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RESEARCH ARTICLE

Compensatory and Adaptive Features of the Cerebellum under Stress

Alexey Rozhentsev[1*], Sergey Lobanov[2], Mikhail Rozhentsev[1], Robert Iagafarov[1]

1. *Federal State Budgetary Educational Establishment of Higher Education «Bashkir State Agrarian University», Ufa, Russian Federation.*
2. *Federal State Budgetary Educational Establishment of Higher Education «Bashkir State Pedagogical University», Ufa, Russian Federation.*

***Corresponding Author: Alexey Rozhentsev**

Abstract

The paper discusses the results of the study of compensatory and adaptive changes in rat cerebellar tissues under stress. As a stress factor, the experiment simulated (hypobaric) hypoxia. Since hypoxia remains one of the central issues in the modern medical science, it is directly or indirectly related to human diseases of various etiologies. To identify the features of compensatory and adaptive changes in the rat cerebellum under the action of hypoxia, we conducted comprehensive histological and histochemical studies. At the early stages of hypoxia, changes in the cerebellar tissue could be found, that were characterized by a significant increase in the volume of intracellular structures. With a prolonged hypoxia, a decrease in the volume of intracellular structures was observed which, in turn, entailed a decrease in total glycosaminoglycans and a change in the ratio of sulfated and non-sulfated glycosaminoglycans. In addition, we noted cerebellar neuron migration into the molecular layer. The experiment revealed that hypoxia has a significant effect on the intensity of metabolic processes in cells, with the generation of intermediate metabolic products leading to a change in pH.

Keywords: *Hypoxia, Cerebellum, Rats, Compensatory and adaptive changes, Glycosaminoglycans.*

Introduction

Human society has accelerated its development pace from year to year. To realize the human's and individual's potential, one shall be able to adapt to a rapidly changing environment [1]. However, modern civilization makes the highest demands on man. Today, it has become common to swim in the ocean depths, to fly at an altitude of over 8,000 meters, and even to stay in space for a long time. All this is associated with various negative factors acting on the human body [2, 6]. One of such common factors is hypoxia; therefore, relevant is the issue of further deepening the knowledge of pathological changes in the body under hypoxia.

The term of HYPOXIA (oxygen deficiency, oxygen starvation) has been defined in the Big Medical Encyclopedia as a state arising from an insufficient supply of body tissues with oxygen or an improper disposal of oxygen in the process of biological oxidation [7]. Under the action of hypoxia, some changes occur in the cell homeostasis that is closely related to metabolic processes [8, 10]. Hypoxia causes significant disturbances in the central nervous system, especially in the tissues of the cerebellum that is involved in controlling high-precision movements and in implementing adaptive mechanisms in the nerve and muscle tissues [11, 12]. Hypoxia, that varies in type of occurrence and in its development mechanisms, as well as in the duration of its action, is a powerful stress factor for the body [13]. Under the action of such factors, the body launches compensatory and adaptive processes, which can develop into maladaptive ones.

Such changes are revealed in the cerebellum, where we can see the signs of increasing anaerobic processes. These processes shift the cells pH towards acidity due to the generation of a significant amount of intermediate metabolic products.

All this leads to the disturbance of energy generation processes in cells and, as a result, to cell dysfunction [14, 17]. Hypoxia affects the cell biosynthesis, the processes of cell renewal and cell the membrane element integrity restoration, as well as the extracellular matrix condition. Hypoxia affects the composition, content and ratio of proteins and lipids that participate in the formation of the cell membrane.

In addition, changes in the composition of glycocalyx are detected on the cell membrane surface [18, 19]. Under prolonged action of hypoxia, we can observe the development of pathological conditions that can develop into a disease [20, 21]. Changes that occur in the nervous system under the action of hypoxic conditions can persist for a long time after their termination [22, 23].Based on the above; the purpose of our study is identifying the compensatory and adaptive features of the cerebellum under stress.

Material and Methods

The experimental study was conducted from 2015 to 2019. The objects of the study were sexually mature VISTAR rats. The research was carried out in full compliance with applicable legal and ethical standards (the State Standard GOST R 53434-2009, the Principles of Good Laboratory Practice; the International Guidelines for Biomedical Research Involving Animals (1985); the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986); the Guide for the Care and Use of Laboratory Animals (the 8th edition, 2011); the Order of the USSR Ministry of Health No. 755 dated August 12, 1977 "On Measures to Further Improve the Organizational Forms of Activities using Experimental Animals").

Experimental animals were kept in a standard vivarium environment, at normal temperature, humidity, and light. In addition, they had free access to water and feed. Specimens had an average body weight of 220 ± 15.2 grams. Rats were divided into control and experimental groups (21 and 37 rats, respectively). As a stressor (a stress factor), the experiments simulated the "hypobaric" hypoxia. Rats were placed in a pressure chamber and exposed to a decrease in atmospheric pressure down to 0.13 atmospheres.

Rats were exposed to hypoxia for 15 minutes one time, until the specimen's complete "unconsciousness", followed by resuscitation procedures. Observations of animals were carried out at fixed intervals for 7 days. Rats were removed from the experiment at the following time intervals: after 1 hour, 6 hours, 12 hours, 24 hours, 72 hours, and 168 hours.

To study the features and arrangement of cerebellar cells, we used histological methods by staining standard sections with hematoxylin-eosin according to the method developed by G.A. Merkulov [24]. To study glycosaminoglycans, histochemical methods were used: staining standard 0.1 to 0.5-micron thick sections (prepared using an ultra tome) with methylene blue and toluidine blue [25]. Various classes of glycosaminoglycans were identified according to the method suggested by C. Lupp [26]. For this purpose, 7-micron thick cryostatic sections were taken, that were stained with alcian blue.

This dye was prepared at different values of pH (1.0 and 2.5) and molarity (the content of $MgCl_2$ in 0.2 to 1.0 mol solution), which made it possible to distribute glycosaminoglycans into classes. The content of glycosaminoglycans in cerebellar tissues was measured using methylation and enzymatic controls. As enzymes, we used (testicular, bacterial, geruidal) hyaluronidases. To study the microvasculature and its features, we used staining of preparations with hematoxylin-eosin and impregnation with nitrous silver according to V.V. Kupriyanov [24].

