DOI 10.26724/2079-8334-2025-4-94-167-172
UDC 614.876:616-055.6:577.122:616-092.4

R.S. Vastyanov, K.O. Talalayev, I.O. Ostapenko, O.A. Hruzevskiy, V.V. Babienko, O.I. Yatsyna[1]
Odesa National Medical University, Odesa, [1]National Cancer Institute, Kyiv

INTRACELLULAR ENERGY DEFICIT AND CONNECTIVE TISSUE BREAKDOWN AS THE LEADING PATHOPHYSIOLOGICAL MECHANISM OF POSTRADIATION ENERGY-MATRIX DYSINTEGRATION

e-mail: rvastyanov@gmail.com

The purpose of the study was to investigate the pathogenetic significance of the correlation between disturbances in the energy balance of connective and muscle tissue cells and changes in collagenolysis after γ-irradiation. Male sexually mature Wistar rats were exposed to ionizing radiation at doses of 1.0 Gy and 4.0 Gy. The content of total oxyproline and its fractions, total glycosaminoglycans, adenyl nucleotides, and alanine- and aspartate aminotransferase activity were determined in animals' skin, blood, skeletal, and cardiac muscles. The data obtained indicated activation of collagen breakdown and structural destabilization of the matrix in response to γ-radiation. Both alanine- and aspartate aminotransferase activities decreased in muscle tissue, paralleled by decreased blood levels in these conditions, indicating membrane damage and enzyme release into the extracellular space. The post-radiation decrease in ATP concentration and the accumulation of ADP and AMP in cardiac and skeletal muscles outline the cellular energy deficit. The authors declare that γ-radiation initiates a complex, dose-dependent set of changes in the "energy metabolism – extracellular matrix" system, manifested by simultaneous disruption of collagen and mitochondrial metabolism, interpreted as post-radiation energy-matrix disintegration and considered a universal mechanism. The data obtained confirm the reasonability of the integral index of energy-matrix condition creation for early diagnosis of radiation-induced tissue damage.

Key words: ionizing radiation, connective tissue, skeletal muscle, cardiac muscle, oxyproline, glycosaminoglycans, alanine aminotransferase, aspartate aminotransferase, adenyl nucleotides, pathogenetic mechanisms.

Р.С. Вастьянов, К.О. Талалаєв, І.О. Остапенко, О.А. Грузевський, В.В. Бабієнко, О.І. Яцина

РОЗВИТОК ВНУТРІШНЬОКЛІТИННОГО ЕНЕРГЕТИЧНОГО ДЕФІЦИТУ ТА РОЗПАД СПОЛУЧНОЇ ТКАНИНИ ЯК ПРОВІДНИЙ ПАТОФІЗІОЛОГІЧНИЙ МЕХАНІЗМ ПОСТПРОМЕНЕВОЇ ЕНЕРГЕТИКО-МАТРИЧНОЇ ДЕЗІНТЕГРАЦІЇ

Метою дослідження було визначення патогенетичної важливості взаємозв'язку порушення енергетичного балансу клітин сполучної та м'язової тканин та змін процесів колагенолізу після γ-опромінення. Експеримент проведено на статевозрілих щурах після γ-опромінювання дозами 1.0 та 4.0 Гр. У шкірі, в скелетному і серцевому м'язах і у крові тварин визначали вміст загального оксипроліну та його фракцій, загальних глікозаміногліканів, аденілових нуклеотидів, активність аланін- та аспартатамінотрансферази. Отримані дані свідчать, що γ-опромінення спричиняє активацію процесів руйнування колагену та структурну дестабілізацію матриксу. Зниження активності аланін- та аспартатамінотрансферази у м'язових тканинах при підвищенні їх рівня в крові за вказаних умов свідчить про мембранне пошкодження й вихід ферментів у позаклітинний простір. Пострадіаційне зменшення концентрації АТФ і накопичення АДФ та АМФ у серцевому та скелетному м'язах висвітлює формування енергетичного дефіциту клітин. Автори стверджують, що вплив γ-опромінення ініціює комплекс дозозалежних змін у системі «енергетичний обмін – позаклітинний матрикс» що визначається як постпроменева енергетико-матрична дезінтеграція і розглядається в якості універсального механізму пошкодження тканин при іонізуючому впливі. Отримані результати обгрунтовують доцільність створення інтегрального показника енерго-матричного стану, який може бути використаний для ранньої діагностики ступеня тканинного ушкодження при радіаційному впливі.

