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ENDERPINE LEVEL IN THE MYOCARDIUM OF ANIMALS EXPOSED TO STRESS

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KEY WORDS: myocardium; enderpines; stress.

The writers showed previously [1-3] that animal tissues contain endogenous alkaloid-like substances which influence vascular tone and the cardiac frequency. These substances, isolated as three chromatographically homogeneous fractions, were named RP1, RP2, and RP3, or enderpines. It was suggested that they play the role of regulators of homeostasis of different forms of catecholamines and indoleamines (free, bound, and so on). The name "enderpines" is derived from the words "endogenous reserpines."

In the present investigation an attempt was made to elucidate the function of the enderpines by determining changes in the content of these substances in the myocardium of animals exposed to stress: immobilization, subcutaneous injection of water and adrenalin, and injection of α-methyldopamine.

EXPERIMENTAL METHOD

Experiments were carried out on 100 male Wistar rats weighing 250-300 g. Isolation of the enderpines from the myocardium and the first stages of their purification were carried out by the method described previously [1]. The enderpine content was determined fluorometrically on the KM-3 chromatogram-spectrophotometer ("Opton") with an excitation wavelength of 270 nm. For this purpose, in the last stages of purification the enderpines were isolated by chromatography on "Silufol" plates ("Cavalier") in a system of acteone–carbon tetrachloride–isooctane–petroleum ether–n-propanol (25:25:25:25:50). Enderpines RP1, RP2, and RP3 with electrophoretic mobilities of 0.78, 0.49, and 0.1 respectively, were eluted with a chloroform–methanol (2:1) mixture and applied as spots 5 mm in diameter to DC-Alufolien Kieselgel 66-Kieselguhr F-254 plates ("Merck"), in the same way as enderpines of known concentration to obtain calibration curves. The results were expressed in micrograms RP1, RP2, and RP3 per gram wet weight of tissue.

Rats were immobilized by stretching them by Selye's method for 3 and 24 h. Intact rats served as the control. α-Methyldopamine (dopegit, from "Egit") was given to the experimental rats by mouth through a catheter in the form of a suspension of crushed tablets in 2 ml milk in a dose of 0.5 mg/100 g body weight once daily for 3 days. Adrenalin bitartrate (from "Sigma") was injected subcutaneously into the rats in 1 ml distilled water in a dose of 0.8 ml/100 g body weight. Control rats received 1 ml of distilled water subcutaneously. The general control consisted of intact animals. The rats were killed by a blow on the head.

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TABLE 1. Concentration of Enderpines (in μ g/g tissue) in Myocardium of Rats Exposed to Immobilization Stress (M ± m)

RP 1			RP 2			RP 3		
control	immobilization		control	immobilization		control	immobilization	
	3 h	24 h		3 h	24 h		3 h	24 h
32,19±1,46 n=15	47,92±6,63* n=18	31,27±2,54 n=15	7,46±0,32 n=15	13,73±1,79* n=18	8,58±0,70 n=15	18,31±0,92 n=15	33,47±4,25* n=18	26,16±1,08 n=15

Legend. *) Difference compared with control significant at P < 0.05; n) number of experiments.

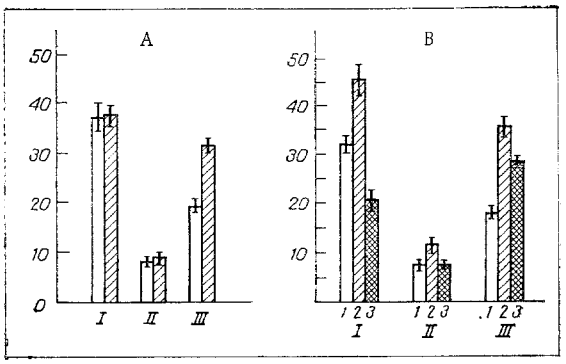

Fig. 1. A) Effect of injection of α-methyldopamine on concentration of enderpines in rat myocardium (in μg/g tissue). Here and in Fig. 2: I) RP1, II) RP2, III) RP3. Unshaded columns – intact animals (n = 10), shaded columns – injection of α-methyldopamine (n = 10). B. Changes in concentrations of enderpines (in μg/g tissue) in myocardium of rats in response to subcutaneous injection of water and adrenalin. 1) Intact animals (n = 18); 2) subcutaneous injection of water (n = 10); 3) subcutaneous injection of adrenalin (n = 15).

