ANTISTRESS EFFECT OF PROLACTIN

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Previous investigations [8, 9] showed that granules of secretion from prolactotrophs are secreted rapidly into the intercellular substance of the adenohypophysis under the influence of extremal factors. This coincides in time with activation of corticotropocytes, but in some cases degranulation of the prolactotrophs is more rapid and complete. These facts led one of us (V. S. S.) to postulate a role for the hormone prolactin in the formation of resistance of the body to unfavorable external environmental factors. Recently many data confirming liberation of prolactin from the pituitary of animals and man during exposure to a wide variety of stressors, which was accompanied by a considerable (by 2-25 times) rise of its peripheral blood concentration [2, 15] have been published but no information could be found on the participation of prolactin in the mechanism of the adaptive properties and in prevention of the stress reaction.

It was accordingly decided to study the role of prolactin in the realization of adaptive reactions during exposure of animals to emotional-painful stress (EPS) and in the prevention of structural damage to the heart arising under these circumstances.

EXPERIMENTAL METHOD

Experiments were carried out on 78 male albino rats weighing 180-200 g, kept under standard animal house conditions. The initial eosinophil count of the rats at 9 a.m. was 220-340 in 1 μl peripheral blood. All animals corresponded in the state of function of their pituitary-adrenal system (PAS), which was determined by studying circadian rhythms of the blood eosinophil count [1]. EPS was produced by the method in [14]. Prolactin in a dose of 2.5 U/100 g body weight was injected subcutaneously into the rats 60 min before exposure to stress. Control animals received 0.5 ml of physiological saline (the solvent for prolactin). The animals were divided into four groups: 1) control, 2) prolactin (killed 9 h after injection of the hormone), 3) EPS + rest for 2 h, 4) prolactin + EPS + rest for 2 h (EPS 1 h after injection of prolactin). For the biochemical tests some rats from all four groups were killed 2 h after the end of EPS. The corticosterone (CS) concentration in blood plasma and in the heart and adrenals was determined by chromatography on silica-gel columns [4], and adrenalin (A) and noradrenalin (NA) in the heart and adrenals were determined by fluorometry [5]. The number of eosinophils in 1 μl of peripheral blood from the remaining animals of these groups was counted every 3 h after the end of exposure to stress for 45 h, in a Goryaev's chamber after staining by Hinkleman's method. The antistress effect of prolactin was estimated quantitatively by the method described previously [3] and calculated by the equation $A=\frac{T_1}{T_2}$ where T_1 is the time from the end of exposure to stress until appearance of the eosinophil peak in the control animals, T the same parameter for the experimental animals, and A the coefficient of adaptation (the higher its value, the greater the antistress effect of the substance studied). Structural lesions in the myocardium were detected in serial topographic sections through the heart by Perls' reaction and counterstained with hematoxylin and eosin, and also by the study of sections in polarized light. For morphological investigations the animals were killed under superficial ether anesthesia, at the time of appearance of the eosinophil peak, for it was shown previously that the structural changes in the organs are most marked at this time [6].

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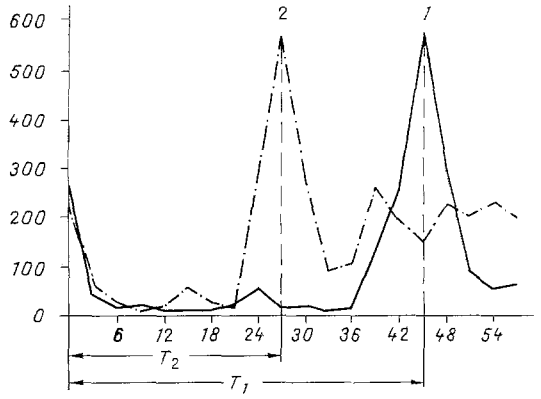

Fig. 1. Effect of prolactin on time of appearance of eosinophil peak in peripheral blood of rats exposed to EPS. 1) Eosinophil peak in control animals after exposure to EPS, 2) eosinophil peak in rats receiving prolactin and exposed to EPS. T_1) Time after beginning of exposure to stress until appearance of eosinophil peak in control rats, T_2) same parameter in animals after preliminary injection of prolactin. Abscissa, time after beginning of exposure to EPS (in h); ordinate, number of eosinophils in 1 μl peripheral blood.

