DOI 10.26724/2079-8334-2023-4-86-217-222
UDC 616.831-007.17:616-036.838:616.89-008.454]-092+557.146.1

I.V. Savytskyi, S.M. Frenkel, R.S. Vastyanov[1], O.M. Stoyanov[1], V.V. Dobrovolskyi[1], L.M. Zayats[2], M.R. Vastianov[1]
PIHE "International Academy of Ecology and Medicine", Kyiv
[1]Odessa National Medical University, Odessa
[2]Ivano-Frankivsk National Medical University, Ivano-Frankivsk

CHANGED CONVULSIVE SENSITIVITY OF ANIMALS AFTER MILD BRAIN TRAUMA IN CONDITIONS OF GENERALIZED SEIZURE ACTIVITY

e-mail: rvastyanov@gmail.com

The purpose of the study was to investigate the change in the intensity of acute generalized convulsive reactions induced by convulsants with different mechanisms of convulsive action during the early posttraumatic period of experimental mild brain trauma. 185 rats were randomized into 5 groups according to the type of convulsant with the help of which the acute generalized convulsive reactions were initiated 6, 12, 24 hours and 3 days after mild brain trauma. A change in convulsive sensitivity was registered within 3 days of the posttraumatic period in the brain of rats which is confirmed by seizure threshold decrease. In case of acute convulsions induction by picrotoxin and pentylenetetrazol their intensity was already higher on the 1st day of posttraumatic period. In case of strychnine-, pilocarpine- and kainic-induced acute generalized seizures the expressed differences were reached on the 3rd day after brain trauma. Convulsive readiness increase and seizure threshold decrease in the dynamics of the posttraumatic period was proved to be a probable pathogenetic mechanism of involuntary self-sustaining seizures occurrence that is the posttraumatic epilepsy clinical basis. The authors believe that obtained results confirm the concept of pathological disintegration of organs and systems in pathological conditions formation which allows us to interpret the pathophysiological mechanisms of traumatic brain damage in mild brain trauma as new type of pathological interaction formation between the cerebral cortex and subcortical formations, which enhances brain convulsive sensitivity including the central GABA-, glycine-, choline-kainate- and monoaminergic neurotransmission participation.

Key words: brain trauma, posttraumatic period, seizure sensitivity, acute generalized convulsions, posttraumatic epilepsy, pathophysiological mechanisms

І.В. Савицький, С.М. Френкель, Р.С. Вастьянов, О.М. Стоянов, В.В. Добровольський, Л.М. Заяць, М.Р. Вастьянов

ЗМІНЕНА СУДОМНА ЧУТЛИВІСТЬ ТВАРИН ПІСЛЯ НАНЕСЕННЯ ЛЕГКОЇ ЧЕРЕПНО-МОЗКОВОЇ ТРАВМИ ЗА УМОВ ВІДТВОРЕННЯ ГЕНЕРАЛІЗОВАНОЇ СУДОМНОЇ АКТИВНОСТІ

Метою дослідження є з'ясування зміни інтенсивності гострих генералізований судомних реакцій, індукованих конвульсантами з різним механізмом реалізації судомної дії, протягом раннього посттравматичного періоду експериментальної легкої черепно-мозкової травми. 185 щурів були розділені на 5 групи відповідно виду конвульсанту, за допомогою якого через 6, 12, 24 години та 3 доби після нанесення легкої черепно-мозкової травми були ініційовані гострі генералізовані судомні реакції. Протягом 3 діб посттравматичного періоду реєструється зміна судомної чутливості в мозку щурів, що підтверджується зниженням судомного порога. У випадку ініціації гострих судом шляхом введення пікротоксину та пентиленететразолу їх інтенсивність вже на 1-й добі посттравматичного періоду була вищою. У випадку стрихнін-, пілокарпін- та каїнат-індукованих гострих генералізованих судом статистичні розбіжності були досягнуті на 3-й добі після нанесення черепно-мозкової травми. Доведено, що підвищення судомної готовності та зниження судомного порогу в динаміці посттравматичного періоду є ймовірним патогенетичним механізмом виникнення мимовільним самопідтримуючихся судом за умов посттравматичної епілепсії. Автори вважають, що отримані результати підтверджують концепцію про формування патологічної дезінтеграції органів і систем при патологічних станах, що свідчить про формування нового типу патологічної взаємодії кори мозку та підкіркових утворень при легкій черепно-мозковій травмі, внаслідок чого підсилюється судомна чутливість мозку в тому числі й за участю центральної ГАМК-, гліцин-, холін,- каїнат- та моноамінергічної нейропередачі.