Ключові слова: іонізуюче опромінення, сполучна тканина, скелетний м'яз, серцевий м'яз, оксипролін, глікозаміноглікани, аланінамінотрансфераза, аспартатамінотрансфераза, аденілові нуклеотиди, патогенетичні механізми.

The study is a fragment of the research project "Mechanisms of epigenetic disorders of the leading links of bioenergetics and nitrogen metabolism in irradiated animals and their descendants", state registration No. 0121U114601.

Ionizing radiation is a decisive exogenous factor that disrupts the structural and metabolic integrity of body tissues and induces complex changes in the energetic, signalling, and matrix systems [4, 13, 15]. Cells after irradiation initiate a complex cascade of pathophysiological reactions, including oxidative stress, cytokine and growth factor responses, excessive collagen synthesis, activation of transforming growth factor β and SMAD-dependent pathways, leading to excessive collagen synthesis of types I and III and fibrosis development [8, 10, 15]. These processes are accompanied by changes in mechanical properties, increased matrix rigidity, failure of cell-matrix interactions, and stable post-radiation dysfunction [6].

Hyaluronic acid (HA), a key glycosaminoglycan that regulates hydration, metabolite diffusion, and cell signalling, plays a special role in the early and delayed phases of radiation-induced cell damage [14]. Low-molecular-weight hyaluronic acid fragments after irradiation are well known to accumulate together with hyaluronidases and metalloproteinases (of the 2nd and 9th types), leading to their activation and the initiation and intensification of an inflammatory microenvironment, resulting in collagen structural degradation and fibrosis progression [1, 14]. A staged reorganization of energy metabolism occurs simultaneously in non-epithelial tissues.

Glycolysis and oxidative phosphorylation are activated, and ATP production increases in the early stages of radiation exposure, demonstrating the cellular adaptive response. The postponed period is characterized by hypoxia, decreased mitochondrial respiratory reserve, increased mitochondrial acidification, reduced ATP production, and mitochondrial morphological disturbances; therefore, one could observe signs of energy depletion and oxidative damage [2, 13].

These changes in energy homeostasis are accompanied by activation of transamination enzymes (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) and accumulation of intermediate metabolites, reflecting a catabolic reorientation of cellular metabolism. Taken together, this leads to an energy-matrix imbalance, in which extracellular matrix degradation is combined with a decline in cellular energy potential. The integrated analysis of collagen metabolism markers (hydroxyproline, glycosaminoglycan) and energy status markers (ATP, ADP, and AMP content, ALT/AST activity) enables the identification of early, dose-dependent biomarkers of tissue destabilization after irradiation [6, 8].

The purpose of the study was to investigate the pathogenetic significance of the correlation between disturbances in the energy balance of connective and muscle tissue cells and changes in collagenolysis after γ-irradiation. Developing an integral index of the energy-matrix state in the post-radiation period was an additional task of the experimental study.

Materials and methods. The studies were conducted on 30 male Wistar rats aged 6 months, weighing 190–250 g, maintained at a constant temperature of 23 °C and 60 % relative humidity on a 12-hour light/dark cycle. Male rats were chosen to avoid the endocrine influences typical of females on ionizing radiation. The animals underwent a seven-day adaptation period before the start of the trials. Rats were housed in plastic cages with metal mesh lids, six animals per cage, with free behaviour and free access to food and water. Wood shavings were used as bedding, which was changed at least once every 48 hrs. The cages were not equipped with any additional materials. The basic requirements of the International Animal Research Reporting Protocols ARRIVE 2.0 were used in these experimental trials.

