FUNCTIONAL MORPHOLOGY OF THE HYPOTHALAMIC–NEUROHYPOPHYSEAL SYSTEM AND JUXTAGLOMERULAR APPARATUS IN ACUTE CIRCULATORY FAILURE

O. K. Khmel'nitskii and A. P. Kurilin

UDC 616.12-008.331.4-092.9-07:
[616.432+ 616.831.41+
616.611-031.64]-091-07

The functional morphology of the hypothalamic–neurohypophyseal system (HNHS) and juxtaglomerular apparatus (JGA) was studied in 50 male cats. In acute circulatory failure induced by ganglion-blocking drugs or exsanguination, an increase in secretory activity of HNHA and JGA was accompanied by accumulation of hormone-containing granules in them. This factor is regarded as a specific feature distinguishing hypotensive stress, namely incomplete utilization of the adaptive powers of the HNHS and JGA under conditions of an acute depressor hormone deficiency.

KEY WORDS: hypothalamic–neurohypophyseal system; juxtaglomerular apparatus; acute circulatory failure.

Hormonal regulation of the arterial blood pressure is achieved through a series of systems the most important of which are the hypothalamic–neurohypophyseal system (HNHS), the adrenals, and the juxtaglomerular apparatus (JGA) of the kidneys. Morphological investigations have been devoted as a rule to the study of only certain components of the neuroendocrine system [1, 2, 6, 7, 10, 12-16]. It was accordingly decided to undertake a combined study of neuroendocrine regulation of the arterial pressure.

EXPERIMENTAL METHOD

The HNHS and JGA, which possess the most powerful pressor factors with systemic and prolonged action, were investigated in 50 male cats.* Acute systemic circulatory failure was produced in anesthetized animals by intravenous drip injection of a ganglion-blocking drug (0.1% solution of Arfonad†) or by partial exsanguination from the femoral artery. The arterial pressure was lowered to 50% of its initial value and kept at that level for 5 h. Intact and anesthetized cats (hexobarbital 0.1 g/kg in a 10% solution, intraperitoneally) were used as the control. The animals were killed immediately or 24 h after the end of the experiment.

The brain and pituitary gland were fixed in Bouin's fluid. Serial paraffin sections were stained by the Gomori–Gabe method and counterstained with Heidenhain's azan. The relative percentages of the different functional types of neurosecretory cells were counted in the supraoptic (SON) and paraventricular (PVN) nuclei and the total content of neurosecretion (NS) was estimated in the neurons and their processes and in the posterior lobes of the pituitary [3]. The kidneys were fixed in Zenker–formol (by Hale's method), paraffin sections were stained with Bowie's stain and counterstained with light green, and the juxtaglomerular index (JGI) was calculated. The nuclei of SON and PVN neurons and of the secretory cells of JGA (JG-cells) were measured and their volume calculated. All quantitative results were subjected to statistical analysis.

*A parallel study of the adrenals in these same experiments was undertaken by N. M. Kochubei [4, 9].
† Trimethaphan camsylate.

Departments of Pathological Anatomy and Pathological Physiology, S. M. Kirov Leningrad Postgraduate Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Smol'yannikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 10, pp. 494-497, October, 1979. Original article submitted February 7, 1979.

