highly active phospholipid repair systems (acyltransferase, cyclo-oxygenase), enabling the system to return to its initial state and thus preventing the accumulation of hydrolyzed residues of phospholipids and free fatty acids in the membranes, where they could change the properties of the receptors.

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EFFECT OF IMMOBILIZATION STRESS ON THE ADRENERGIC INNERVATION OF THE RAT MESENTERY AND DURA MATER

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UDC 612.338:612.339]-06:613.863-02:612.766.2

KEY WORDS: adrenergic innervation; immobilization stress; mesentery; dura mater.

Adrenergic (sympathetic) innervation structures are inseparable components of peripheral catecholaminergic systems which, together with central systems, play an important role in the mechanisms of onset and development of the response to stressors. Processes of tissue metabolism and the adaptive activity of the organism at different levels of its integration are directly linked with the trophic and trigger (effector) function of peripheral adrenergic nerves [1-3, 9]. Meanwhile the problem of the morphological and functional state of the peripheral adrenergic innervation under extremal conditions has not attracted the attention it deserves from the research worker. There have been only single investigations which have shown directly or indirectly that it participates in the general reaction of the body to stress [4, 5]. Essentially, however, the dynamics of mediator activity of adrenergic nerves at the various stages of stress has not been seriously studied, nor have any reliable criteria been developed for the objective assessment of the corresponding processes.

Accordingly, in the investigation described below a model of immobilization stress was used to study the adrenergic innervation of the rat mesentery and dura mater.

EXPERIMENTAL METHOD

Experiments were conducted on male rats weighing 180 ± 30 g. The animals were immobilized for 1, 4, 6, 16, and 24 h. The duration of the experiments was determined by analysis of the dynamics of the somatic manifestations of the animal's stressor reaction in this particular model of immobilization stress established previously by the writers [6]. Total preparations of mesentery of the small intestine and dura mater were studied. Adrenergic structures were detected histochemically by the fluorescence-microscopic method of Falk and Hillarp, in the writers' modification [10]. The morphological and functional state of the adrenergic innervation of the mesentery and dura mater was estimated by qualitative (visual) and quantitative methods. The latter consisted of determining the intensity of luminescence of the adrenergic nerves by means of an FÉU-19 photosensitive attachment to the ML-2 lumines-

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(Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Kupriyanov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 96, No. 11, pp. 8-10, November, 1983. Original article submitted April 8, 1983.

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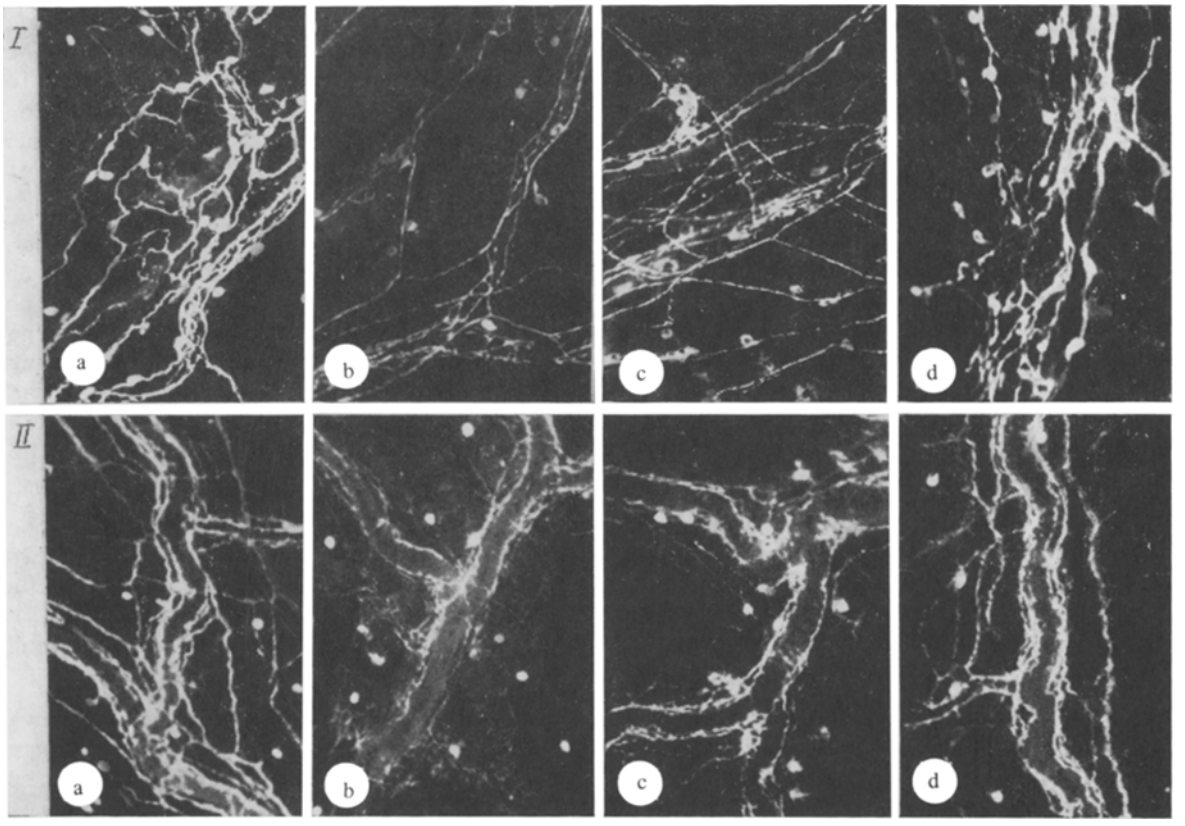