Rats were removed from the experiment using an anesthesia overdose followed by decapitation. Then, during the first 8 to 10 minutes, the skull box was opened; the brain was extracted and placed in formalin (10 % solution of neutral formalin on phosphate buffer at pH of 7.2 to 7.6). For electron microscopy, 1×1 mm pieces of cerebellum were taken.

They were placed in 2.5 % solution of glutaraldehyde on phosphate buffer at pH of 7.2 to 7.6 followed by additional fixation in 1 % solution of osmium tetroxide (OsO_4) for one hour. Then, these pieces were transferred to alcohol in an ascending concentration from 50% to 100% and pure acetone, and covered

with EPON-812 resin. Using LKB-III ultratome, we prepared ultra-thin sections about 700 angstroms thick followed by contrasting with uranyl acetate and lead citrate according to Reynolds. Sections were studied in a JEM-100 S transmission electron microscope (JEOL Ltd., Japan) at an accelerating voltage of 90 kV. The results of these studies were subjected to statistical processing in the Windows 7 operating system using the STATISTICA application (Stat Soft Inc., USA).

Results and Discussion

Comprehensive morphological studies revealed the dynamics of changes in the cerebellum of experimental animals exposed to a stressor (hypoxia). The histological studies of rat cerebellar tissue preparations showed that, as early as by the end of the first hour, under the action of the stressor, structural features of cellular and non-cellular elements were observed. We noted that cerebellar neurocytes had relatively clear contours, although some of their areas looked blur. In this period, cerebellar neuron cells featured uneven staining, whereas the cerebellar tissue on histological preparations became mosaic (cell elements could have light, intensely stained, or intermediate forms). It is the uneven staining observed in the preparations of both neurocytes and glia cells that highlighted the functional activity unevenness of these cell structures.

Hypoxia as a stressor has a significant effect on the functional condition of nerve cells, on the intensity of metabolic processes, on the generation of intermediate metabolic products, which change the medium pH, along with many other changes. All this could be seen in the form of lighter colored areas around neurocytes. In the cerebellar cells themselves, a more saturated staining of their elements was observed, which looked replete in histological preparations. Nerve cell nuclei had a deeper staining as compared to their cytoplasm (Fig. 1).

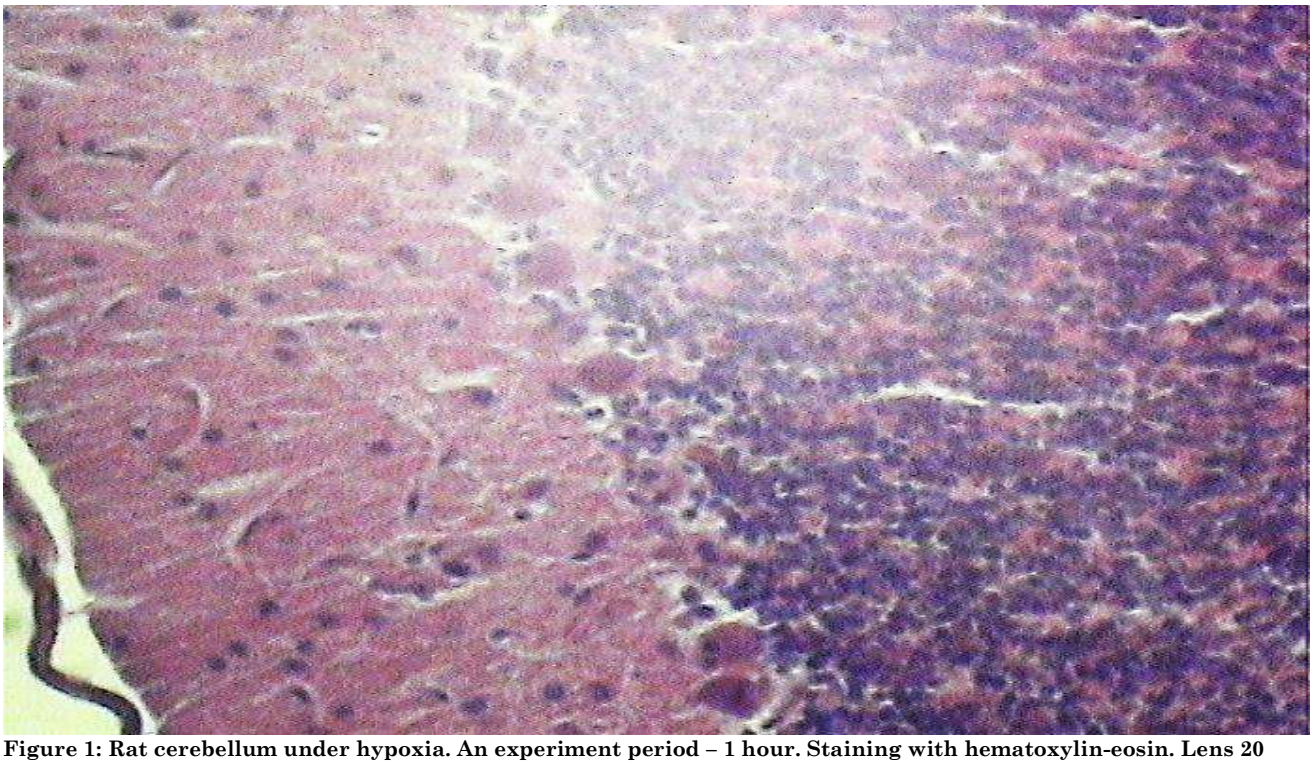

Figure 1: Rat cerebellum under hypoxia. An experiment period – 1 hour. Staining with hematoxylin-eosin. Lens 20

At this stage of hypoxia, we could see the development of functional hyperemia processes from the side of the microvasculature blood vessels; this was especially noticeable in the capillary link vessels. In the capillary and post-capillary link vessels of the microvasculature, we could see blood corpuscles, among which erythrocytes prevailed, that were arranged in the form of coin columns. The clearance between these microvasculature structural elements had a diameter of approximately 1.5 to 2 times greater than under normal conditions. The results of histochemical studies allowed to see the features of the glycosaminoglycans distribution, to trace the dynamics of changes in their quantitative parameters under hypoxia and, in addition, to determine the ratio of different classes of glycosaminoglycans (Fig. 2).