0007-4888/79/8810-1225 $07.50

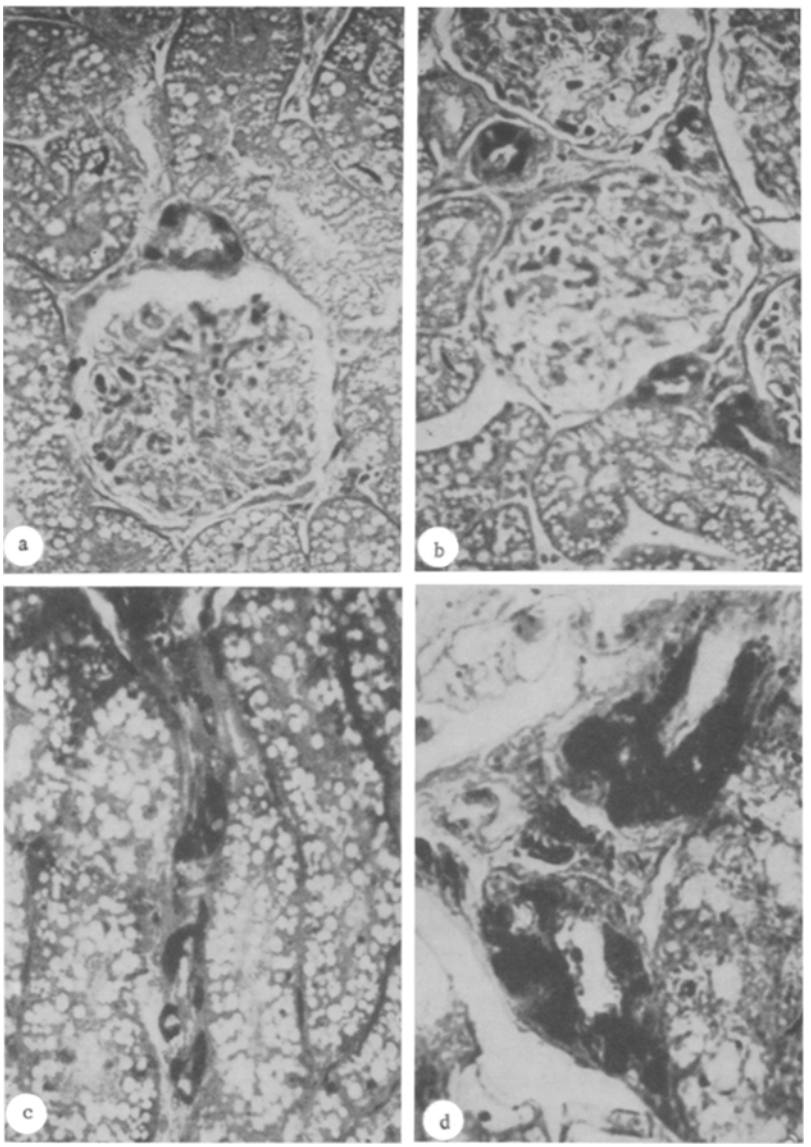

Fig. 1. JGA of a cat: a) JGA of control cat (hexobarbital anesthesia), degree of granulation +2 (after Hartroft); b, c, d) JGA of animals during hypotension, degree of granulation +4 (after Hartroft). Stained by Bowie's method and counterstained with light green. a, b, c) 600 x, d) 1500 x.

EXPERIMENTAL RESULTS

The HNHS of male cats has a structure basically similar to that of other mammals and man. The only characteristic differences were a looser arrangement of the neurons of SON and PVN and a deep infundibular recess, penetrating into the neurohoyphysis. These features have been observed by other workers also [5]. Gomori-positive nuclei of the anterior hypothalamus consisted mainly of active neurons (type I) with a varied content of neurosecretion, whereas the PVN was distinguished by a higher content of neurosecretion. Neurons with low synthetic activity (type II) were practically absent. There was a fairly high percentage of "degenerative" forms.

Analysis of the cell formulas showed that the HNHS undoubtedly reacts to administration of hexobarbital, ganglion-blockers, and exsanguination. Under hexobarbital anesthesia there was a shift of the cell formulas of SON and PVN in the direction of neurons with a low NS content. Under conditions of hypotension and blood loss, on the other hand, the number of forms with a high NS content was increased, evidence of a slower rate of its liberation. The number of neurons reached in NS was reduced 24 h after the end of artificial hypotension, and the cell formulas shifted toward "pale" cells.

The character of the cell formulas corresponded to the total content of NS in the various parts of HNHS. Under hexobarbital anesthesia the NS content in the cytoplasm of the neurons, their processes, and the neurohypophysis decreased, during hypotension (and exsanguination) it increased, and 24 h after the end of hypotension it returned to its initial level.