EXPERIMENTAL RESULTS

After the end of exposure to EPS activation of PAS was observed during the first 39-42 h, as shown by eosinopenia, followed after 45 h by a temporary increase in the number of eosinophils (Fig. 1). Considerable social necrotic and contractural lesions of the heart muscle were found at this time (Fig. 2a, b). The CS concentration in the blood plasma 2 h after EPS was increased fourfold. The CS and A concentrations in the heart also were increased, but the NA level was reduced almost by half. A considerable increase in the CS concentration and a sharp decrease in the A concentration were observed in the adrenals (Table 1).

Preliminary injection of prolactin shortened the delay before appearance of the eosinophil peak after exposure to EPS to 27 h (by more than one-third), evidence of the strong antistress (adaptive) effect of this hormone (A = 1.67). This is also shown by the results of the biochemical test; the concentrations of CS in the blood plasma and heart were increased by a lesser degree and its concentration in the adrenals did not increase at all; the catecholamine levels in the organs studied were virtually indistinguishable from those in intact animals, except for a small but significant decrease in the adrenalin concentration in the adrenals.

The protective action of prolactin also was manifested by the fact that it prevents development of necrosis in the myocardium and severe contractural lesions in the myofibrillary apparatus in the cardiomyocytes. Only individual muscle cells or small groups of them with some increase in isotropy, with contracture of the myofibrils of the I-II degree, and with weakening of cross-striation (Fig. 2c, d) could be observed in the histological preparations, but only 45 h after the end of EPS pathomorphological changes were virtually absent in the heart of the animals receiving prolactin.

It can be concluded from these results that prolactin has a marked antistress action. It shortens the duration and weakens the degree of activation of the PAS and prevents the development of severe necrotic and contractural lesions of the heart muscle. The ability of prolactin to prevent metabolic and structural disturbances under conditions of stress in skeletal muscles, cerebral cortex, and other organs was demonstrated by the writers previously [10, 13]. By virtue of its ability to interact directly with prolactin receptors of

TABLE 1. Effect of Prolactin on CS and Catecholamine Levels in Blood Plasma and Organs of Rats 2 h after Exposure to EPS (M ± m)

Experimental conditions	CS, μg%			Adrenalin, μg/g		NA, μg/g	
	blood plasma	heart	adrenal	heart	adrenal	heart	adrenal
Control – physiological saline (n=12)	4,8±0,7	12,6±1,4	986±107	0,05±0,009	450,0±38,0	0,98±0,11	117,8±20,5
Prolactin (n=12)	5,8±0,1	16,8±4,9	1172±146	0,05±0,008	396,8±41,2	0,81±0,07	121,4±16,8
EPS + rest for 2 h (n=12)	19,6±1,4**	27,3±1,9**	1994±138***	0,09±0,01*	176,6±21,4***	0,55±0,07**	106,4±13,6
Prolactin - EPS + rest for 2 h (n=12)	8,7±0,6*	17,9±1,6*	1093±129	0,06±0,007	348,7±26,8	0,78±0,08	119,4±17,1