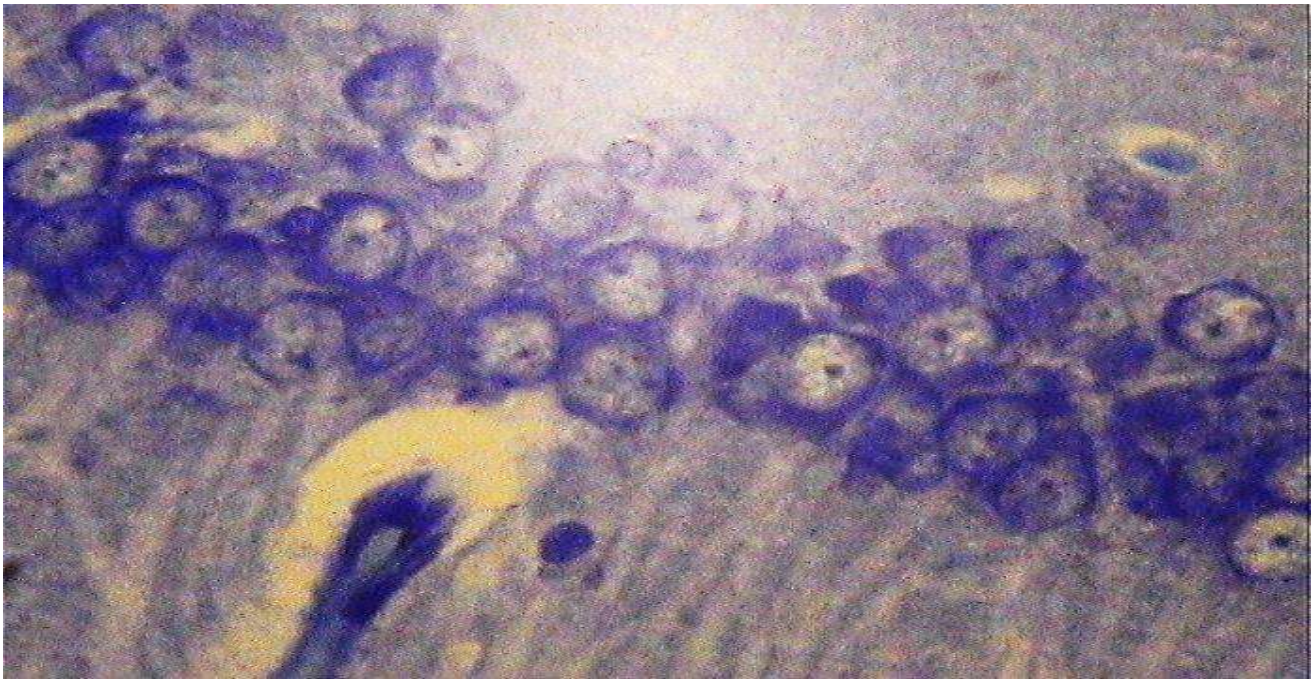

Figure 2: Rat cerebellum under hypoxia. An experiment period – 1 hour. Staining with toluidine blue. Lens 40

The data obtained using electron microscopy made it possible to determine the features of structural changes in the cerebellum cellular elements, their intracellular structures, and the intercellular matrix. It was found that nerve cells of the cerebellum granulose layer had different sizes and shapes. These neurocytes were characterized by light and dark shapes of varying degrees of osmiophilism, which also indicated that they featured different functional activity. In addition, according to electron microscopic studies, it was found that mainly neurons of a polygonal shape were found in the granulose layer. These cells were arranged relatively closely to each other. On their surface and processes, numerous cytoplasmic outgrowths were observed and intercellular contacts could be traced (Fig. 3).