The maintenance, handling and manipulation of animals were carried out in accordance with the "General Ethical Principles of Animal Experiments" approved by the Fifth National Congress on Bioethics (Kyiv, 2013), while being guided by the recommendations of the European Convention for the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes (Strasbourg, 1985), the methodological recommendations of the State Clinical Research Center of the Ministry of Health of Ukraine "Preclinical Studies of Drugs" (2001) and the rules for the humane treatment of experimental animals and conditions approved by the Bioethics Commission of Odesa National Medical University (No 19, September 14, 2023).

For the experiment, sexually mature animals were subjected to total single-time gamma irradiation with ^{60}Co in special chambers made of organic glass, in the morning on an empty stomach on the "Agat" telegammatherapy device. The distance to the absorption source was 75 cm, and the dose rate was 0.54 Gy/min. The animals were randomized as follows: group 1 – intact rats; group 2 – rats with the absorbed dose of 1.0 Gy; group 3 – rats with the absorbed dose of 4.0 Gy. There were 10 animals in each group.

1 rat in each group (2 and 3) died after exposure to ionizing radiation; however, there were 10 animals in each group in the final analysis, and mortality was not accounted for in the statistical analysis.

For biochemical studies, the animals were removed from the experiment by euthanasia under propofol (iv, 60 mg/kg) anesthesia. After the animals were dissected, blood from the tail vein was collected and centrifuged at 3000 rpm for 10 min to obtain serum.

To determine biochemical parameters in tissues, the liver, heart, and anterior thigh muscle group were removed, washed with chilled saline, ground, and homogenized in a 9–fold volume of 0.32 mol sucrose in 0.05 mol Tris buffer, pH=7.36, in a homogenizer with Teflon surfaces and subjected to differential centrifugation.

To determine biochemical parameters in the tissues, the skin, heart, and the fronto-thigh muscle group were removed. Skin samples with the long side along the back were cleaned of subcutaneous fat and hair. Tissue samples were immersed in liquid nitrogen and ground into a powder. Our attention was focused on determining the content of total oxyproline and its fractions, total glycosaminoglycans, ALT, AST, and adenyl nucleotides.

Serum level of total, free, and bound oxyproline was determined by a modified spectrophotometric method (spectrophotometer V-1200, spectral range 325–1000 nm, spectral bandwidth 4 nm, "Shanghai Mapada Instruments Co., Ltd", China) [9]. Oxyproline calibration solutions were prepared using Pierce reagents (Netherlands). Results were expressed in mg/day for urine and in μmol/l for serum.

The quantitative content of glycosaminoglycans was determined after enzymatic hydrolysis using Clostridium histolyticum collagenase (600 units). The results were expressed as μmol of HA per 1 mg of tissue, using HA as a standard to create a calibration curve [12].

Both ALT and AST activity in tissues and blood serum, as well as the determination of adenine nucleotide (ATP, ADP, AMP) content, were performed spectrophotometrically [3]. The activity of ALT and AST in tissues is expressed in μmol of pyruvate/g•hr, in blood in μmol of pyruvate/l•hr.

The power analysis conducted before the start of the experimental trial allowed for determining a sufficient sample size for adequate statistics and convincing results. Statistical analysis of the results was conducted, accounting for the sample distribution. Normality of distribution was tested using the Shapiro-Wilk test. The parametric one-way ANOVA was used to compare groups when the data were normally distributed. The nonparametric Mann-Whitney test was used if the distribution deviated from normality. The minimum statistical probability was determined at $p<0.05$.