Ключові слова: черепно-мозкова травма, посттравматичний період, судомна чутливість, гострі генералізовані судоми, посттравматична епілепсія, патофізіологічні механізми

The study is a fragment of the research project "To investigate the chronic convulsive syndrome pathogenetic mechanisms on the model of pharmacological kindling and to study the efficacy of its complex pathogenetical correction by anticonvulsant mechanisms activation", state registration No 0122U000081.

The relevance and importance of traumatic brain injury problem does not lose its significance with the progressive development of diagnostic and treatment capabilities [12]. Traumatic diseases rank third in frequency after oncological and cardiovascular diseases in terms of causes of disability and mortality [10]. From the entire share of traumatic diseases, the dominant one – up to 70 % – belongs to brain trauma (BT). The BT frequency in peaceful conditions increases annually by an average of 2 %, the frequency of skull injuries during military operations reaches 35 % of the total number of wounded, and skull damage – 76 % of the number of victims of a neurological profile [2]. Therefore, the situation with traumatic brain injury requires the primary attention of specialists in many fields of medicine since the BT consequences cause

social and labour maladjustment with loss of work capacity, especially among young people, which gives this problem global general medical and socio-economic significance [13].

Mild BT given the numerous undesirable consequences in the delayed, posttraumatic period, is the most unfavourable in the prognostic aspect [10]. Brain trauma has a direct generalized influence on the body causing an initial general adaptation reaction manifested by a complex of pathophysiological and morphological changes not only in the centre of direct mechanical damage but also in various organs and systems of the body [12]. Taking into account the above-mentioned features of the altering traumatic impact, our attention is drawn to brain excitability increase during the posttraumatic period, ictal convulsive manifestations development with posttraumatic epilepsy (PTE) formation [12].

From neuropathophysiological point of view, a complex of cascading pathophysiological reactions occurs in the dynamics of the posttraumatic period which reflect a wave-like change in compensatory and decompensatory processes (or processes of incomplete compensation) activity, which further development contributes to regulatory mechanisms irreversible disruption with the persistent pathological dysregulation development [10]. A similar loss of regulatory control, the formation of pathologically enhanced excitation generator in the brain, a significant loss of inhibitory GABA-ergic control with seizure threshold decrease, pathological epileptogenic system hyperactivation [5] is the reason for PTE development within 1 week after the mild BT [12].

We decided to follow the experimental animals' nervous system sensitivity changes during the mild BT early posttraumatic period to determine the pathogenetic mechanisms of posttraumatic convulsions and PTE formation.

The purpose of the study was to investigate the change in the intensity of acute generalized convulsive reactions induced by convulsants with different mechanisms of convulsive action during the early posttraumatic period of experimental mild brain trauma.

Materials and methods. Experimental studies were performed on 185 white matured male Wistar rats. The animals were kept in standard vivarium conditions. Experimental animals keeping and manipulation was done in accordance with the "General Ethical Principles of Animal Experiments" adopted by the Fifth National Congress on Bioethics (Kyiv, 2013) and was guided by the recommendations of the European Convention for the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes (Strasbourg, 1985) and guidelines of the State Pharmacological Center of the Ministry of Health of Ukraine on "Preclinical studies of drugs" (2001) as well as rules of humane treatment of experimental animals and conditions approved by the Committee on Bioethics of Odesa National Medical University (Prot. N17-C from 12.10.2021).

Mild TBI in rats was reproduced by falling load (m=50 g) impact from a height of 50 cm on the occipital-parietal region of the skull [3]. For this purpose, rats under ether Rausch anaesthesia were fixed in such a way that the trajectory of the load was perpendicular to the surface of their skull.