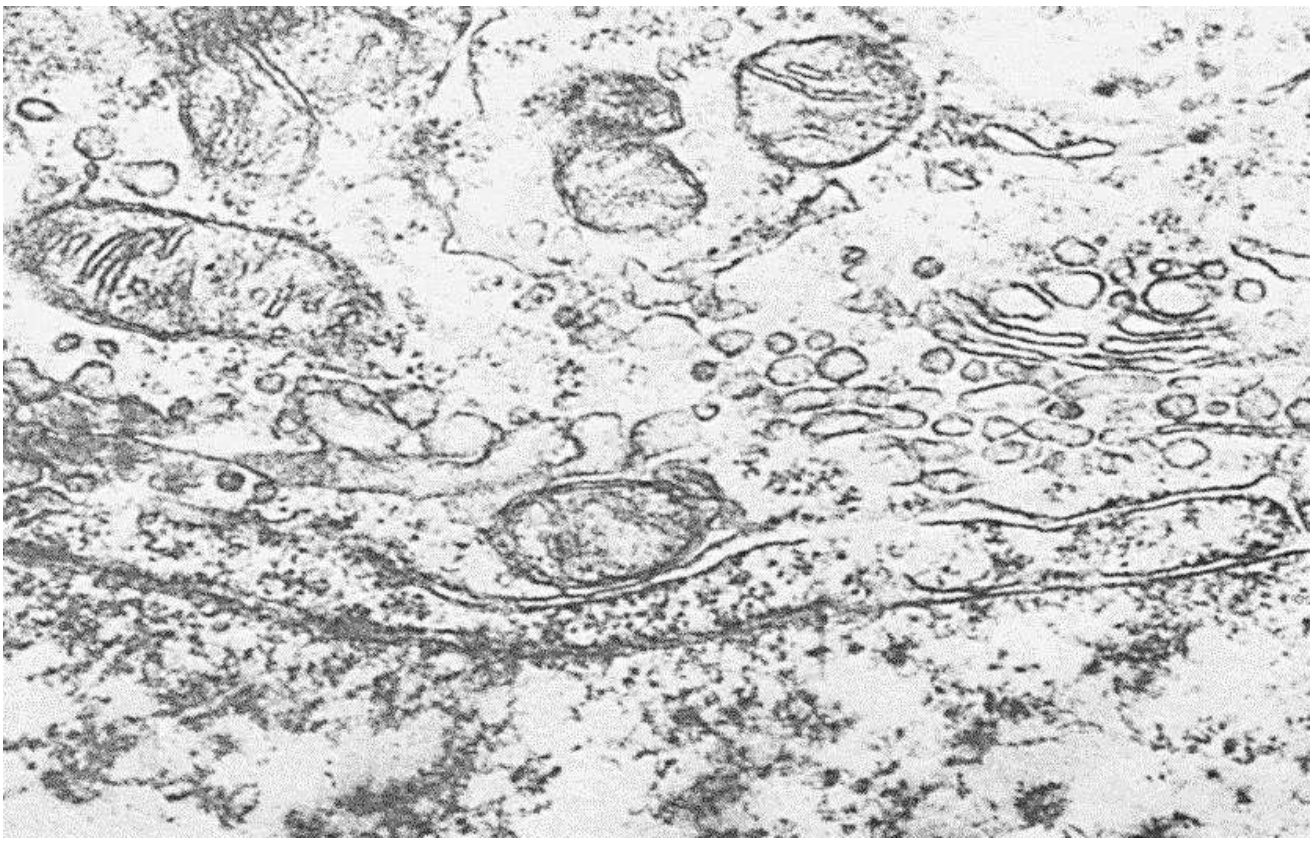

Figure 3: Cerebellar neuron under the action of hypoxia. An experiment period – 1 hour. Areas with hypertrophy and destruction of the Golgi complex, vesicle proliferation. Enlarged 40000 times

Neurons located in the ganglion layer were represented by large cells – Purkinje cells. These neurons had different osmiophil staining and were represented by relatively light and dark forms characterizing their functional condition. In an ultra structural study, cerebellar neurocytes had relatively clear contours. Their cell membrane and the intracellular structure membranes in some areas had lost the contour clarity and became slightly "blurry". More pronounced "blurring" was observed among intracellular membrane structures. The data of electron microscopic studies identified the dynamics of changes in clarity and some contour violations among cellular ultrastructural elements.

Under hypoxia, the experimental animals' cerebellum nerve cells acquired pronounced nuclei polymorphism. This was manifested in the irregular sizes, contour features, and varying degrees of nucleoplasm osmiophilism of such cell elements, which reflected the heterogeneity of their functional condition. In this period, the electron diffraction patterns of the cerebellar neurocytes studied showed an uneven saturation of their chromatin.

Experiments showed that cerebellar neuron nuclei interacted differently with salts of heavy metals. Under these conditions, nerve cells were found that had nuclei with poorly stained chromatin, with chromatin located on the nucleoplasm periphery, or with its uniform distribution. The cerebellar neurons of the experimental group animals contained nuclei in their cytoplasm that had invaginations in the nucleoplasm. The nuclei of these cells included one or two nucleoli of a high degree of osmiophilism, as compared to the nucleoplasm. The nuclear membrane preserved its double-contoured structure. In some areas, we could observe areas of extensions and contractions. The nucleoplasm revealed an integrity violation of the nuclear membrane outer leaf.

The nuclear membrane had areas with recesses and protrusions on its surface, giving it a peculiar appearance. In the cytoplasm of neurons and glia cerebellum cells, lysosomes of different osmiophilism were present. These lysosomes were in the immediate vicinity of mitochondria, which led to local melting of their membranes and violation of the mitochondrial matrix integrity. During this period, mitochondria were detected that varied in size and in the matrix staining intensity. In addition, we could see an increase in the number of medium-sized mitochondria. These mitochondria showed an increase in the number of cristae whose contours were not the same everywhere. Among mitochondria, forms that had lost their two-contoured structure were found; the reason for this was the destruction of their inner membrane. It should also be noted that mitochondria were unevenly located in different parts of the nerve cell cytoplasm. These energy-generating structures were detected near the nuclear zone, in areas of invagination, both isolated and in groups. Cristae in these mitochondria featured a parallel arrangement.

The endoplasmic reticulum was represented by moderately dilated tubules. In the studied preparations, there were areas where flat endoplasmic reticulum was smoothly transforming into granular one. Fibrillar structures occurred in small groups; separate microtubules were located next to them. Six hours after hypoxia, changes in the cerebellar tissue of the experimental group animals were described as a mild edema. In histological preparations, this was manifested as lighter areas around cells.

In microvasculature vessels, hyperemia persisted in almost all links. An ultrastructural research showed signs of pinocytosis in the capillary walls, in endotheliocytes forming the same, the intensity of which increased, in comparison with the early period. The changes that occurred in the microvasculature under hypoxia were differently manifested. To a greater extent, this was manifested among the vessels of the venular link, because of their greater diameter, as compared to that of arterioles.

In the studied preparation, we could see vascular dilatation, i.e. an alternation of their extensions and contractions. In some areas of rat cerebellar tissue, perivascular edema was observed. At the sixth hour of the experiment, when conducting histochemical studies, we found that the rat cerebellar tissue was characterized by an uneven

distribution of glycosaminoglycans and different ratios of their classes (Table 1, Fig. 4).