Results of the study and their discussion. Significant dose-dependent changes in connective tissue metabolism indices were detected after exposure to ionizing radiation. The total content of oxyproline in intact animals' blood serum was equal to 121.4±6.15 μmol/l (Table 1). This index shows a moderate increase after irradiation with 1.0 Gy, indicating activation of collagenolysis and mobilization of the amino acid pool. After irradiation at 4.0 Gy, this index decreased to 114.6±5.81 μmol/l, indicating exhaustion of the collagen reserve and suppression of fibroblast synthetic activity due to matrix damage.

Table 1

Blood hydroxyproline and skin glycosaminoglycans content in intact and sexually mature animals irradiated by different doses (M±m)

Investigated indexes	Tissues	Groups of animals (n=30)		
		Group 1	Group 2	Group 3
Total oxyproline, μmol/l	Blood	121.44±6.15	132.43±6.52	114.64±5.81
Free oxyproline, μmol/l	Blood	12.11±0.36*	14.51±0.68*#	17.22±0.82*##
Bound oxyproline, μmol/l	Blood	112.34±5.36	117.92±5.86	95.42±4.15#
Glycosaminoglycans, μmol/g	Skin	463.18±28.10	476.78± 28.50	559.73±29.41#

Notes: * – p<0.001 – statistical differences of the investigated indexes compared with the corresponding indexes of total oxyproline; # – p<0.05; ## – p<0.01 – statistical differences of the investigated indexes compared with the corresponding indicators in intact animals.

The free fraction of oxyproline showed a clear dose-dependent increase up to 14.5±0.68 μmol/l ($p<0.05$) and 17.0±0.82 μmol/l ($p<0.01$) after irradiation with 1.0 Gy and 4.0 Gy, respectively. The bound oxyproline content in animals irradiated by a dose of 1.0 Gy increased slightly, but after irradiation with a dose of 4.0 Gy, it decreased by 15.3 % when compared with the analogous control indicator ($p<0.05$).

An increase in glycosaminoglycan content was observed in the skin, and only after irradiation with the maximum dose did the studied index turn out to be significantly (by 20.8 %) higher than in intact rats ($p<0.05$).

ALT and AST activity in muscle tissue of intact animals indicated a stable level of reamination necessary for maintaining energy homeostasis. A moderate decrease in both enzymes' intramuscle activity with a slight increase in the blood was observed after irradiation with a dose of 1.0 Gy, which had an adaptive nature. A significant ALT (by 2.2 times) and AST (by 1.4 times; in both cases $p<0.05$) activity inhibition in cardiac muscle was observed at a higher irradiation dose of 4.0 Gy (Table 2).

Table 2

ALT, AST, and nucleotide content in tissues of intact and sexually mature animals irradiated by different doses (M±m)

Investigated indexes	Tissues	Groups of animals (n=30)		
		Intact animals	Irradiated at a dose of 1.0 Gy	Irradiated at a dose of 4.0 Gy
ALT	Cardiac muscle	8.12±0.71	6.35±0.42	3.62±0.21*
AST		11.03±0.98	9.25±0.73	7.96±0.69*
ATP, μmol/g		5.312±0.483	4.368±0.351	3.022±0.260*
ADP, μmol/g		0.282±0.043	0.341±0.049	0.186±0.016
AMP, μmol/g		0.163±0.026	0.189±0.029	0.474±0.042**
ALT	Skeletal muscle	8.11±0.64	6.94±0.51	7.12±0.48
AST		10.23±0.92	8.41±0.67	9.04±0.71
ATP, μmol/g		3.234±0.276	2.742±0.243	1.658±0.154**
ADP, μmol/g		0.463±0.054	0.518±0.058	0.356±0.032
AMP, μmol/g		0.289±0.032	0.324±0.038	0.765±0.064**
ALT	Blood	3.14±0.31	3.46±0.37	5.97±0.42*
AST		3.42±0.39	3.97±0.46	4.98±0.35*

* – p<0.05 and ** – p<0.01 – statistical differences of the investigated indexes compared with the corresponding indicators in intact animals.

