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ADRENAL GLANDS: MORPHOFUNCTIONAL REORGANIZATION BASED ON THE INFLUENCE OF EXOGENOUS AND ENDOGENOUS FACTORS

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Abstract

The adrenal glands are the subject of many researches in biology and medicine. They have unique histoarchitectonics of the parenchyma and structure of the bloodstream. They also perform a number of important functions necessary for the normal vital activity of the body under stress. A large number of scientific papers are devoted to the study of changes in the structural organization of this organ at the micro- and submicroscopic levels under the influence of various external and internal factors. Morphofunctional changes in the gland after experimental thermal burns of the skin remain poorly understood, which requires further experimental studies in this area.

The purpose of this study was to review the scientific literature on the effects of factors of different origins on the morphofunctional structure of the adrenal glands.

The article analyzes scientific publications devoted to the study of the effects on the adrenal morphology of stress factors, heavy metals, drugs and toxic substances, alcohol,

smoking, starvation, hypergravity, physical exercises, hypothermia, poisoning, dehydration, drugs, diabetes, and viral infections. It was found that the factors we mentioned cause the reorganization of the structural components of the adrenal glands, violations of their histoarchitectonics, in particular microcirculatory bed, at the micro- and submicroscopic level. In most cases, there were phenomena of pericellular and perivascular edema, focal hemorrhage, connective tissue growth, thickening of the connective tissue capsule of the organ with signs of edema, vacuolation and edema of the cytoplasm, and the appearance of pyknotic nuclei. In the long term that followed after the experiment, the stabilization of morphofunctional elements of the gland and the microcirculatory bed was recorded, but complete restoration of the structural integrity of the organ did not occur.

Key words: adrenal glands; morphological and functional changes; exogenous and endogenous factors.

Introduction. An important role in the process of adaptation of the organism is played by organs of the endocrine system such as the adrenal glands, so their morphofunctional state affects the development of adaptive mechanisms [22, 31]. So, they are involved in optimizing gluconeogenesis and metabolic reactions. It is known that the body's response to stress is staged and, in particular, distinguishes the following three stages of such a reaction: alarm reaction, resistance and exhaustion [6]. It was also found that the action of any stress factor, both exogenous or endogenous, is accompanied by a complex of nonspecific changes in the body, which are manifested in the activation of the hypothalamic-pituitary system [35]. Thus, under the influence of adrenocorticotropic hormone of the pituitary gland, the adrenal glands produce hormones that play an important role in the body's response to stress. That is why this is a sensitive organ responsible for the body's adaptation to new conditions [8].

Description of the state of knowledge

The scientific work of many scientists was aimed primarily at a comprehensive study of various morphological characteristics of the adrenal glands under stress as an extreme factor. It has been found that chronic stress leads to the morphofunctional changes in the body [24, 33]. Thus, in the adrenal glands of rabbits there is an increase in the concentration of cortisol in the serum and an increase in the total mass of organs. At the microscopic level, changes in the thickness of the structural and functional zones of the adrenal cortex in percentage were established. In addition, hyperplasia of subcapsular cells, local angiogenesis and stromal component dystrophy due to hemomicrocirculation, as well as the phenomenon of degeneration and apocytosis and apoptosis were observed [29].

Researches performed to study the effects of immobilization stress on the adrenal glands, which showed an increase in cortisol levels in the blood, indicating a significant activation of glucocorticoid function of the adrenal glands. Conducted morphological studies of the gland confirmed a significant increase in its secretory activity under immobilization. The morphofunctional rearrangement of light cells was microscopically described, which was explained by the high content of lipid inclusions. A small number of dark cells rich in ribosomes was noted, which indicated the predominance of enzyme systems synthesis and subsequently provided steroidogenesis [16, 21].

In the morphometric study of the adrenal glands under conditions of pre-mortem stress, changes in the ratio of the size of the adrenal cortex in animals of different experimental groups were observed, which is due to changes in the physiological activity of the organ [10]. In particular, the increased secretion of glucocorticoid hormones under stress was accompanied by the swelling of the cells of the zona fasciculata with its simultaneous expansion. Weakening of the secretion of glucocorticoid hormones with the use of anti-stress substances was manifested by a reduction of the zona fasciculata and the expansion of the zona reticularis.

When studying the effect of chronic stress on the adrenal glands, hypertrophy of the organ was noted, and subsequently, its depletion, as well as circulatory disorders at the level of the microcirculatory bed and various damage at the cellular level, manifested by tissue dystrophy and necrosis. Thus, the phenomena of granular and fine-vacuolar dystrophy, hypertrophy of cortex cells (mainly zona glomerulosa and zona fasciculata) and adrenal medulla were observed. Signs of pericellular and perivascular edema, punctate hemorrhage, and focal proliferation of connective tissue between the cortex and medulla were present [7].

