## EFFECT OF ELEVATION TO DIFFERENT ALTITUDES ON STRUCTURAL ORGANIZATION OF ADRENAL CORTEX IN RATS DIFFERING IN THEIR TYPE OF AUTONOMIC RESPONSE

S. I. Safronova and V. V. Lopukhova

UDC 612.453.014.2.06:612.275.1].06:612.89

KEY WORDS: adrenals; hypoxia; type of autonomic response

The question of individual typological features under normal conditions and during stress has recently been discussed in medicine and biology. The urgent importance of this question is due to the fact that it is closely connected with the problem of homeostatic mechanisms. The general reactivity of an organism is determined by the typological features of higher nervous activity, the structural and functional state of the central and autonomic nervous systems, activity of glands of internal secretion, and also the level of metabolism [2, 4, 6, 12].

The existence of individuality in the physiological status of an organism is demonstrated most clearly on exposure to increased demands. On the one hand, in response to various external factors the body responds with a general universal reaction, correlating both with the strength of the stimulus and the duration of its action. On the other hand, universality of response is always coupled with the individual features of an organism. These are closely linked with resistance to the action of extremal factors and to the ability of the organism to restore disturbed structural and functional parameters. There is virtually no information in the literature on individual typological features of organs and systems responsible for adaptation to changing environmental conditions. We therefore set out to analyze some morphological characteristics of the adrenal cortex in rats with different types of autonomic response, under normal conditions and during elevation in a pressure chamber to different altitudes.

## EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino rats weighing 200-250 g, which were divided into three groups depending on their type of autonomic response (change in heart rate in response to subcutaneous injection of adrenalin in a dose of  $100 \,\mu$ g/kg body weight): 1) with a predominantly sympathetic type of response (sympathotonics — S), 2) with a predominantly parasympathetic type of response (parasympathotonics — P), 3) intermediate group (mesotonics — M). The experimental groups of rats (10 animals in each group) were lifted in a pressure chamber to an altitude of 2, 6, 8, and 11 km at the rate of 1 km/min. On reaching the above-mentioned altitudes, the animals were immediately killed by rapid decapitation with a guillotine. Control rats were kept in the pressure chamber for 15 min without elevation. The left adrenal gland was removed and fixed in silver nitrate by the method of Giroud and Leblond. Paraffin sections were cut through the plane of maximal area of the medulla, 5  $\mu$  thick, and stained with hematoxylin and eosin [3]. Morphometric investigations were carried out by the method in [11]: the width of the adrenal cortex and of the zonae glomerulosa, fasciculata, and reticularis and the diameter of the cell nuclei in these zones were measured.

## **EXPERIMENTAL RESULTS**

As Table 1 shows, definite correlation was found between the type of autonomic response and certain morphometric parameters of the adrenal cortex in the control animals. In the S group, for instance, the smallest width of the cortex and of the zona glomerulosa was observed. The ratio of the width of the zona glomerulosa to the zonae fasciculata and reticularis in the

Department of Physiology, Research Institute of Biology and Biophysics, V. V. Kuibyshev Tomsk University. (Presented by Academician of the Academy of Medical Sciences of the USSR N. V. Vasil'ev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 110, No. 7, pp. 105-108, July, 1990. Original article submitted June 23, 1989.

TABLE 1. Morphometric Parameters of the Adrenal Cortex in Rats with Different Types of Autonomic Response to Elevation to Different Altitudes  $(M \pm m)$ 