Statistical analysis showed that the cell formula itself is not a sufficiently sensitive index of the change in neurosecretory activity. The types of neurosecretory cells studied characterized not so much differences in their secretory activity as differences in the rate of NS liberation [3]. An attempt was accordingly made to assess the morphological and functional state of SON and PVN neurons by the use of karyometry. The results of karyometry provide reliable evidence of an increase in the volume of the nuclei of neurons under conditions of hypotension (and blood loss) that could be interpreted as the result of an increase in their functional activity.

Hexobarbital thus had a relatively weak effect on the HNHS, consisting simply of emptying of the NS which had accumulated previously. The increase in functional activity of the neurons during artificial hypotension was accompanied by marked accumulation of NS in the cytoplasm of the cells, their processes, and the the neurohypophysis. The secretory activity of the neurons fell 24 h after the end of hypotension and the rates of NS liberation increased.

The JGA of intact and anesthetized cats was characterized by a low content of granular JG-cells, as other workers also have observed [8]. Granular JGA were distributed mainly near the hilum of the glomeruli in the subcapsular zone. After hypotension (or blood loss) for 5 h the number of granular JG-cells increased and they were found both in the subcapsular zone and in the depth of the cortex; they were discovered not only in the juxtaglomerular segments of the afferent arteriole, but also frequently over its whole extent and even in the wall of the interlobular artery. Besides the increase in the number of granular cells during hypertension, the degree of their granularity also increased (Fig. 1).

Analysis of the JGI – a quantitative indicator of the degree of granulation of the JGA – showed that under hexobarbital anesthesia it showed a tendency to decline, during hypotension there was a significant increase in JGI, and 24 h after the end of hypotension JGI was again reduced.

Since there is no general agreement at the present time about the reliability of JGI as an indicator of functional activity of the JGA [7, 15], karyometry was used as an additional morphofunctional criterion. The results of karyometry showed a significant increase in the volume of the nuclei of the JG-cells under the influence of the ganglion-blocker and of blood loss which was interpreted as a reflection of their increased functional activity.

Hexobarbital thus had practically no effect on the functional activity of JGA. The increased synthetic activity of the JG-cells during hypotension (and blood loss) was accompanied by a marked increase in the number of renin-containing granules in their cytoplasm. The secretory activity of the JG-cells was reduced 24 h after the end of artificial hypotension and the rate of liberation of the granules was increased.

A comparative morphological study of HNHS and JGA showed that during prolonged and deep hypotension they responded by a considerable increase in their secretory activity, which was confirmed by the accumulation of hormone-containing granules in the cytoplasm of the cells. Meanwhile a distinctive "blockade" of liberation of hormone-containing Gomori-positive and Bowie-positive granules was observed and was evidently linked with the severe disturbance of the microcirculation taking place under these experimental conditions.

LITERATURE CITED

1. B. V. Antipov, Arkh. Patd., No. 5, 69 (1971).
2. L. B. Bebeneva and A. E. Biochenko, in: Mechanisms of Some Pathological Processes [in Russian], No. 4, Part 1, Rostov-on-Don, pp. 94-103.
3. Z. D. Kn orre, A. L. Polenov, and M. V. Propp, Arkh. Anat., No. 7, 17 (1969).
4. A. L. Polenov, Hypothalamic Neurosecretion [in Russian], Leningrad (1971).
6. B. A. Saakov, E. S. Gul'yants, V. A. Vorontsov, et al., Fiziol. Zh. SSSR, No. 6, 901 (1970).
7. V. A. Skuratov, Patol. Fiziol., No. 5, 28 (1966).
8. A. F. Ushkalov and A. M. Vikhert, Arkh. Patol., No. 9, 3 (1972).
9. O. K. Khmelnitsky and N. M. Kotchubey (O. K. Khmel'nitskii and N. M. Kochubei), Acta Morphol. Acad. Sci. Hung., 24, 1 (1976).
10. B. S. Garber, F. W. McCoy, E. R. Hayes, et al., Arch. Int. Pharmacodyn., 12, 275 (1959).
11. P. Hartroft and W. Hartroft, J. Exp. Med., 97, 415 (1953).
12. K. Hirashima and F. Takaku, Blood, 20, 1 (1962).
13. G. Kaley and H. Demopoulos, Fed. Proc., 22, 664 (1963).