Under experimental acetic acid poisoning, the most significant changes in the structural components of the adrenal glands were observed in the zona fasciculate of the cortex, which was manifested by focal lesions, the degree of which varied: the less prominent changes after acute stress response and the most pronounced after chronic stress. During acute stress, the mass of the organ increased and the phenomena of hypertrophy of cortical cells was observed. There was a change in the parenchymal-stromal ratio, the size of corticocytes and their nuclei, as well as an increase in the volume of the vascular bed. In chronic stress, there was a decrease in organ mass, hypotrophy of the cortex, a decrease in the volume of the vascular bed with a sharp decrease in corticosterone level [15].

Under the conditions of exposure to ionizing radiation on the adrenal glands of adult rats, compensatory hypertrophy of the organ occurred, which depended on the radiation dose.

It was studied that the glands are characterized by a high level of regeneration of the cortex due to compensatory hypertrophy, and the recovery of the adrenal medulla occurs in the presence of a small number of undamaged chromafinocytes [4, 12].

With prolonged tobacco intoxication in the cortex of the adrenal glands, a typical increase in the width of the zona reticularis occured, which indicated an increase in the secretion of hormones in this zone, as a sign of the implementation of the general adaptation syndrome. In the zona fasciculata there was a decrease in the number of corticocytes due to their cytolysis, an increased size of their nuclei, and a slight vacuolation of the cytoplasm. These changes indicate compensatory-adaptive reactions in the organs of animals of experimental groups [36].

The researchers studied the effect of changing the length of daytime on the morphofunctional state of the adrenal glands of rats. Ultramicroscopic examination of corticocytes of animals that were under constant light showed that all cells were polygonal in shape with a round nuclei. In the corticocytes of the zona fasciculata of rats there was a decrease in the number and size of secretory inclusions, and their boundaries were poorly contoured. Light vacuoles and expansion of cysterns of a smooth endoplasmic reticulum were found in cytoplasm. The Golgi complex consisted of tubular structures that were partially expanded, which is related with their participation in the intermediate stages of corticosteroid synthesis. The main part of the mitochondria is of round shape, with an osmiophilic matrix. A significant number of free ribosomes are visible between mitochondria. Ultramicroscopic examination of the structure of the adrenal medulla of the experimental animals showed that typical changes in epinephrocytes were determined during the experiment. The cytoplasm is vacuolated in some cells; large vacuoles were observed in certain places, the number of secretory granules was markedly reduced [13, 25]. Histological and morphometric studies showed that the existence of animals in altered light stimulated the morphofunctional activity of the adrenal cortex zona fasciculata and inhibited the activity of endocrinocytes of the zona glomerulosa and zona reticularis, indicating hyperproduction of corticosteroids and hypoproduction of aldosterone and steroid hormones in animals. The results of the experiment showed that animals that were kept in conditions of changes in the duration of daylight have a smaller mass of the adrenal glands, compared with animals that were kept in conditions as close as possible to natural light. There was also a decrease in the mass of the adrenal glands in groups of animals kept in round-the-clock lighting, which was more pronounced in rat-males [26, 30].

Under the influence of red sludge (highly toxic waste generated during aluminum production) on the body of animals during 14 days of experiment there is an increase in the functional activity of adrenocorticocytes of the adrenal cortex, accompanied by corresponding changes in the ultrastructure of these cells and morphometry data. At the same time, signs of dystrophic changes (cytoplasmic edema, hyperchromic and shrunken nuclei) were found in some cells. On the 45th day after the experiment, the action of red sludge caused a decrease in the function of adrenocorticocytes and a significant dystrophic-degenerative rearrangement of their ultrastructure. On the 180th day of the experiment, the reorganization of the cells of the zona fasciculata indicated the activation of the processes of intracellular reparative regeneration. There was an increase in the number of nuclear pores, ribosomes, liposomes, and a significant expansion of the perinuclear space. The mechanism of glucocorticoid hormone production was intensified [5].

Due to the action of heavy metals in combination with the influence of ionizing radiation in the adrenal cortex, more significant changes were detected than under the action of each of these factors separately. Total irradiation of white rats in combination with the load of heavy metal salts for 1 - 3 months caused progressive dystrophic-destructive processes, inhibition of functional activity and disruption of adaptive responses of adrenocorticocytes of the adrenal cortex, which depended on the intensity and duration of exposure [17].

When modeling experimental streptozotocin diabetes in the early stages of its development, researchers [20, 27, 38] described different stages of reactive changes in response to metabolic disorders in the body. In particular, on the 7th day after the experiment, within the cortex of the adrenal glands, there was a thickening of the zona fasciculata, and a decrease in the size of endocrinocytes of this zone. Such morphometric changes were associated with a decrease in the bulk density of lipid droplets in the cytoplasm of cells. On the 14th day of streptozotocin-induced diabetes mellitus, an increase in morphofunctional activity was observed in the adrenal cortex, which manifested in the thickening of all its zones; significant increase in the size of endocrinocytes of all zones and their nuclei; an increase in the bulk density of lipid granules in the endocrinocytes of the zona fasciculata and an increase of the cortisol levels in the blood.