Similar, but less expressed, changes were observed in skeletal muscle. In addition, a significant increase in blood transaminase activity was observed compared with intact animals, suggesting a disturbance in plasma membrane permeability.

The ATP content was significantly reduced in cardiac muscle of intact animals only after irradiation by a dose of 4.0 Gy (by 1.8 times; $p<0.05$). A gradual ADP and AMP concentration was recorded, also accompanied by the ATP/ADP ratio. Similar trends were also observed in skeletal muscle, where the decrease in ATP content was accompanied by ADP and AMP accumulation, indicating a disturbance in mitochondrial phosphorylation capacity.

Thus, the data obtained allow us to state that γ-radiation initiates a complex dose-dependent set of changes in the system "energy metabolism-extracellular matrix," manifested by simultaneous alterations in collagen and mitochondrial metabolism. Among all the data received for further discussion, we consider it appropriate to outline the following three positions.

Firstly, the established free hydroxyproline and glycosaminoglycan levels increase, coupled with a decrease in the bound hydroxyproline fraction, indicating collagen destruction, collagen fiber degradation, and the release of their breakdown products into the blood, a characteristic sign of ionizing irradiation. The dynamics of bound hydroxyproline levels indicate the presence of mature collagen fibers and the loss of connective tissue structural integrity. Glycosaminoglycan levels are expected to be associated with hyaluronate-dependent hyperhydration and compensatory remodeling of the extracellular matrix aimed at osmotic and colloidal homeostasis after collagen framework damage. The detected changes indicate a disruption in the balance between the processes of connective tissue component synthesis and degradation. One could see adaptive-reparative reactions prevail at moderate radiation exposure (1.0 Gy), whereas at higher doses, a catabolic type of remodeling develops, reflecting matrix structural-metabolic destabilization and the background for fibrogenesis.

Secondly, the ALT and AST activities decrease in muscle tissue, with their levels increasing in blood after ionizing radiation, indicating membrane damage and the release of these enzymes into the extracellular space. We are confident that the opposite trends in compatibility – ALT/AST activity decreasing in tissues while increasing in serum – highlight the disconnection of tissue energy metabolism and are a systemic marker of damage. Intratissue transamination suppression indicates a catabolic shift and energy deficiency, while elevated serum transaminases indicate structural damage and disrupted membrane integrity. All together, these data confirm the formation of post-radiation energy-matrix disintegration.

The third, the post-radiation decrease in ATP concentration and the accumulation of ADP and AMP in cardiac and skeletal muscles, outlines the process of cellular energy deficiency, which is consistent with protein catabolic restructuring. Such energy balance shifts, a marker of intracellular energy deficiency, occur in parallel with suppression of transaminase activity and activation of catabolic processes.

ATP levels decrease concomitantly with increases in GAG and oxyproline, demonstrating the unity of energy and matrix mechanisms in the pathogenesis of post-radiation remodeling. These changes result in energy-matrix discoordination, a universal mechanism of tissue damage during ionizing radiation.

The revealed correlations among adenine nucleotide levels, transaminase activity, and markers of collagen metabolism indicate a close functional relationship between the energetic and matrix mechanisms of organisms' adaptation to radiation [11], which also included modulation of specific neurotransmitter systems [3].

To perform a comprehensive analysis of the data obtained, we suspected that the scientific investigation of radiation-induced connective tissues in both experimental and clinical settings was limited. With this aim, we provided literature searches with PubMed from January 2000 to December 2024 using the keywords "radiation", "ionizing radiation", "gamma irradiation", "ultraviolet radiation", "visible light", "skin', "muscle tissue", connective tissue", and "pathogenesis". The search was limited to English, Italian, and Spanish language articles. Articles were selected depending on their relevance.