Generalized convulsions were induced in rats 6, 12, 24 hrs and 3 days after mild BT by i.p. picrotoxin (PTX, 2.0 mg/kg), pentylenetetrazol (PTZ, 40 mg/kg), strychnine nitrate (1.0 mg/kg), pilocarpine hydrochloride (a 20 % solution was prepared from the powder dissolved in a 0.9 % NaCl physiological solution, 280 mg/kg) and kainic acid (15 mg/kg; all used convulsants are of "Sigma-Aldrich", Germany) administration. The animals of the control groups under these conditions were injected with similar volumes of 0.9 % NaCl physiological solution.

After convulsants injections the rats were placed in individual transparent plastic chambers (10 cm x 25 cm x 30 cm), and the severity of convulsive reactions were evaluated on a 6-point scale [14]. The first convulsive reactions latency was also estimated. The number of rats with generalized clonic-tonic seizures was also counted. In each experimental group there were 7 rats, in the control (convulsants injections without BT) – 9 rats.

The data obtained were statistically analyzed with the help of parametric ANOVA test followed by Newman-Keulls test and the non-parametric Krushkal-Wallis test. The minimal statistical probability was determined at $p<0.05$.

Results of the study and their discussion. Picrotoxin administration caused in 7 out of 9 rats the development of acute generalized convulsions in the form of generalized clonic-tonic seizures, with animals falling on their side, autonomic disorders and post-seizure depression. Repeated generalized seizures were recorded in 1 rat (Table 1). PTX injection 6 hrs after BT did not change the severity of acute PTX-induced seizures ($p>0.05$). A similar intensity of PTX-induced seizures was noted 12 hrs after BT ($p>0.05$). Picrotoxin-induced seizures 24 hrs after BT were characterized by generalized clonic-tonic seizures in all rats, and in 2 rats these seizures were recorded repeatedly. The intensity of seizures in these rats was higher than in the control group, and the latency of their development was on 30.3 % shorter

compared to such indexes in the control group (in both cases, p<0.05). In the case of PTX administration 3 days after TBI, their intensity was greater (p<0.01), the number of rats with repeated generalized clonic-tonic seizures was also greater (p<0.05), and the first convulsions reactions latency was on 41.85 % shorter (p<0.05) when compared with the corresponding indexes in control observations.

The intensity of acute generalized PTZ-induced seizures in the posttraumatic period 24 hrs after the BT was significantly greater than in control, and their latency of development was on 35.3 % less than that in intact rats (in both cases p<0.05). PTZ introduction 3 days after BT resulted in generalized clonic-tonic seizures development in all 7 rats – the intensity of PTZ-induced seizures and the number of rats with repeated generalized clonic-tonic seizures was greater (in both cases p<0.05). The latency of seizures initiation was 2.1 times shorter (p<0.01) in relation to such indicators in the control group of rats.

Table 1

The intensity of acute generalized seizures induced in rats by picrotoxin, pentylenetetrazole and strychnine in the dynamics of posttraumatic period

Experimental groups	Number of rats with seizures intensity						P, vs control	Latency M±m, min
	0	1	2	3	4	5		
Picrotoxin injections								
Control, n=9	0	0	0	2	6	1	-	12.2±1.4
6 hrs after BT, n=7	0	0	0	2	5	0	>0.05	11.3±1.3
12 hrs after BT, n=7	0	0	0	2	5	1	>0.05	9.4±0.8
24 hrs after BT, n=7	0	0	0	0	5	2	<0.05	8.5±0.7*
3 days after BT, n=7	0	0	0	0	2#	5#	<0.01	7.1±0.8*
Pentylenetetrazole injections								
Control, n=9	0	0	0	3	5	1	-	1.7±0.2
6 hrs after BT, n=7	0	0	0	1	5	1	>0.05	1.8±0.2
12 hrs after BT, n=7	0	0	0	1	3	3	>0.05	1.2±0.2
24 hrs after BT, n=7	0	0	0	0	3	4#	<0.05	1.1±0.1*
3 days after BT, n=7	0	0	0	0	2	5#	<0.01	0.8±0.1**
Strychnine injections								
Control, n=9	0	0	0	2	5	2	-	4.6±0.4
6 hrs after BT, n=7	0	0	0	1	5	1	>0.05	4.4±0.4
12 hrs after BT, n=7	0	0	0	0	6	1	>0.05	3.8±0.4
24 hrs after BT, n=7	0	0	0	0	5	2	>0.05	3.4±0.3
3 days after BT, n=7	0	0	0	0	2	5#	<0.05	2.9±0.3*

Notes: seizure intensity statistical differences were calculated using Kruscall-Wallis criterion; * – P<0.05 and ** – P<0.01 – statistical differences of the investigated parameters compared with the same in the control group (ANOVA + Newmann Keuls criteria); # – P<0.05 – statistical differences of the investigated indexes compared with the same in the control group (Kruscall-Wallis criterion).