Group of animals	Altitude,	Width, μ, of			Diameter of	Diameter of nu-
		cortical layer	zona glomerul- osa	zona fasci- culata	nuclei in zona glomerulosa	clei in zona fasciculata
P	0	771+7.02	54±0.68	335±4,15	5,8±0,01	6,7±0,03
	$\overset{\circ}{2}$	$733\pm 7,20$	$79\pm 0.72$	$455\pm 4.05$	$5,4\pm0,03$	$6.3\pm0.05$
	6	$704 \pm 7,65$	$70 \pm 0.45$	$450 \pm 3,60$	$5,5\pm0,02$	$6.5\pm0.01$
	8	$640 \pm 5{,}40$	$72\pm0,47$	$336 \pm 3,15$	$5,3\pm0,02$	$6,4\pm0,04$
S	11	$680 \pm 4{,}50$	$61 \pm 0,27$	$453 \pm 2,71$	$5,9\pm0,03$	$6,5\pm0,01$
	0	$658 \pm 5,15$	$48 \pm 0,32$	$405 \pm 3,15$	$5,6\pm0,01$	$6,1 \pm 0,04$
	2	$668 \pm 4,05$	$73 \pm 0,45$	$413 \pm 2,70$	$5,6\pm0,03$	$6,3 \pm 0,04$
	6	$671 \pm 5,40$	$78 \pm 0.35$	$432 \pm 4,51$	$5,3\pm0,01$	$6,4\pm0,03$
	8	$638 \pm 8,55$	$84 \pm 0,38$	$326 \pm 4{,}06$	$5,3\pm0,01$	$6.3 \pm 0.01$
	11 -	615 <u>+</u> 4,23	$64 \pm 0,45$	$437 \pm 3{,}33$	$5,9\pm0,03$	$6.3 \pm 0.02$
М	0	$806 \pm 2,15$	$67 \pm 0,45$	$552 \pm 3{,}05$	$5,8\pm0,01$	$6,2\pm0,01$
	2	$594 \pm 2,70$	$69 \pm 0,54$	$408 \pm 3,15$	$5,2\pm0,07$	$6,0\pm 0,01$
	6	$621 \pm 4{,}50$	$80 \pm 0,36$	$361 \pm 4,05$	$5,1 \pm 0,04$	$6,0\pm 0,02$
	8	$667 \pm 2,72$	$82 \pm 0.37$	$317 \pm 2,70$	$4,6\pm0,01$	$6.2 \pm 0.03$
	11	$680 \pm 2,72$	$59 \pm 0,27$	$464 \pm 5{,}40$	$5,7\pm0,03$	$6,1 \pm 0,04$

animals of this group was 1:8:4. The diameter of the nuclei in all the cells likewise was less than in the other groups; the nuclei of the zona glomerulosa, moreover, were dentate in shape and were basophilic, whereas near some of the nuclei in the zona reticularis, concentration of small granules of ascorbic acid was observed. Mainly the ascorbic acid granules were in the vascular wall of the radial blood vessels or inside them. In some places in the zona reticularis a columnar structure was observed.

In the P group the width of the cortex was greater than in S, but the zona fasciculata was narrower than in the other groups. The ratio of width of the zona glomerulosa to the zona fasciculata and zona reticularis was 1:6:6. The zone of compression between the zonae glomerulosa and fasciculata was well defined and consisted of cells with large hyperchromic nuclei and basophilic cytoplasm. Here also a large concentration of medium-sized ascorbic acid granules was observed at the periphery of the cells. At the same time, the number of ascorbic acid granules in the radial vessels of the zona fasciculata was considerably smaller. Elements of medullary substance were found in the zona fasciculata, and characterized by a zonal distribution with dark cells in the inner layers and pale cells in the outer layers. The diameter of the nuclei of cells of the zonae glomerulosa and fasciculata was greater than in rats of the other groups.

The M group was characterized by hypertrophy of the cortex and of its zones. The ratio of the width of the zona glomerulosa to the zona fasciculata and zona reticularis was 1:8:3. The diameter of the nuclei of cells of the zona glomerulosa was the same as in animals of the P group, but in the zona fasciculata this parameter was close in its value to the S group. Because of the well marked intercellular spaces, the structure in the cortical layer was loose. Ascorbic acid granules were found in the intermediate zones and in vessels of the zona fasciculata.