The data we found indicated that specialists' attention, in the majority of cases, was limited to visible epidermal damage in response to both ultraviolet and visible high-energy radiation exposure. Possible muscle activity pathologies were ignored in these conditions. It's worth noting that intensive pathobiochemical studies focused on bone pathology following γ-irradiation [4]. Moreover, data similar to our results, showing increased muscle tissue catabolism, were obtained in experimental conditions in response to low-dose ionizing radiation [11].

After a particularly high-energy visible light impact, as well as in combination with infrared radiation, reactive oxygen species are generated, matrix metalloproteinases are expressed, collagen degradation is increased, and even DNA molecules are damaged in the upper layers of the skin, especially in keratinocytes [7]. These data are generally consistent with ours and emphasize the leading pathogenic role of inflammation, with pathobiochemical catabolic reactions strengthening and ultimately leading to subsequent cellular death in response to ionizing radiation.

Studies have reported increased matrix metalloproteinase-1 activity in fibroblasts, which mediates collagen synthesis under normal conditions and serves as a marker of cellular death following γ-irradiation [7].

The increase in expression of proteins associated with apoptosis, the increase in mast cell numbers, the increase in tryptase expression, the increase in reactive oxygen species and heat shock proteins, together with a decrease in type I procollagen synthesis, are also considered markers of radiation-induced tissue damage [5]. It should be noted that the data available in the scientific literature are consistent with our results and indicate a complex cascade of interrelated pathophysiological reactions, whose consequences include an inflammatory response, restructuring of biochemical metabolism, energy deficiency, and cell death via necrosis and/or apoptosis.

To resume, we note that damage from ionizing radiation causes post-radiation energy-matrix disintegration, characterized by energy resource depletion, enhanced connective tissue degradation, and loss of metabolic coordination between tissue systems. The sequence of pathophysiological mechanisms is a universal mechanism of tissue damage induced by ionizing radiation. The proposed approach to simultaneous evaluation of energy and collagen indexes can serve as the basis for an integrated energy-matrix condition appropriate for early diagnosis of radiation-induced tissue damage.

Conclusions

1. Free hydroxyproline and glycosaminoglycan content increase, combined with the bound hydroxyproline level decrease, indicate the collagen breakdown activation and structural destabilization of the matrix in response to γ-radiation.

2. Both alanine aminotransferase and aspartate aminotransferase activity decrease in muscle tissue, coupled with their blood levels in response to ionizing radiation, indicating membrane damage and enzyme release into the extracellular space.

3. The post-radiation ATP concentration decrease and both ADP and AMP accumulation in cardiac and skeletal muscles outline the cellular energy deficit.

4. The influence of γ-radiation initiates a complex of dose-dependent changes in the "energy metabolism – extracellular matrix" system manifested by collagen and mitochondrial metabolism, simultaneous disruption, which we interpret as post-radiation energy-matrix disintegration and consider to be a tissue damage universal mechanism.

5. Such an approach to energy and collagen index simultaneous evaluation can serve as the basis for integrated energy-matrix condition creation appropriate for radiation-induced tissue damage early diagnosis.

Prospects for further research include additional studies to establish the prognostic efficacy of connective tissue metabolism dysregulation markers for evaluating possible systemic dysfunctions following ionizing radiation exposure.

References

1. Averbeck D, Rodriguez-Lafrasse C. Role of Mitochondria in Radiation Responses: Epigenetic, Metabolic, and Signaling Impacts. Int J Mol Sci. 2021; 22(20): 11047. doi: 10.3390/ijms222011047.

2. Buss LG, Rheinheimer BA, Limesand KH. Radiation-induced changes in energy metabolism result in mitochondrial dysfunction in salivary glands. Sci Rep. 2024; 14: 845. doi:10.1038/s41598-023-50877-9.

3. Dimov AO, Stepanov GF. Pathophysiological mechanisms of nitrogen metabolism dysregulation under the influence of ionizing radiation. World of Medicine and Biology. 2025; 2(92): 169–173. doi: 10.26724/2079-8334-2025-2-92-169-173.