Fig. 1. Adrenergic innervation of mesentery of small intestine (I) and dura mater (II) of rat. a) Control, b) 1 h, c) 4 h, d) 24 h of immobilization. Falk–Hillarp method, 250 ×.

TABLE 1. Quantitative Characteristics of Adrenergic Innervation of Mesentery and Dura and of Somatic Manifestations of Stress Reaction in Immobilized Rats

Period of immobilization, h	Intensity of luminescence of adrenergic nerves, conventional units		Weight, % of weight in intact animals			Thickness of lipid layer of adrenal, conventional units
	mesentery	dura mater	of thymus	of spleen	of adrenal	
Control	26,2±2,5*	20,5±1,8	100±16,6**	100±17,5**	100±8,5**	6,3±1,4
1	13,7±1,6	12,4±1,5	78,6±13,4	61,3±13,6	91,5±22,1	2,8±0,9
4	16,6±1,8	14,8±1,6	100,1±16,5	102,0±13,0	95,7±8,8	6,4±1,7
6	18,3±1,9	15,6±1,6				
16	19,1±2,2	16,5±1,7	103,6±19,0	71,6±13,2	144,7±15,1	6,6±1,8
24	19,7±2,1	16,9±1,8	92,5±10,0	65,5±12,5	155,3±13,7	6,2±1,5

Legend. *) Confidence limits of mean at P = 0.05; †) the 100% weight levels adopted were: for the thymus 137.6 ± 22.8 mg, for the spleen 199.8 ± 34.9 mg, for the adrenal 4.7 ± 0.4 mg.

cence microscope. The measurements were made in conventional fluorescence units based on the digital readings of the microammeter. The total (integral) intensity of luminescence of adrenergic nerve plexuses within standard fields of vision was recorded (with a No. 10 objective, the linear visual field was 2.1 mm^2). The results were subjected to statistical analysis [8].

EXPERIMENTAL RESULTS

Both in the mesentery and in the dura of normal (control) rats fluorescence microscopy of catecholamines revealed a reasonably complete picture of the adrenergic innervation, which in most cases was characterized by bright luminescence of fibers and of preterminal and terminal divisions, abundantly supplied with expansions (Fig. 1a).

The data given in Table 1 summarize the intensities of luminescence of adrenergic nerves and were obtained by statistical analysis of numerical parameters recorded from 10 scattered fields of vision from all preparations of the mesentery and dura that were studied. To obtain more reliable parameters of quantitative analysis, areas (or zones) comparable in histoarchitectonics and density of adrenergic nerve structures were conventionally distinguished in these preparations. An important guide at this stage was the system of branching of the microvessels with which most adrenergic nerves are connected.

According to our observations, even in the early stages of immobilization (during the first hour) there was a considerable decrease in luminescence of nerve plexuses over the whole area of total preparations of the mesentery and dura. Many adrenergic fibers were without varicosities and resembled weakly fluorescent threads. The total number of luminescent axons was appreciably reduced, and this led to a universal reduction in the density of adrenergic nerve plexuses (Fig. 1b). Quantitative analysis of the preparations at this stage of immobilization showed a reduction in the overall intensity of luminescence of the adrenergic innervation of mesentery and dura by 40-50% compared with the initial (control) level.

In the next stages of immobilization (4-6 h) a gradual increase in the intensity of luminescence of the adrenergic nerves and a more complete picture of the structure of their preterminal and terminal divisions were observed. The latter reacquired their characteristic bead-like outlines, due to bright noradrenalin luminescence of the varicosities. The architectonics of the perivascular adrenergic plexuses was appreciably restored (Fig. 1c). These changes significantly affected the parameters of overall intensity of luminescence of the adrenergic nerves of the mesentery and dura (increased to 60-70%).

