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CHANGES IN CONTRACTILE FUNCTION OF THE HEART IN EMOTIONAL-PAINFUL STRESS

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Previous investigations have shown that severe emotional-painful stress (EPS) is accompanied by phasic changes in the metabolism and structure of the heart, and also in the blood eosinophil count, which reflects the response of the pituitary-adrenal system [2, 3, 6, 7]. It was found that the greatest disturbances of the oxidative and phosphorylating functions of the cardiac mitochondria and injuries to the structure of the cardiomyocytes of focal contractural and necrotic type are observed after the end of EPS — at a time when the eosinopenia induced by stress is suddenly replaced by eosinophilia [3-5, 9]. The question of how the dynamics of changes in the contractile function of the heart (CHF) correlates with the development of disturbances of cardiac metabolism and structure in EPS has not yet been answered.

The aim of this investigation was to study CHF of the heart in animals at times after EPS corresponding to the temporal parameters of responses of the pituitary-adrenal system, and also to the phases of development and regression of stress-induced disturbances of metabolism and structure of heart muscle [3, 5, 8].

EXPERIMENTAL METHOD

Experiments were carried out on 111 male Wistar albino rats weighing 200-300 g, divided into four groups. The control group (experiments of series I) consisted of 30 animals. EPS in the form of an anxiety neurosis was produced in the course of 6 h in 81 rats by the method described in [10]. The animals were anesthetized 2 h (series II, 24 rats), 45 h (series III, 34 rats), and 96 h (series IV, 23 rats) after the end of the procedure with pentobarbital sodium in a dose of 8 mg/100 g body weight, artificially ventilated, after which the chest was opened and the pressure in the left ventricle measured by means of a VI 6-6 TN electromanometer and N-105 oscilloscope [1] or RM-6000 polygraph (Nihon Kohden, Japan). CFH was estimated on the basis of the following parameters: the developed pressure P_d, the rate of contraction V_c and relaxation V_r of the ventricle, the index of intensity of functioning of structures (IFS) — the product of the heart rate (HR) and developed pressure, divided by the weight of the left ventricle. CHF was analyzed under conditions of relative rest and maximal load on the heart, due to compression of the aorta for 30 sec. Calculation of CSH and statistical analysis of its values under isometric conditions were done after 5 and 25 sec.

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TABLE 1. CHF of Rats in the Course of EPS (M ± m)

Parameter studied	Series of experiments	Relative rest	Change, %	Compression of aorta			
				5 sec	Changes, %	25 sec	Changes, %
P_d, mm Hg	I Control	105±4,2	—	208,5±8,2	—	195,1±9,7	—
	II	113±5,7	—	192,3±10,9	—	184,0±11,4	—
	III	90,3±4,7*	—14	146,8±10,1***	—19,6	129,5±11,1***	—33,6
	IV	93,2±5,7	—	199,0±5,9	—	180,3±9,4	—
HR, beats/min	I Control	375±17	—	370±15	—	336±17	—
	II	371±18	—	339±18	—	309±17	—
	III	357±12	—	347±15	—	303±19	
	IV	376±16	—	365±21	—	311±14	
IFS, mm Hg/min·mg	I Control	87,4±4,2	—	176,6±9,4	—	137,9±6,7	—
	II	84,8±5,3	—	138,0±11,0*	—18	127,2±9,0	—
	III	69,7±6,3*	—20	108,0±6,3***	—35,6	83,4±7,7***	—39,5
	IV	88,4±7,2	—	137,3±11,1*	—18,1	116,2±11,8	—
V_c, mm Hg/sec	I Control	4316±240	—	6723±309	—	6170±340	—
	II	4783±312	—	7183±649	—	6533±448	—
	III	3636±207*	—15,8	4994±362**	—25,7	4266±233***	—30,8
	IV	4090±366	—	6059±455	—	6000±626	—
V_r, mm Hg/sec	I Control	2678±161	—	3509±297	—	3014±210	—
	II	2650±433	—	3250±359	—	2917±302	—
	III	2235±147*	—16,5	2169±148***	—38,2	1794±94***	—40,5
	IV	2442±213	—	3020±170	—	2699±187	—

Legend. *P < 0.05, **P < 0.01, ***P < 0.001.