14. W. Oliver and G. Brody, Circulat. Res., 16, 83 (1965).
15. S. Osnes, Br. Med. J., 2, 1387 (1958).
16. G. Reeves, L. Lovenstein, and S. Sommers, Am. J. Med. Sci., 245, 184 (1963).

STRUCTURAL CHANGES IN THE RAT MYOCARDIUM DURING ADAPTATION TO MOUNTAIN HYPOXIA

V. A. Kononova

UDC 612.172.6-06:612.275.1

Changes in weight indices for different parts of the heart, the area of cross sections of the myocytes, and vascularization of the myocardium during adaptation to hypoxia were studied in experiments on rats exposed to high-altitude hypoxia (3200 m above sea level). The morphological manifestation of compensatory and adaptive reactions of the rat heart to hypoxia is an increase in its weight, chiefly on account of hypertrophy of the myocardium of the right ventricle. Increasing hypertrophy of the myocardium is accompanied by the corresponding increase in its vascularization.

KEY WORDS: myocardium; hypoxia; morphometry.

The effect of mountain conditions on man and animals is a subject that increasingly attracts the attention of research workers. Even a short stay under conditions of high-altitude hypoxia in the mountains evokes a response primarily of the cardiovascular system [2, 4, 10, 12]. However, all the extensive evidence so far available is concerned mainly with functional manifestations of adaptation of the cardiovascular system to hypoxia [1, 13, 14]. There are few data on the structural manifestations of adaptation of the system. Among the most important morphological criteria of adaptation to hypoxia are hypertrophy of the myocardium of the right ventricle and an increase in the blood supply to the tissues. However, information on the dynamics of development of hypertrophy and vascularization of the hypertrophied myocardium is frequently contradictory [8, 11].

The object of this investigation was to study the dynamics of weight indices of the heart, the area of cross section of the myocytes, and vascularization of the myocardium during adaptation of animals to mountain hypoxia.

EXPERIMENTAL METHOD

Noninbred male rats weighing 200-250 g were used. The control consisted of 16 animals killed in the city of Frunze (760 m above sea level). The experimental rats (75 animals) were taken up to Tyuya-Ashu Pass, at an altitude of 3200 m above sea level in the mountains of Kirghizia. The duration of the experiment was counted as the number of days of exposure of the rats to mountain hypoxia. Tests were carried out on the 1st, 3rd, 7th, 15th, 30th, and 45th days. To determine the weight indices of the heart, the heart was weighed by Müller's method in Il'in's modification [5] separately in six rats at each of the above-mentioned times of the experiment. The absolute weight of the heart, the weight of the right and left ventricles and septum, and the cardiac and ventricular indices were determined. The numerical results were expressed per 100 g body weight. The area of cross section of 100 muscle fibers from the right and left ventricles of each rat was determined in the same animals in histological sections cut after embedding in paraffin wax by the method of direct microplanimetry. The area of the arterial microcirculatory system was measured in frozen sections cut from rat hearts perfused with an aqueous solution of ink (six rats at each time of the experiment). The area of the myocardial vessels in the right and left ventricles was calculated in 10 fields of vision as a percentage of the total area of the myocardium. The method of direct microplanimetry, with the aid of a microprojector, was used for this investigation. The numerical data were subjected to statistical analysis. The coefficient of correlation was calculated by the method of squares.

Khirghiz Research Institute of Obstetrics and Pediatrics, Frunze. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Smol'yannikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 10, pp. 497-500, October, 1979. Original article submitted January 7, 1979.

 0007-4888/79/8810-1228 $07.50