4. Donaubauer A-J, Deloch L, Becker I, Fietkau R, Frey B, Gaipl US. The influence of radiation on bone and bone cells—differential effects on osteoclasts and osteoblasts. Int J Mol Sci. 2020; 21(17): 6377.

5. König A, Zöller N, Kippenberger S, Bernd A, Kaufmann R, Layer PG. et al; Non-thermal near-infrared exposure photobiomodulates cellular responses to ionizing radiation in human full thickness skin models. J Photochem Photobiol B. 2018; 178: 115–123. doi: 10.1016/j.jphotobiol.2017.11.003.

6. Kreuder L, Bissey PA, Yip KW, Liu FF. Exploring radiation-induced fibrosis: biological mechanisms and new frontiers in research and therapeutics. Int J Radiat Biol. 2025: Sep 2: 1–16. doi: 10.1080/09553002.2025.2540353.

7. Lim HW, Kohli I, Ruvolo E, Kolbe L, Hamzavi I. Impact of visible light on skin health: the role of antioxidants and free radical quenchers in skin protection. J Am Acad Dermatol. 2022; 86(3S): 27-37. doi: 10.1016/j.jaad.2021.12.024.

8. Park J, Choi J, Cho I, Sheen YY. Radiotherapy-induced oxidative stress and fibrosis in breast cancer treatment: role of TGF-β and ECM remodelling. Sci Rep. 2022; 12: 16104. doi: 10.1038/s41598-022-20050-9.

9. Pavlov SB, Pavlova GB. Study the role of intercellular mediators in the metabolism of connected tissue in children with cardiomyopathy and osteopeny. Journal of Education, Health and Sport. 2016; 6(9): 902–916. doi: 10.5281/zenodo.163528.

10. Peng D, Fu M, Wang M, Wei Y, Wei X. Targeting TGF-β signal transduction for fibrosis and cancer. Mol Cancer. 2022; 21(1): 104. doi:10.1186/s12943-022-01569-x.ф

11. Stepanov GF, Vastyanov RS. The peculiarities of low-dose ionizing radiation influence on muscles metabolism in experimental animals. World of Medicine and Biology. 2023; 2(84): 233–238. doi: 10.26724/2079-8334-2023-2-84-233-238.

12. Talmoudi N, Ghariani N, Sadok S. Glycosaminoglycans from Co-Products of "Scyliorhinus canicula": Extraction and Purification in Reference to the European Pharmacopoeia Requirement. Biol Proced Online. 2020; 22: 1. doi: 10.1186/s12575-019-0113-1.
13. Wang KX, Ye C, Yang X, Ma P, Yan C, Luo L. New Insights into the Understanding of Mechanisms of Radiation-Induced Heart Disease. Curr Treat Options Oncol. 2023; 24(1): 12–29. doi: 10.1007/s11864-022-01041-4.
14. Wu SY, Chen YT, Tsai GY, Hsu FY, Hwang PA. Protective effect of low-molecular-weight fucoidan on radiation-induced fibrosis: inhibition of TGF-β1/Smad3 and collagen I accumulation. Mar Drugs. 2020; 18(3): 136. doi: 10.3390/md18030136.
15. Zhou L, Zhu J, Liu Y, Zhou PK, Gu Y. Mechanisms of radiation-induced tissue damage and regeneration. MedComm (Berlin). 2024; 5(2): 725. doi:10.1002/mco2.725.

Стаття надійшла 15.10.2024 р.