On elevation to an altitude of 2 km the width of the cortical layer in the S and P groups was increased by 1.5 and 2%, and the width of the zona glomerulosa in these groups was increased by 52 and 46% respectively. Meanwhile the width of the zona fasciculata was considerably increased (by 35%) in P, whereas in S it showed only a tendency to increase. The width of the zona reticularis was reduced in both groups. In the M group the width of the cortical layer and of the zona fasciculata was reduced by 26%. In P and M the diameter of the nuclei in the cells of the zona glomerulosa and zona fasciculata was reduced. At this altitude the ratio of the width of the zona glomerulosa to the zona fasciculata and zona reticularis in M and P was 1:6:2, compared with 1:6:3 in S. In animals of all groups ascorbic acid granules disappeared from the blood vessels of the zona fasciculata. Initial stages of pinching off of the cortical substance were noted: evagination of the surface due to the formation of lacunae in the zona fasciculata and zona reticularis. In this same group of rats the compression zones were observed to disappear.

With an increase in altitude to 6 km, the width of the cortical layer in P was reduced somewhat on account of the zona glomerulosa and zona fasciculata. The opposite picture was observed in the S animals: very slight widening of the cortex on account of these same zones. In the M group the cortical layer began to widen, mainly due to an increase in width of the zona glomerulosa (by 19%), whereas the width of the zona fasciculata continued to decrease. The ratio of the widths of the zona glomerulosa to the zona fasciculata and zona reticularis at this altitude was 1:6:2 in S, 1:6:3 in P, and 1:5:2 in M.

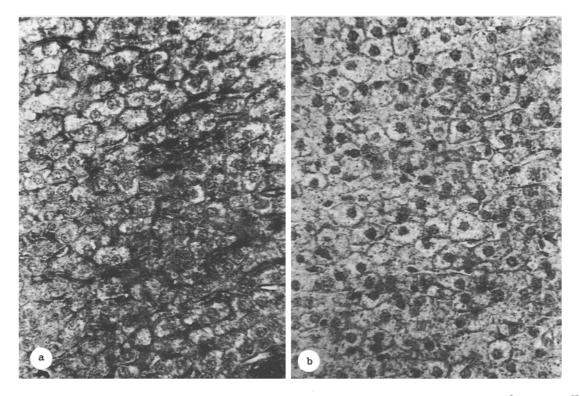


Fig. 1. Outer part of zona fasciculata of rat adrenal cortex on elevation to an altitude of 8 km. Here and in Fig. 2: a) P, b) S. Figs 1-5: stained with hematoxylin and eosin,  $160 \times$  (Figs. 1, 2, 4, and 5).

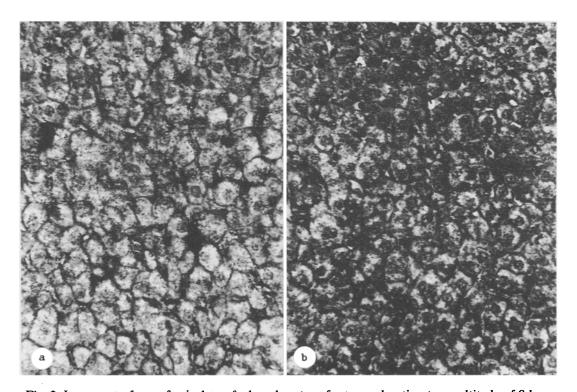


Fig. 2. Inner part of zona fasciculata of adrenal cortex of rats on elevation to an altitude of 8 km.

On elevation of the animals to an altitude of 8 km, the width of the cortical layer in the S and P groups was reduced, whereas in M the width of the cortex continued to increase. In S and M at this altitude the zona glomerulosa reached its maximal width, whereas in P it remained almost the same as at an altitude of 6 km. The width of the zona fasciculata was re-

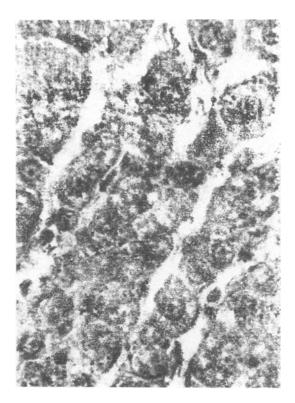


Fig. 3. Area of zona reticularis of adrenal cortex in rat from group S on elevation to an altitude of 11 km.  $400\times$ .