EXPERIMENTAL RESULTS

Exposure of rats to stress in the form of immobilization for 3 h caused a sharp and significant (P< 0.01) increase in the contents of all three fractions of enderpines in the myocardium compared with intact animals (Table 1). Immobilization of the rats led after 24 h to a significant increase in the level of RP3 only, whereas the concentrations of RP1 and RP2 remained close to those in the control animals.

Injection of α-methyldopamine into the rats was followed by changes in the RP3 level in the myocardium: It was significantly increased compared with the control (Fig. 1A). The RP1 and RP2 levels in animals exposed to the same procedures were virtually unchanged. Subcutaneous injection of adrenalin into rats caused a significant increase in the content of the RP3 fraction only, whereas subcutaneous injection of 1 ml distilled water led to a significant change in the levels of all three types of enderpines compared with the corresponding levels in intact animals (Fig. 1B).

All procedures used in this investigation on the rats are undoubtedly stress factors and give rise to metabolic changes in the body as a whole and, in particular, in the myocardium.

The fall in the enderpine level obtained in the animals in this investigation after immobilization for 24 h compared with the concentration of these factors in rats immobilized for only 3 h and the approximation of this index to the control values can be explained on the grounds that enderpines, responding to stress by a change in their concentration due to changes in their synthesis, breakdown, and accumulation, play an adaptogenic role, facilitating adequate work of the heart under unfavorable conditions.

The results do not contradict the hypothesis of the regulatory role of enderpines in relation to catecholamine metabolism [3]. It is well known that sudden changes in the structure of emotions are accompanied by the liberation of adrenalin into the blood stream. This hypothesis is confirmed by experiments in which water and adrenalin were given. Subcutaneous injection of water invariably makes it necessary to increase the pool of free endogenous adrenalin in the myocardium on account of emotional and pain stress in the experimental animals and the concentrations of all three types of enderpines are reduced compared with their level in the experiment with injection of water (Fig. 1B).

Consequently, the mechanisms connected with metabolism of the enderpines and their function are connected with changes in the free adrenalin (and, probably, of other catecholamines also) level and they respond to this level by a feedback mechanism, i.e., they carry out the homeostasis which we postulated previously [3].

The action of α-methyldopamine (an inhibitor of catecholamine synthesis) also can evidently be explained similarly. This substance probably induces a compensatory increase in the concentration of one fraction of enderpines (RP3) in response to a fall in the catecholamine level produced by that substance.

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ENERGY METABOLISM IN THE LIVER AND KIDNEYS DURING THE FIRST DAY AFTER ACUTE BLOOD LOSS IN RATS

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Experimental investigations of energy metabolism in different organs during shock and after blood loss, published in the literature, describe its changes during the first 3-4 h after the beginning of development of the pathological process. However, in patients with third-degree traumatic shock the period of unstable hemodynamics lasts much longer (according to data given by the I. I. Dzhanelidze Emergency Aid Research Institute, up to 16 h). Accordingly it was decided to study the dynamics of changes in energy metabolism during the 24-h period after acute blood loss in the liver and kidneys, the functions of which are disturbed very significantly in this process.

EXPERIMENTAL METHOD

Fifty male rats weighing 220-320 g were used. The animals were fixed to a frame, pentobarbital was injected (40 mg/100 g intraperitoneally), and the femoral artery was catheterized to measure the arterial blood pressure (BP). Bleeding (2.5% of body weight) was carried out for 10 min. Anesthesia was maintained throughout the experiment. The fixation of the rats was subsequently released somewhat. Heparin was injected in fractional doses (total dose not more than 500 units) into the femoral artery. Depending on the course of the posthemorrhagic period the animals were divided into four groups. In the rats of group 1, BP fell immediately after blood loss on average to 9 mm Hg, after which it became stabilized at between 40 and 60 mm Hg (in 50% of the animals it did not exceed 45 mm Hg), after which it again fell progressively. Energy metabolism was investigated 3.6 h after blood loss, when the mean value of BP was 39 mm Hg. In the animals of groups 2, 3 and

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