After long periods of immobilization (16-24 h) the state of the adrenergic innervation showed no significant change compared with that described above. Only a tendency toward enhancement of the fluorogenic properties of the nerve fibers and their terminal portions could be observed. On the whole, however, the adrenergic innervation of the mesentery and dura at this stage of immobilization was characterized by stability of its morphological and functional parameters (Fig. 1d), and this was reflected also in the results of quantitative analysis. As Table 1 shows, the overall intensity of luminescence of adrenergic nerves by the end of the first day of immobilization had reached 70-75% of the control level.

These observations indicate that the most important morphological and functional shifts in the state of the adrenergic innervation of the tissue-vascular substrate of the mesentery and dura take place in the early stages of immobilization, when the somatic and hormonal manifestations of the animal's response to stress are most marked [7, 11-13]. It is in this period, which corresponds to the stage of fear, that the maximal decrease in weight of the lymphoid organs (thymus and spleen), a tendency for the weight of the adrenals to decrease, and a sharp reduction in thickness of the lipid layer in their cortex were observed (the appropriate data are summarized in Table 1).

Release of noradrenalin from terminals (synapses) of adrenergic nerves on a large scale, which regularly accompanies the initial stage of immobilization, leads not only to excessive utilization of active mediator, but also to exhaustion of its reserves in the axoplasm of the nerve fibers. The state of the adrenergic innervation thus observed in the mesentery and dura can be regarded as a distinctive indicator of their functional desympathization. With the transition to the stage of adaptation (4-6 h after the beginning of the experiment) this state gives way to an increase in the noradrenalin luminescence of the adrenergic nerves. At the same stage of immobilization a positive trend was observed in the somatic parameters of the response to stress: the weight of the thymus, spleen, and adrenals was restored to normal and the lipid concentration in the adrenal cortex returned to its initial level (Table 1). In the later stages of the experiments (16-24 h) the morphological and functional parameters of the level of mediator activity of the adrenergic nerves observed under these conditions corresponded exactly to the stability of the somatic manifestations of adaptation which is maintained for a long period of immobilization of the rats. As Table 1 shows, at the end of 24 h of immobilization the weight of the lymphoid organs and the thickness of the lipid layer of the adrenals are close to normal again.

Morphological and functional changes in the adrenergic innervation of the mesentery and dura in immobilized rats described above reflect the dynamics of its neuromediator activity in different stages of this model of stress. They not only demonstrate the direct participation of peripheral catecholaminergic innervation systems in the general reaction of the body

to stress, but they can also be regarded on their own account as criteria for evaluating this reaction at the level of nerve-tissue relations.

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DISTURBED EXTENSIBILITY AND DEPRESSION OF CONTRACTILITY OF THE MYOCARDIUM IN STRESS TREATED WITH URIDINE, A COFACTOR IN GLYCOGEN RESYNTHESIS

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UDC 616.127-009.12-02:613.863]-085.31:547.963.3]

KEY WORDS: stress; myocardium; glycogen; uridine; extensibility.

It has recently been shown that the myocardium of rats exposed to stress differs from that of control animals by a marked decrease in its extensibility.

This phenomenon is accompanied by depression of the tension capable of being developed by the myocardium and, as a first approximation, it was explained by a disturbance of relaxation, as a result of which an excess of actomyosin bridges remained in the myofibrils of the "stressor" myocardium in diastole [1, 3, 5]. Analysis of this phenomenon must pay heed to the fact that under the influence of stress disturbances of glycolysis regularly develop in the myocardium, where they are expressed as a fall in the concentration and inhibition of resynthesis of glycogen [4]. Since glycolysis plays an important role in the functioning of the membrane Ca^{++} pump, which is responsible for relaxation [2, 6], it seemed probable that it was disturbances of ATP regeneration in the glycolysis system that could be an important link in the chain leading to disturbances of extensibility and depression of contractility during stress. In that case correction of the disturbances arising in the glycolysis system by the creation of an excessive concentration of substrate or administration of cofactors of glycogen resynthesis could abolish the stressor disturbances of extensibility and the depression of contractility of the myocardium. To test this hypothesis, the effect of high concentrations of glucose and the glycogen resynthesis cofactor uridine on extensibility and contractility of isolated atria from animals exposed to stress was studied.

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(Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 96, No. 11, pp. 11-13, November, 1983. Original article submitted February 1, 1983.