Fig. 4. Additional cortical structure in capsule of adrenal gland of group P rat on elevation to an altitude of 11 km.

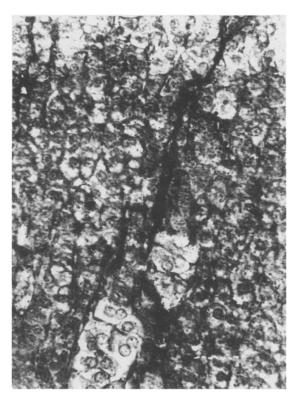


Fig. 5. Islets of medulla in cortical layer of adrenal gland of rat from group P on elevation to an altitude of 11 km.

duced in P to the control values, but hypertrophy of the nuclei in this case was observed in cells of the outer part of the zona fasciculata, with disappearance of ascorbic acid granules from the cells and with a decrease in vacuolation of the cytoplasm (Fig. 1a). In M the width of the zona fasciculata was reduced by 43% and in S by 20% compared with the control. The ratio of the widths of the zona glomerulosa and zona fasciculata and zona reticularis was 1:4:3 in M and S and 1:5:3 in P.

Nuclei of the cells of the outer layer of the zona fasciculata were smaller in the S than in the P group (the mean diameters of the nuclei for the whole zona fasciculata were about equal in the two groups), and the cytoplasm of most cells was vacuolated and contained ascorbic acid granules (Fig. 1b). The inner layers of the zona fasciculata in the animals of these groups also had definite differences on elevation to an altitude of 8 km. In the S group, a mosaic arrangement of the pale and dark cells was observed in this layer, with ascorbic acid granules distributed predominantly in the intercellular spaces and along the nuclear membranes. In the P group cells of the inner layer of the zona fasciculata were mainly pale, whereas granules of ascorbic acid were concentrated in the intercellular spaces and in the blood vessels (Fig. 2a, b).

On elevation to an altitude of 11 km, a decrease in width of the zona glomerulosa was observed in rats of all groups, but in the P rats it remained 13% higher than in the control, in S it was 33% above the control, but in the M rats 12% below the control value. In M and P an increase was again observed in the width of the cortical layer, although it remained 16 and 4% respectively below the control values. In S the width of the cortex was reduced by 7% compared with the control. In the animals of all groups, at an altitude of 11 km, widening of the zona fasciculata was observed. The ratio of the width of the zona glomerulosa to the zona fasciculata and zona reticularis was again 1:8:3 in M, in S it was 1:7:2, and in P it was 1:7:3. All groups were characterized by a marked zonal distribution of the adrenal cortex: a very pale zona glomerulosa contrasted with the zona fasciculata and zona reticularis, deeply stained with eosin. In S and, to some extent, in M dilatation of the radial vessels was observed in the zona reticularis, as a result of which it acquired the structural features of the zona fasciculata (Fig. 3). Furthermore, the appearance of radially oriented connective-tissue layers in the zona glomerulosa and in the outer part of the zona fasciculata was noted in these animals. Additional cortical structures were often found, especially in P but infrequently in M, in the capsule of the organ and beneath it (Fig. 4). In the rats of these same groups, on elevation to an altitude of 11 km bands of medullary substance were often seen across the whole cortical layer (Fig. 5). In the animals of all groups, just as at an altitude of 2 km, the ascorbic acid granules again disappeared from vessels of the zona fasciculata. At the same time a small compression zone appeared between the zona glomerulosa and zona fasciculata, the cells of which contained many ascorbic acid granules.