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

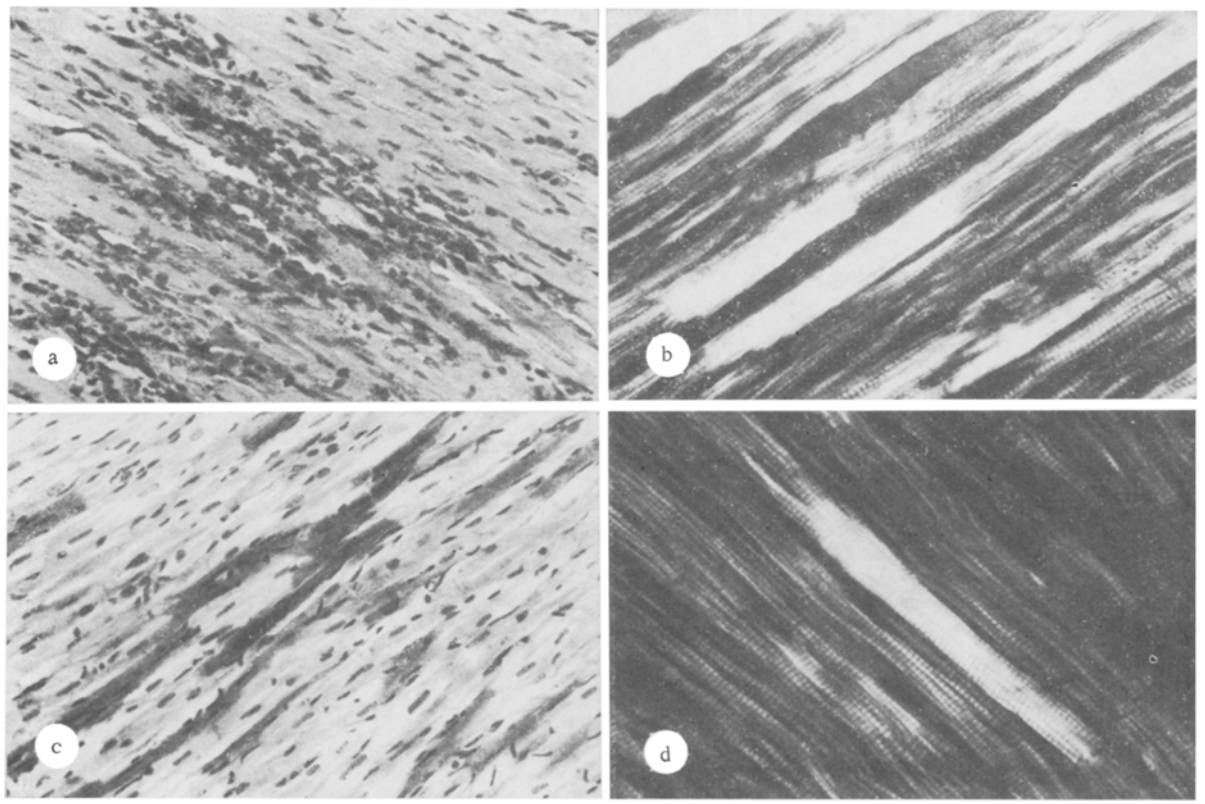

Fig. 2. Ultrastructure of rat myocardium after EPS. a) Large foci of necrosis in myocardium of control rats 45 h after exposure to EPS; b) contractural lesions and fragmentation of myofibrils in muscle fibers of rat myocardium 45 h after exposure to EPS; c) moderately severe reversible degenerative changes in individual cardiomyocytes in myocardium of experimental animals 27 h after exposure to EPS; d) weakening of anisotropy and partial injury to myofibrils in individual cardiomyocytes of experimental rats 27 h after exposure to EPS. a, c) Staining with hematoxylin and eosin, 56 ×; b, d) polarization microscopy, 280 ×.

cells and to act indirectly through peripheral organs of internal secretion, prolactin thus increases the resistance of the cells through changes in their metabolism [7, 11, 12] and it is thus the second principal pituitary hormone which, equally with ACTH, participates in the formation of the adaptive reactions of animals and man. By limiting excessive response of the hypothalamo-hypophyseo-adrenal system prolactin adjusts the level of response of the body to match the quantitative and qualitative characteristics of the harmful factor acting on it.

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