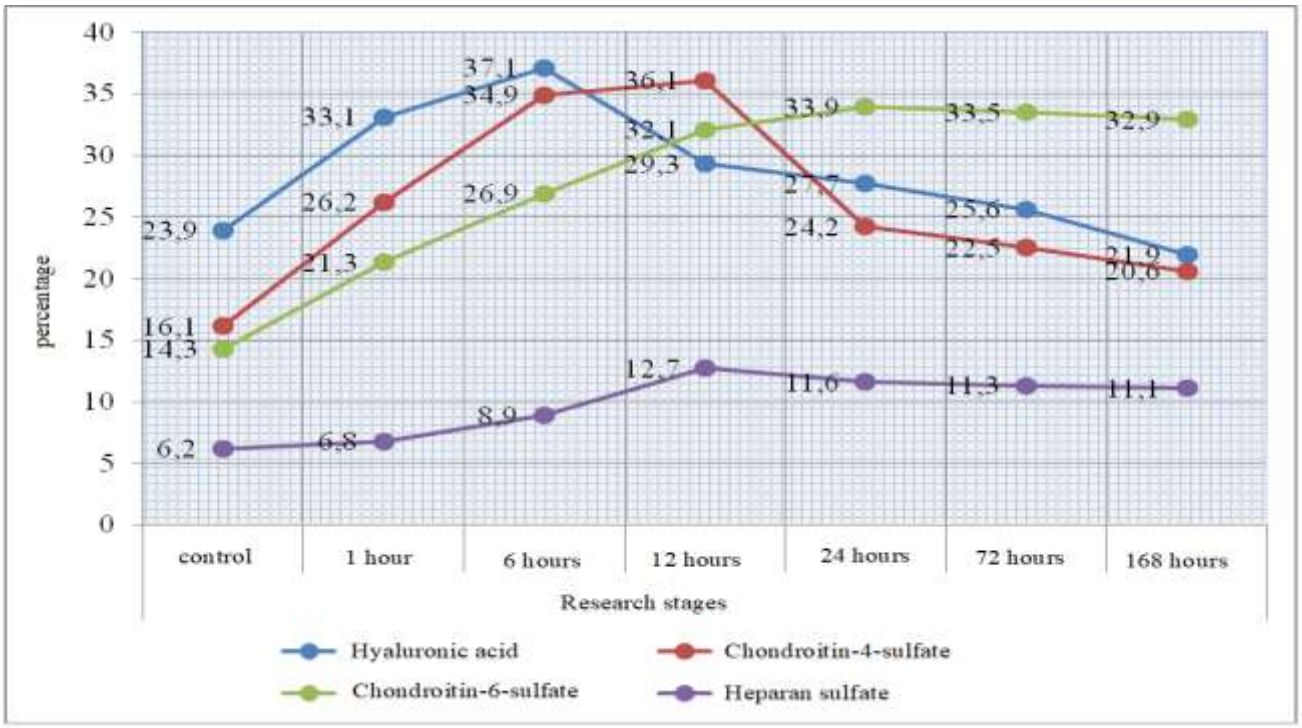

Figure 4: Percentage of different GAG classes in rat cerebellar tissue under hypoxia

Table 1: Percentage of different GAG classes in rat cerebellar tissue under hypoxia

Name	Control group	Research stages					
		1 hour	6 hours	12 hours	24 hours	72 hours	168 hours
Hyaluronic acid	23.9	33.1	37.1	29.3	27.7	25.6	21.9
Chondroitin-4-sulfate	16.1	26.2	34.9	36.1	24.2	22.5	20.6
Chondroitin-6-sulfate	14.3	21.3	26.9	32.1	33.9	33.5	32.9
Heparan sulfate	6.2	6.8	8.9	12.7	11.6	11.3	11.1

Hypoxia changed the reaction of intracellular elements of neurocytes and glia cells. In the studied preparations, we found significant changes in mitochondria. They differed in their shape, volume, the mitochondrial matrix composition, and the inner membrane composition.

Hypoxias contributed to functional overstrain of mitochondria as energy-generating elements of the cell, what was manifested by lighter color of their matrix, a fuzzy structure of the inner membrane. Experimental simulation of hypoxia in rats revealed that morphological and functional restructuring of cerebellar nerve cells were observed as early as in the first twelve to twenty-four hours. Neurocytes located in the granulose layer differed in their shape, size, and staining intensity. Among these neurons, there were intensively stained, “light” stained cells, and intermediate forms.

In addition, similar phenomena were observed among the nerve cells of the ganglion layer-Purkinje cells. Inhomogeneous staining of the cerebellar tissue was found in the study of various levels of structural and functional organization of the cerebellar tissue-both at the light-optical and electron microscopic levels.

Cerebellar neurocytes forming the ganglion layer were quite well stained and swelled. In histological preparations, this was manifested as lighter areas around the cells. These cells contained well-stained nuclei; in some of them, nucleoli were present. Similar changes were observed in granulose layer neurons. Electron microscopic studies of the cerebellar tissue showed that glia cells’ swelling was weakly expressed in comparison with adjacent neurons.

These nerve cells had an oval or oblong shape and an increased volume as compared to earlier periods of the experiment. In histological preparations, neurocytes processes were poorly stained and hardly distinguishable. In electron micrographs, neurocytes were detected that had nuclei with sufficiently good osmiophilism. In the nuclei of some nerve cells, nucleoli were intensely stained, as compared with nucleoplasm, i.e. they were highly osmiophil.

The nucleoplasm contained heterochromatin in the form of clumps located on the nucleus periphery. The nuclear pores were open. In the space between the inner and outer nuclear membranes, we could see subtle, fine-grained, and finely fibrillar material of an uneven electron density. Intracellular membrane structures were well expressed in these nerve cells. Clear contours were characteristic of cytoplasmic elements such as the Golgi complex, the endoplasmic reticulum, and mitochondria. In the clearance between the Golgi complex and the endoplasmic reticulum, there was a finely granular and finely fibrillar material. In this time interval, mitochondria were quite large, with a destroyed inner membrane, which was presented in the form of fragments (Fig. 5).