Thus the results are evidence that, despite the similarity in the general organization of the cortical parenchyma of the adrenals, different background values of the structural parameters of the adrenal cortex which we studied were discovered in rats with different types of autonomic response. This finding suggests that the nerve cells of the adrenals, which possess a definite level of bioelectrical activity, which changes in different autonomic situations in the body [8], are permanently acting cells due to the arrival of information destined for corticosteroid cells. Since the character of autonomic function is connected with the individual-typological features of nervous activity [7], so also the structural and functional properties of the adrenal cortex, as an effector component in autonomic regulation, acquire individual typological features. The latter may to a certain degree (together with the strength and duration of the factor) determine the character and direction of function of the controlled organ in stress reactions.

In the present experiments a decrease in width of the cortical layer observed during hypoxia [9] in the M group was noted at an altitude as low as 2 km (at a time when its values in the control were maximal). Meanwhile in the S group, which had the smallest values of the width of the cortex in the control, at an altitude of 2 km some widening of the cortex was observed, subsequently followed by narrowing, which was particularly marked at an altitude of 11 km. The time course of the change in width of the cortex in the P group was similar to that in the S group. More or less the same pattern was found in the change in width of the zona fasciculata at altitudes of 2 and 6 km for the various groups. Later the qualitatively similar changes in width of the zona fasciculata (narrowing at an altitude of 8 km in animals of all groups, but widening at an altitude of 11 km, also in all animals) had quantitative differences among the groups. Widening of the zona glomerulosa observed during hypoxia [5] reached peak values in the P group on elevation to an altitude of 2 km, whereas in animals of the other two groups, on elevation to an altitude of 8 km.

Signs of a columnar structure in the zona reticularis, sometimes appearing under the influence of stress [10], were observed in the present experiments in the S group even in the control situation, and on elevation to an altitude the columnar structure of the zona reticularis became even more marked in the S rats and appeared de novo in some group M rats. It has been suggested that this restructuring of the zona reticularis is connected with a change in the character of corticosteroid synthesis, when a certain proportion of cells of the zona reticularis begin to produce glucocorticoids, which are mainly formed in the inner layers of the zona fasciculata. Furthermore, in the animals of this group additional structures began to appear in the capsule at an altitude of 11 km, and which evidently were responsible for the increased synthesis of glucocorticoids [1]. Possibly the additional structures arose under the influence of catecholamines of the medulla, islets and bands of which penetrated in rats of the P group through the whole cortical layer as far as the zona glomerulosa.

## LITERATURE CITED

- 1. N. K. Bogdanovich, Arkh. Patol., 28, No. 5, 50 (1966).
- 2. V. S. Gorozhanin, Probl. Éndokrinol., No. 4, 33.
- 3. V. I. Kononski, Histochemistry [in Russian], Moscow (1956).
- 5. Yu. A. Medvedev, Problems in Pathological Anatomy [in Russian], Leningrad (1970), pp. 203-218.
- A. M. Monaenkov, Immunologic Reactivity and Type of Nervous System [in Russian], Moscow (1970).
- 7. N. A. Patkina, V. B. Zagustina, and B. G. Bershadskii, Zh. Vyssh. Nerv. Deyat., 31, No. 6, 1224 (1981).
- 8. Yu. A. Pines, Fiziol. Cheloveka, 8, No. 3, 477 (1962).
- 9. Ya. A. Rakhimov, L. E. Étingen, V. Sh. Belkin, and I. U. Usmanov, Morphology of the Internal Organs Under High Altitude Conditions [in Russian], Dushanbe (1969).
- 10. M. R. Sapin, Vessels of the Adrenal Glands [in Russian], Moscow (1974).
- 11. V. F. Sidorova and E. N. Stepanov, Ukr. Biokhim. Zh., 53, No. 5, 97 (1981).
- 12. R. Williams, Biochemical Individuality [Russian translation], Moscow (1960).