a moderate increase in the indices of cardiac function at relative physiological rest. Only the systolic pressure in the right ventricle changed significantly, to 33 ± 3 mm Hg, 58% above the control level.

The creation of EPS in these animals did not cause any significant change in the indices of contractile function of the myocardium of the left (Table 2) and right ventricles, but the gastric ulcers remained.

Adaptation to mountain conditions at an altitude of 2 km thus prevented a decrease in the maximal indices of contractile function of the myocardium during functional loads. Presumably the observed prophylactic effect, like the analogous result obtained during adaptation of the animals in a pressure chamber [4], was due to two factors. First, the series of changes in the energy-providing system arising under the influence of adaptation [1] increases the functional capacity of the heart muscle during loading [1, 3] and increases the power of adrenergic regulation of the heart [5]. This series of changes can limit the harmful effect of sudden excitation of the sympathico-adrenal system in EPS. Second, under the influence of adaptation the synthesis of nucleic acids and proteins is activated, and this is accompanied by an increase in the degree of preservation of temporary connections and an increase in the resistance of the brain to electric shock and to other extraordinary stimuli [1] and, in particular, to EPS.

When the roles of these two factors are compared it must be remembered that disturbance of catecholamine synthesis under the influence of picolinic acid, a dopamine decarboxylase inhibitor, prevents damage to the heart but does not prevent the formation of gastric ulcers during stress [8, 9]. Meanwhile the development of ulcers and also of heart lesions is prevented by butyryl derivatives of picolinic acid penetrating into the brain. γ-Hydroxybutyric acid, which activates the inhibitory strionigral system in the brain, has a similar effect [6].

Factors with a central inhibitory action can thus prevent not only the disturbance of cardiac activity during stress, but also the formation of gastric ulcers. Adaptation to hypoxia does not have this effect, and it can therefore be concluded that this factor exerts its prophylactic effect through adaptive changes in the heart and in its regulatory apparatus.

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CHANGES IN THE NICOTINAMIDE NUCLEOTIDE CONTENT IN THE BRAIN AND MYOCARDIUM OF RATS EXPOSED TO FACTORS INDUCING NEUROGENIC DYSTROPHIES

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The content of nicotinamide nucleotides in the brain and myocardium of rats was investigated during electrical stimulation of the animals and administration of toxic doses of noradrenalin. The level of total nicotinamide nucleotides and their oxidized forms was reduced but the content and rate of synthesis of nicotinamide nucleotide-phosphates were increased. The results point to a disturbance of oxidation–reduction processes and to an increase in the activity of the pentose pathway of carbohydrate utilization in the tissues in neurogenic dystrophies caused by extremal stimulation.

KEY WORDS: neurogenic dystrophies; nicotinamide nucleotides; energy metabolism; brain; heart.

Extremal stimulation causes a disturbance of nervous regulatory influences on metabolism in the tissues, with the consequent development of dystrophic changes in them. Disturbance of the functions of the sympathetic nervous system, a deficiency of catecholamines in the tissues, and marked inadequacy of energy metabolism are observed in such cases. The creatine phosphate level in the tissues falls, glycolysis is disturbed, the glycogen concentration is reduced, lactic acid accumulates, and oxidative phosphorylation is depressed [1, 4, 5, 7].

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