EXPERIMENTAL RESULTS

It was found that 2 h after the end of exposure to stress, at a time corresponding to the phase of development of disturbances of the structure and energy metabolism of the heart, and also of eosinopenia, slight changes in the values of the CHF parameters were observed (Table 1). Only under conditions of isometric contraction induced by occlusion of the aorta for 5 sec was a significant fall in IFS observed in the stressed animals, by 18% of the control valve, indicating a decrease in the maximal functional capacity of the heart muscle tissue.

Considerable depression of CHF was observed 45 h after EPS, i.e., at a time of high eosinophilia, when profound contractural and necrotic lesions had formed in the heart and inhibition of oxidation and phosphorylation in the heart muscle mitochondria was maximal. Whereas in a state of relative rest the parameters characterizing CHF were reduced by 15-20%, 5 sec after compression of the aorta the parameters of CHF were reduced by more than 30%. Even more marked changes in CHF were found in these animals after the heart had worked for 25 sec under isometric conditions. P_d and V_c of the left ventricle were reduced by 1.5 times, and IFS and V_r by more than 1.7 times under these circumstances compared with their control values.

The parameters of CHF of the animals 96 h after EPS were virtually the same as in the controls, both in a state of relative rest and after compression of the aorta. Only IFS, which characterizes the upper limit of functional capacity of the heart muscle, remained depressed by 18%. This indicates that at this time, in the phase of recovery of the metabolism and structure of the heart muscle, latent disturbances of CHF are still present.

The investigation thus demonstrated the phasic character of poststress disturbances of CHF and that the time course of their formation corresponds to that of the phases of development and recovery of cardiac metabolism and structure from the changes arising during EPS.

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EFFECT OF SOME VITAMIN PREPARATIONS ON EPILEPTIC ACTIVITY

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The development of rational treatment of epilepsy with the aid of natural metabolites is one of the most important trends in the problem of creating comprehensive pathogenetic therapy of this disease. A matter of great importance in such research is the choice of adequate models of epileptogenesis and, in particular, the production of states that closely resemble chronic epileptization of the brain. One such model is the method of pharmacologic kindling. In models of acute epileptic foci the writers previously demonstrated the effectiveness of nicotinamide, pyridoxal-5-phosphate, and α-tocopherol [3, 6]. The next important step was to study the effects of these substances on the development of epileptization of the brain on a kindling model.

The aim of this investigation was to study the effect of nicotinamide (NA), pyridoxal-5-phosphate (PP), and α-tocopherol (α-T) on developing epileptic activity (EA) and as a means of preventing its formation.

EXPERIMENTAL METHOD

Mice and rats were used. The animals received a daily intraperitoneal injection of a subconvulsant dose of metrazol (30 mg/kg). The EEG and behavioral responses were recorded. The intensity of seizures was expressed in points (for a detailed account of the technique, see [7]). NA and PP were injected in 0.1 ml of 0.9% NaCl solution 25 min, and an oily solution of α-T 24 h before injection of metrazol (in the group of animals with developed kindling). All drugs were injected intraperitoneally. Control animals in each series of experiments received an injection of physiological saline in the same volume as the test drug. The results were subjected to statistical analysis by variance and nonparametric methods.

EXPERIMENTAL RESULTS

During daily injections of metrazol progressive development of epileptization of the brain was observed, as shown by an increase in the number of animals with seizures and the greater severity of the seizure reactions from single shakings of the head and trunk to a

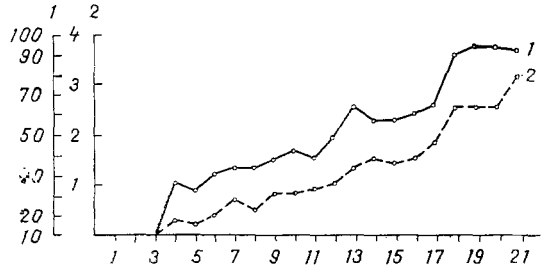

Fig. 1. Severity of seizure responses and number of animals with seizures evoked by subthreshold doses of metrazol. Abscissa, days of experiments; ordinate: 1) number of animals with seizures (in %); 2) severity of seizures (in points).

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