Strychnine-induced acute generalized convulsions 3 days after BT were characterized by generalized clonic-tonic convulsions occurrence when all the animals fell on their side with post-seizure depression, and similar seizures were recorded repeatedly in 5 rats. The intensity of convulsions, the number of rats with the seizure reactions maximal severity and their latency had significant differences with such indexes in the control group of rats (p<0.05).

Pilocarpine administration 3 days throughout the posttraumatic period caused the generalized clonic-tonic seizures development in 100 % of rats, with repeated generalized seizures in 6 out of 7 rats (p<0.05, Table 2). The first convulsive reactions latency in this case was equal to 9.7±1.1 min which turned out to be 36.6 % shorter when compared with such a control indicator (p<0.05).

Kainic-induced acute generalized convulsions had a similar character. Their intensity exceeded the corresponding control index only on the 3rd day of the posttraumatic period (p<0.05). 6 out of 7 rats demonstrated repeated generalized clonic-tonic convulsive seizures with side-falling and post-seizure depression (p<0.05). The latency of the first convulsive reactions was on 31.9 % shorter than in the control (p<0.05).

Thus, the data obtained indicate a change in convulsive sensitivity in the posttraumatic period dynamics. Our total period of observation lasted for 14 days but we consider it reasonable to indicate such a 3-day posttraumatic interval, since it is possible to clearly trace the dynamics of the seizure threshold change related to first seizure reactions initiation. Important that used convulsants have a different mechanism of convulsive action which makes possible to draw conclusions about the increased convulsive sensitivity pathophysiological mechanisms and the rat brain altered convulsive readiness in the posttraumatic period dynamics.

Our data indicate seizure threshold decrease during the posttraumatic period. In case of acute convulsions induction by PTK and PTZ their intensity was already higher on the 1st day of posttraumatic period than in control observations. In the remaining cases, statistically significant differences were reached on the 3rd day after BT.

Table 2

The intensity of acute generalized seizures induced by in rats pilocarpine and kainic acid in the dynamics of posttraumatic period

Experimental groups	Number of rats with seizures intensity						P, vs control	Latency M±m, min
	0	1	2	3	4	5		
Pilocarpine injections								
Control, n=9	0	0	0	2	6	1	-	15.3±1.6
6 hrs after BT, n=7	0	0	0	1	6	0	>0.05	14.9±1.6
12 hrs after BT, n=7	0	0	0	0	6	1	>0.05	12.2±1.3
24 hrs after BT, n=7	0	0	0	0	6	1	>0.05	10.9±1.4
3 days after BT, n=7	0	0	0	0	1#	6#	<0.05	9.7±1.1*
Kainic acid injections								
Control, n=9	0	0	0	1	6	2	-	9.1±0.9
6 hrs after BT, n=7	0	0	0	1	6	0	>0.05	9.3±0.9
12 hrs after BT, n=7	0	0	0	0	5	2	>0.05	8.6±0.9
24 hrs after BT, n=7	0	0	0	0	4	3	>0.05	7.4±0.7
3 days after BT, n=7	0	0	0	0	1#	6#	<0.05	6.2±0.5*

Notes: seizure intensity statistical differences were calculated using Kruscall-Wallis criterion; * – P<0.05 – statistical differences of the investigated parameters compared with the same in the control group (ANOVA + Newmann Keuls criteria); # – P<0.05 – statistical differences of the investigated indexes compared with the same in the control group (Kruscall-Wallis criterion).

Summarizing, one should conclude that according to all used parameters – the seizure reactions intensity, their latency and the number of rats with single and repeated generalized clonic-tonic seizures – precisely on the 3rd day of the posttraumatic period convulsive reactions had significant differences from the point of view of their aggravation compared with similar convulsive manifestations in rats without mild BT. We consider this result fundamental in this series of experiments since from the point of view of neuropathophysiology we obtained evidence of inhibitory control expressed loss and brain cytoarchitectonics serious reorganization during the 72-hour posttraumatic period, which is sufficient for the behavioural demonstration of convulsive reactions due to the generator of pathologically enhanced excitation formation and pathological epileptogenic system hyperactivation with brain antiepileptic system activity suppression.