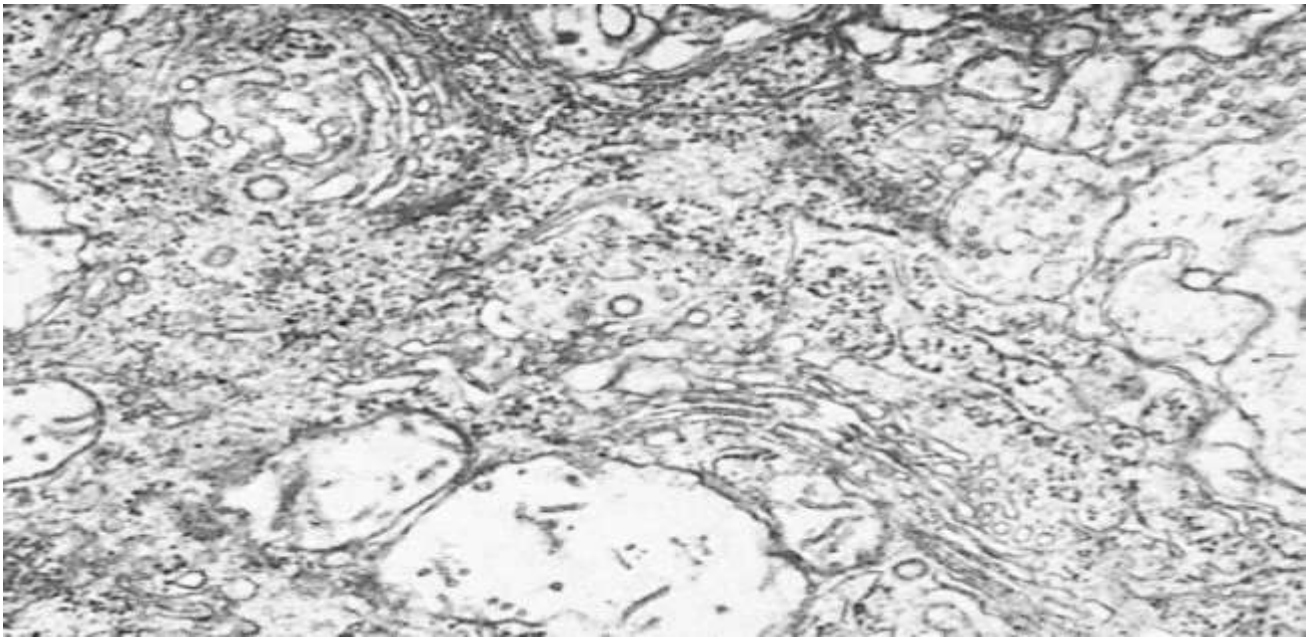

Figure 5: Cerebellar neuron under hypoxia. An experiment period – 12 hours. Activity of intracellular elements. Proliferation of the Golgi complex, enlarged bordered vesicles, swollen and disrupted mitochondria. Enlarged 45000 times

At this stage of the experiment, cells with oval or bean-shaped nucleus prevailed among cerebellar neurocytes. The nerve cell nucleus membrane had many invaginations in the form of depressions and protrusions. Histochemical studies that were used to identify the glycosaminoglycans location in cells, the glycocalyx, and the intercellular matrix, allowed us to identify their uneven distribution. At this stage of experimental research, neurons hardly absorbed dyes, what was manifested in their pale staining.

The cell contours were blurry; this indicated an increasing generation of intermediate products by both neurocytes and glia cells. In addition, cells swelled and reduced their functional activity. By the end of 24 hours, after simulating experimental (hypobaric) hypoxia, edema signs persisted in rat cerebellar tissue, judging by the lighter areas around neurocytes and microvasculature blood vessels. These phenomena could be observed when staining preparations with hematoxylin-eosin and when staining them with dye to detect glycosaminoglycans. Light-optical methods revealed the microvasculature blood vessels hyperemia in the cerebellar tissue of the experimental group animals. The venular link vessels had a larger diameter, as compared with arterioles, approximately 2.5 to 3 times. It should be noted that these blood supply processes were irregular; there were areas with extensions and contractions.

Uneven lighter areas were observed around these vessels. In ultrastructural examination of cerebellar tissues, a high content of pinocytotic vesicles in endothelial cells was

found. The cytoplasmic matrix of these cells had a lighter staining and lower osmiophilism. Blood capillaries had uneven lumen; inside them, deformed blood corpuscles were observed. In this time period of the experiment, histochemical studies revealed a more intense staining of cerebellar tissue. Around neurocytes and their processes, intense staining was observed, which indicated an increase in the content of different classes of glycosaminoglycans in these areas (Fig. 6).

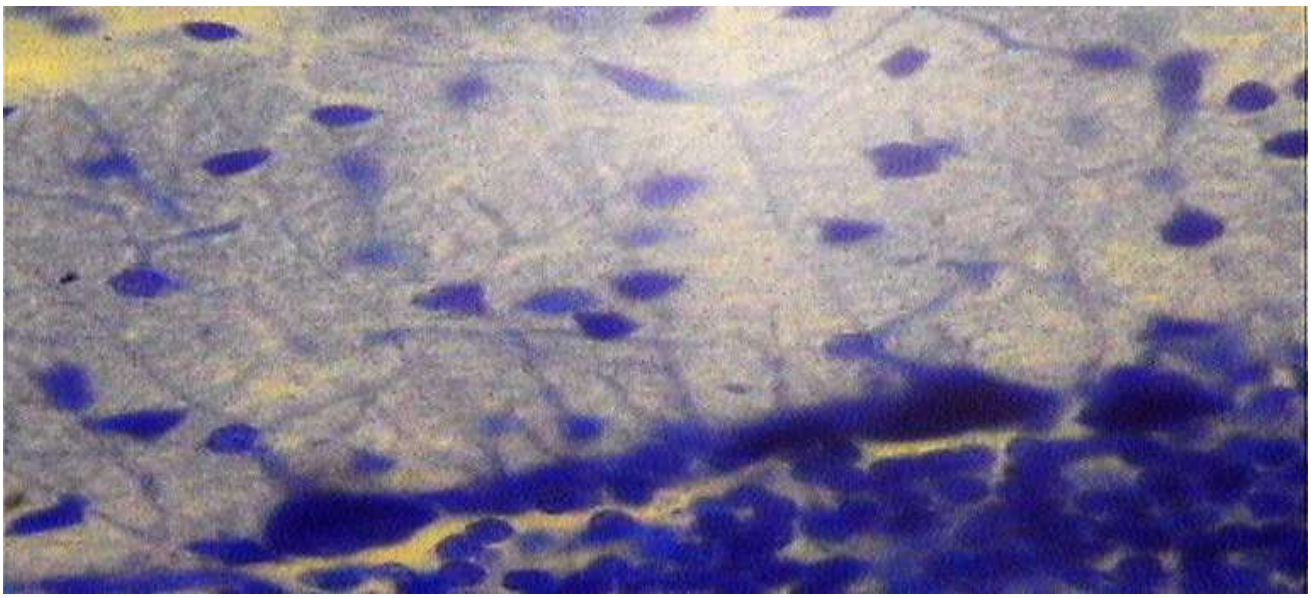

Figure 6: Rat cerebellum under hypoxia. An experiment period-24 hours. Granular, ganglionic, molecular layers. Staining with methylene blue Lens 10

In this period, electron-microscopic studies allowed to determine the features of morphological and functional changes occurring in neurons and glia cells. Hypoxia, acting as a stressor on cerebellar tissue, promoted the activation of compensatory and adaptive processes. These processes were manifested by the formation of numerous vesicles next to the Golgi complex. Inside these structures, an osmiophil material was found that had a fine-grained or flaky appearance. Note the relative hypertrophy of the Golgi complex.