The morphological changes of the adrenal glands under combined alcohol and drug intoxication in the experiment and in humans were also studied. Scientists have identified signs of functional activity of cells that are characteristic of the stress response, as well as hemodynamic disorders of the microcirculatory bed. In particular, these include the development of compensatory maladaptive changes in the cortex and medulla of the adrenal

glands, the expansion of the hemocapillaries' lumen, pyknosis of the nuclei, and intracellular edema of cortical endocrinocytes and chromafinocytes. There are sludge-phenomena, point hemorrhages, and loss of cytoarchitectonics of endocrinocytes in the zona glomerulosa of the adrenal cortex [3, 23].

In the study of the effect of low temperatures on the adrenal glands, it was found that in the structural components of the wall of different parts of the hemomicrocirculatory bed and in the parenchyma of the organ there were successive changes that depended on the duration of hypothermia. Thus, on the 1st day of the post-hypothermic period, reactive edema was observed in the cellular structures of the vessel wall and gland parenchyma with areas of arterial spasm and dilatation of the venous area of the bloodstream, as well as an increase in blood cortisol and adrenaline. On days 3 and 7, destructive-compensatory changes in the structural components of the organ were characteristic, which was manifested by partial destruction of cellular and extracellular components and partial hypertrophy of the zona fasciculata. On days 14 and 30, compensatory-restorative signs were detected, which indicated an increase in the activity of intracellular regenerative processes. The result was the restoration of angioarchitectonics of the organ and signs of regenerative processes in the walls of blood vessels and parenchyma of the adrenal glands [9, 18].

Changes in the morphofunctional state of the adrenal glands were also observed in acute inflammation. Macroscopically, from the first day of peritonitis, adrenal hyperemia was observed. Histological examination of the cortical substance revealed hemorrhages of different sizes [34].

In the study of the systematic effect of hypergravity on the adrenal glands, adaptive responses of the body to stress and changes in hemodynamic conditions were observed. Significant ultrastructural destructive changes were most pronounced with prolonged exposure to this factor [28].

Significant changes in the glands occurred when exposed to high temperatures and physical activity. It was found that the complex effect of chronic hyperthermia and physical activity leads to pronounced morphological changes in the adrenal glands of rats at different times of readaptation, which indicate functional depletion of organs. The degree of morphofunctional changes in the body depends on the duration of exposure to these exogenous factors [1, 2].

General hypoxia, overheating, and genetically determined metabolic disorders also caused significant ultrastructural changes in the adrenal glands. With the acute action of these factors there was atrophy of the adrenal cortex, and with prolonged exposure - hypertrophy of

the adrenal cortex. Phenomena of adrenocorticocyte delipidization, cambial cell hyperplasia, hemodynamic disorders (blood vessels plethora, erythrocyte sludge and stasis), cell necrobiosis and resorption, growth of connective tissue component (especially in the zona glomerulosa and zona reticularis) of the organ allow us to trace the patterns of reorganization of the gland due to the actions of these extreme factors [19, 37].

Studies of the adrenal glands of rats with transplanted carcinosarcoma and chemotherapy have shown that antitumor drugs can impair the morphology and function of the adrenal glands. Under the influence of cytostatic drugs, lipid inclusions in the cells of the zona fasciculata almost disappeared and less glucocorticoids were synthesized. The secretion of adrenaline and noradrenaline decreased in the adrenal medulla. The most prominent changes in the adrenal glands of experimental rats were observed in the zona fasciculata, the least - in the zona glomerulosa. All this data suggests that the use of chemotherapy adversely affected the morphofunctional state of the adrenal glands [32].

In the study of the structure of the adrenal glands under conditions of 15 days of readaptation after experimental extracellular dehydration of mild degree, the hormonal status of experimental animals was characterized by signs of instability, which is explained by the example of the development of compensatory-adaptive processes in response to water-salt balance [11].

The study of the adrenal glands due to influenza A (H1N1) and COVID-19 viruses is relevant today. Thus, the researchers found specific histological changes in the adrenal glands in these diseases, characterized by edema and partial destruction of endocrine cells of both the cortex and medulla parts, but with COVID-19 there was more significant damage to the medulla with loss of endocrine cells of Chromogranin A substrate. In case of COVID-19, in the cortical and cerebral layers of the adrenal glands, there is small amount of blood in the vessels of the microcirculatory bed with a decrease in their lumens in contrast to cases of influenza A (H1N1), in which there are signs of plethora and vasodilation. Hypoxic damage in COVID-19 is accompanied by accumulation of lipofuscin granules in the cytoplasm of endocrine cells - a marker of activation of free radical oxidation of lipids [14].

Conclusions

Thus, the results of the analysis of scientific works suggest that under the influence of factors of different genesis in the adrenal glands there are significant structural and functional changes, which is confirmation of the adaptive and compensatory mechanisms of animals in response to stress. The results of the influence of various factors have both typical and specific features, depending on the conditions and duration of the experiment. Under short-

term action of factors, initial destructive changes of adrenal glands were revealed, and under long action - significant degenerative changes were observed, that testify to compensatory processes in an organ and signs of adaptation of an organism of experimental animals.

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