DOI 10.26724/2079-8334-2025-4-94-172-178
UDC 612.43;612.018;615.252;591.147.4

G.A. Eminova, Yu.B. Ismayilov, T.V.Rustamova[1], Z.Y. Veliyeva, A.M. Jafarova, T.H. Kerimova[2], T.N. Gasimzade[2]
Azerbaijan Medical University, Baku
[1] Ganja State University, Ganja, [2] Odlar Yurdu University, Baku, Azerbaijan

EFFECT OF HYPOTHALAMIC PREOPTIC NUCLEUS ELECTRICAL ACTIVITY CHANGES ON GONADAL HORMONE REGULATION IN NORMAL AND EXTREME STATES

e-mail: mic_amu@mail.ru

With the purpose to examine the changes in the activity of gonadal hormones resulting from the effects of hydrogen sulfide gas and electrode implantation on the preoptic nucleus of the hypothalamus 35 female rabbits were observed. The activity of follicle-stimulating hormone, luteinizing hormone, and estradiol in the blood were evaluated after stress. On the 5th day follicle-stimulating hormone decreased by 0.26 IU/l; luteinizing hormone decreased by 0.18 IU/l, estradiol increased by 207.4 pg/ml ($P<0.001$) from the normal value. In the post-model period, electroencepfalografic waves and hormones do not return to normal levels. On the 30th day of gas exposure, follicle-stimulating hormone, luteinizing hormone, and estradiol decreased significantly ($P<0.001$). Thus, the preoptic nucleus of the hypothalamus has a complex structure that plays a key role in the regulation of the biological functions of the body and occupies an essential place in the endocrine regulation of the pituitary-gonadal system.

Key words: hypothalamus, preoptic nucleus, hormone, hydrogen sulfide, toxic and mechanical stress.

Г.А. Емінова, Ю.Б. Ісмаїлов, Т.В. Рустамова, З.Ю. Велієва, А.М. Джафарова, Т.Х. Керімова, Т.Н. Гасимзаде

ВПЛИВ ЗМІН ЕЛЕКТРИЧНОЇ АКТИВНОСТІ ПРЕОПТИЧНОГО ЯДРА ГІПОТАЛАМУСА НА РЕГУЛЯЦІЮ СТАТЕВИХ ГОРМОНІВ У НОРМІ ТА В ЕКСТРЕМАЛЬНИХ СТАНАХ

З метою вивчення змін активності статевих гормонів, зумовлених впливом сірководню та імплантацією електродів у преоптичне ядро гіпоталамуса, було проведено спостереження за 35 самками кроликів. Після стресу оцінювали активність фолікулостимулюючого гормону, лютеїнізуючого гормону та естрадіолу в крові. На 5-у добу рівень фолікулостимулюючого гормону знизився на 0,26 МО/л, лютеїнізуючого гормону – на 0,18 МО/л, естрадіолу – збільшився на 207,4 пг/мл ($P<0{,}001$) від норми. У постмодельний період електроенцефалограма і рівень гормонів не поверталися до норми. На 30-й день газового впливу рівні фолікулостимулюючого гормону, лютеїнізуючого гормону і естрадіолу достовірно знизилися ($P<0{,}001$). Таким чином, преоптичне ядро гіпоталамуса має складну структуру, відіграє ключову роль у регуляції біологічних функцій організму і займає важливе місце в ендокринній регуляції гіпофізарно-гонадної системи.

Ключові слова: гіпоталамус, преоптичне ядро, гормон, сірководень, токсичний і механічний вплив.

From the perspective of modern directions of neurophysiology and neuroendocrinology, the investigation of the role of the integrative activity of the hypothalamus and the study of the mechanism of interaction between the hypothalamic-pituitary-gonadal system in various functional states of the organism remains one of the most pressing issues for the science of physiology. Thus, in extreme situations, the manifestation of stress reactions occurs with the participation of the integrative centers of the hypothalamus [6]. Since these centers regulate homeostatic processes and adaptive reactions, it is important to study the neurohormonal relationships of the organism in extreme situations of various origins. However, in the modern globalized world, the interaction between the monoaminergic functional activity of the organism and the neuroendocrine system, as well as the neurophysiological mechanisms underlying this relationship, remains insufficiently studied [1, 6, 11].

On the other hand, when harmful environmental substances enter the body in inadequate quantities, they not only cause the development of serious functional disorders, but also have a significant negative