The study of preparations revealed that the granular endoplasmic reticulum was presented in the form of oblong or oval fragments with a larger number of fixed ribosomes on its membrane. As compared to the surrounding endoplasmic matrix, the granular endoplasmic reticulum tubules had a higher electron density. In the immediate vicinity, there were “tomentose” vesicles that also had a high electron density.

The cytoplasm of both neurocytes and glia cells contained many ribosomes, both isolated and in groups or polysomes of different sizes. They occurred freely in the cytoplasm or were fixed on endoplasmic reticulum membranes. When researching Purkinje cells in this time interval, we found fragments of both granulose and non-granulose endoplasmic reticulum. In the endoplasmic reticulum tubule lumen, a fine-grained material of increased electron density was found. The studied preparations showed a more intense staining of the neuronal hyaloplasm as compared to the nucleoplasm.

This was also characteristic of glia cells. Vesicles were detected in neurocyte cells and glia cells; they were represented by fringed and smooth-contoured forms. They were also different in size and composition. The ultra structure study revealed that mitochondria had an elongated shape of varying length in this period. They were located unevenly in the cell cytoplasm. In addition, we observed mitochondria arranged in groups at the base of the processes, in the area of the spine apparatus.

Some of these energy-generating apparatuses were found near the endoplasmic reticulum tubules, both granulose and non-granulose ones. At the same time, it should be noted that the inner mitochondrial membrane had quite pronounced contours and well-defined cristae; the matrix featured a high electron density. Microtubules and microfilaments in nerve cells were found in small quantities;

they were mainly observed in the processes and on the cell periphery. At this stage of the study, single lysosomes were found in the cell cytoplasm, which are usually found near the Golgi complex.

Morphological studies within the range of 24 to 72 hours after the simulated hypoxia showed a change in the granular cell activity, which were detected between Purkinje cells in this period. In isolated cases, these cells were also found in the molecular layer. The neurons that form the ganglion layer of the cerebellar cortex featured heterogeneous staining and acquired a mosaic appearance, which indicated a heterogeneous functional condition of these cells.

It should also be noted that part of the nerve cells of this area showed the signs of apoptosis, whereas other cells show autolysis. These processes are found not only in the cells themselves, but also in the surrounding intercellular matrix. In the cerebellar tissue of the experimental group animals, we revealed not only a change in the composition of the intercellular substance, but also a reduction in the number of Purkinje cells, which subsequently entailed an increase in the granular cells migration activity and their penetration into the molecular layer. At this stage of the experimental activity, the microvasculature vessels were marked by hyperemia and dilatation processes from their vascular wall.

Endothelial cells that covered the capillary lumen were located on the basal, wavy-shaped membrane. In addition, the endotheliocyte cytoplasm featured a high content of pinocytotic vesicles. Hypoxia has a significant effect on cerebellar tissue; the result is restructuring of the functionality of all cellular elements. Under hypoxia, both compensatory and adaptive mechanisms are activated, which help restore cell activity in the new altered conditions. By the end of 168 hours of the hypoxia simulation experiment, functional activity increased in the cerebellar tissue (Fig. 7).

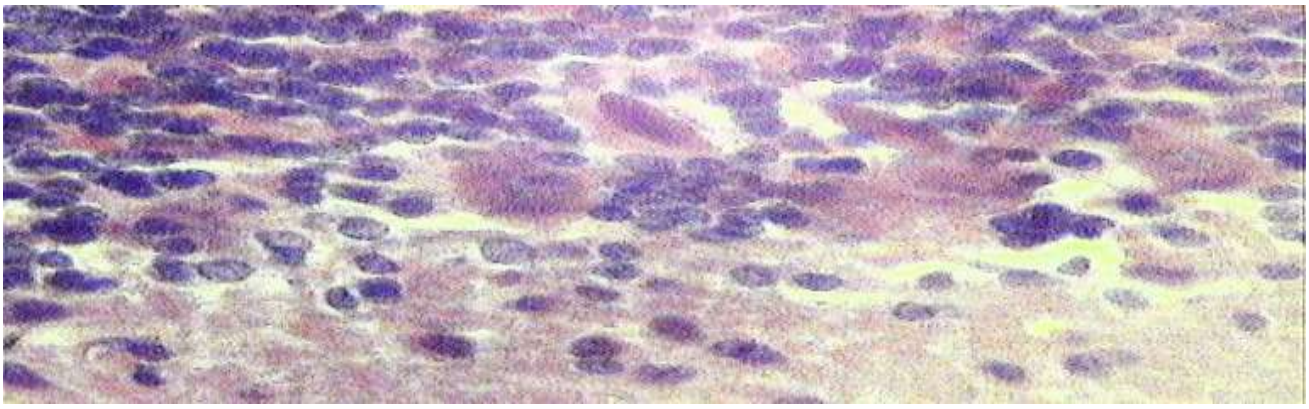

Figure 7: Rat cerebellum under hypoxia. An experiment period – 168 hours. Granular, ganglionic, molecular layers. Staining with hematoxylin-eosin. Lens 10

We associate these changes with an increase in the enzymatic activity of glia cells, restructuring and re-composition of the intercellular matrix, a change in the composition and ratio of different classes of glycosaminoglycans (Fig. 8).

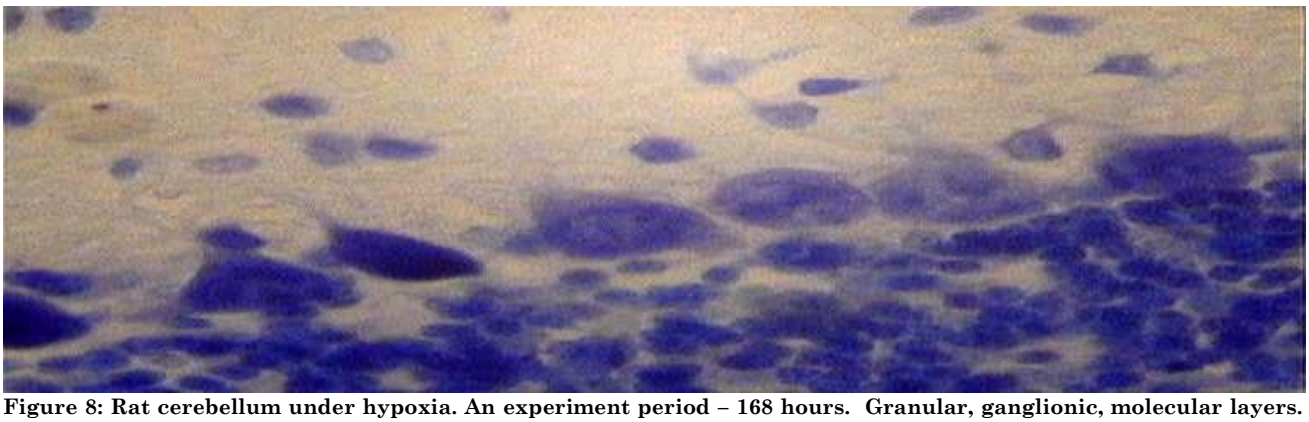

Figure 8: Rat cerebellum under hypoxia. An experiment period – 168 hours. Granular, ganglionic, molecular layers. Staining with methylene blue. Lens 10

The cytoplasm of both neurons and glia cells showed a decrease in the tigroid substance content. This was manifested in a decreased osmiophilism of the endoplasmic reticulum, the Golgi complex, and various vesicles. The content of cytogranules decreased in the cytoplasm, which acquired a relatively weak staining. Cell nuclei contain heterochromatin, which was relatively evenly distributed in the nucleoplasm. The nuclear membrane was quite well contoured with nuclear pores observed therein. Grain and Purkinje cells contained lysosomes varying in size, shape, and their matrix nature. The number of these structural elements in cells varied significantly. Among these lysosomes there were structures, such as autophagic vacuoles, which contained fragments of mitochondrial cristae and myelin-like figures. Lysosomes were located in different areas of the cytoplasm; they could be located near mitochondria, near the Golgi complex, etc. In these areas, there was a decrease in osmiophilism. Neurofibrils in the form of thin protofibrils were found in the neuron cytoplasm. Between them, homogenization areas were observed. Mitochondria in the neuron cytoplasm differed in shape, size, and the matrix condition. Among these mitochondria, forms with moderate matrix swelling persisted, this was manifested by contours blurring and a decrease in staining (Fig. 9).

Figure 9: Rat cerebellum under hypoxia. An experiment period – 168 hours. Purkinje cell. Swollen and disrupted mitochondria. Edema and destruction of cristae, osmiophilic formations. Enlarged 45000 times

In this period, cerebellar neuron cells were characterized by an increased content of large and branched mitochondria. Ribosomes in this period were heterogeneous in structure and composition. Ribosomes freely located in the cytoplasm were grouped in the form of polysomes of different sizes, shapes, and electron densities. Other ribosomes were attached to the endoplasmic reticulum tubule membranes. At this stage of the experiment, the endoplasmic reticulum was quite well expressed and increased in volume. The endoplasmic reticulum tubules along their length were crimped, with an uneven lumen. In the lumen of these tubules, a pronounced material was observed, having a medium electron density.

Conclusions

Using a set of histological, histochemical, and electron microscopic research methods revealed the features of compensatory and adaptive changes in cerebellar tissues under the action of a stressor such as hypoxia. Simulation of hypoxia led to a change in the cerebellar neurons ultrastructure and composition. We observed a decreased osmiophilism of cell membranes and the glycocalyx content. At the same time, there was a decrease in the content of ribosomes on the endoplasmic reticulum membranes. In the endoplasmic reticulum itself, matrix enlightenment was observed, what was detected at different time periods of the experiment.

During the experiment, compensatory-adaptive features were observed in rat cerebellar tissues under hypoxia, which were characterized at the early stages by a significant increase in the volume of intracellular structures (mitochondria, Golgi complex, endoplasmic reticulum by 12.9 %, 18.7 %, and 23.4 %, respectively, with $p < 0.05$).With prolonged action of hypobaric hypoxia, a decrease in the intracellular

structures volume was observed (mitochondria, Golgi complex, endoplasmic reticulum by 8.9 %, 17.1 %, and 19,3 %, respectively, with $p < 0.05$). It should also be noted that, during the experiment, there were changes in the content of glycosaminoglycans and the ratio of sulfated and non-sulfated forms, which indicated the activation degree of compensatory-adaptive processes in the cerebellar tissues. In some preparations, apoptosis was reported, which was manifested in fewer nerve cells. At the same time, there were changes not only in neurocytes, but also in the surrounding pericellular space. Under these conditions, we observed the neuron migration from one layer to another. However, neurocytes and glia cerebellum cells under hypobaric hypoxia retained relatively high morphological and functional activity, which allowed them to activate compensatory and adaptive mechanisms .These cell elements, which are closely interconnected, start functioning in new conditions, maintaining a sufficiently high plastic activity. Cerebellar neurons, together with glia cells, started compensatory and adaptive processes in the first three days; then, both degeneration and activated physiological regeneration processes were observed in these cells. The paper shows that, even under the action of hypoxia, the cerebellum, as a highly organized and specialized structure, activates a set of protective mechanisms aimed at preserving its specialized functional activity.

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