Thus, the obtained data indicate convulsive readiness increase and convulsive threshold decrease in the dynamics of the posttraumatic period which is a probable pathogenetic mechanism of involuntary self-sustaining seizures that is the PTE clinical basis.

Taking into account the mechanisms of the used convulsants epileptogenic effect implementation it seems reasonable that convulsive posttraumatic activity is more likely to be initiated in case GABA-ergic (which is inherent in PTK, PTZ) and glycine-ergic inhibition (in the case of strychnine) blockade [9]. In contrast, on the 3rd day of the posttraumatic period, cholinergic mechanisms and the system of excitatory amino acids hyperactivation are already involved into the pathogenetic convulsive mechanisms [8].

It should be noted that both serotonin and dopaminergic neurotransmission involvement in traumatic brain injury was proved [3] which extends the existing ideas about the self-sustaining seizures in PTE pathogenetic mechanisms. The obtained data from the point of view of systemic-antisystemic relationships also testify in favour of pharmacological compounds testing reasonability that are able to modulate the activity of the abovementioned neurotransmitter systems aimed to possible posttraumatic convulsive activity suppression.

In this regard, the data about the Mexiprim and Semax antiepileptic effects are interesting, since their anticonvulsant effect during the posttraumatic period is realized due to the contrainflammatory and antioxidant effects of both drugs [1], and also activates peptidergic mechanisms [14], which has a pathogenetic rationale, activates the brain antiepileptic system and indicates the need for a pathogenetically oriented influence on all links of a convulsive syndrome [6, 15]. There is also evidence that posttraumatic seizures severity determined by immune disorders, which allows us to consider the cytokines and growth factors receptors block as promising antiepileptic measures [4, 7, 11].

The obtained results from a fundamental point of view confirm the concept of the formation of pathological disintegration of organs and systems in pathological conditions [5, 14] which allows us to

interpret the pathophysiological mechanisms of traumatic brain damage in mild BT as new type of pathological interaction formation between the cerebral cortex and subcortical formations, which enhances brain convulsive sensitivity including the central GABA-, glycine-, choline-kainate- and monoaminergic neurotransmission participation. We are sure that brain neurons alteration due to traumatic and/or hypoxic influences as well as these brain structures functional activity should be restored due to pathogenetically oriented pharmacological correction, the leading focus of which should be the highlighted intracerebral neurotransmission modulation, reducing the brain convulsive sensitivity, brain antiepileptic system hyperactivation and its reactivity restoration.

Conclusions

1. A change in convulsive sensitivity was registered within 3 days of the posttraumatic period in the brain of rats which is confirmed by seizure threshold decrease.

2. In case of acute convulsions induction by picrotoxin and pentylenetetrazol their intensity was already higher on the 1st day of posttraumatic period. In case of strychnine-, pilocarpine- and kainic-induced acute generalized seizures the expressed differences were reached on the 3rd day after brain trauma.

3. On the 3rd day of the posttraumatic period convulsive reactions had significant differences from the point of view of their aggravation compared with similar convulsive manifestations in rats without mild BT which is in favour for the inhibitory control expressed loss and brain cytoarchitectonics serious reorganization during the 72-hour posttraumatic period, sufficient for the behavioural demonstration of convulsive reactions due to the generator of pathologically enhanced excitation formation and pathological epileptogenic system hyperactivation with brain antiepileptic system activity suppression

4. Convulsive readiness increase and seizure threshold decrease in the dynamics of the posttraumatic period was proved to be a probable pathogenetic mechanism of involuntary self-sustaining seizures occurrence that is the posttraumatic epilepsy clinical basis.

5. Convulsive posttraumatic activity is initiated in case of both GABA-ergic and glycine-ergic inhibition block as well as cholinergic mechanisms and the system of excitatory amino acids hyperactivation involvement.

6. The obtained results confirm the concept of pathological disintegration of organs and systems in pathological conditions formation which allows us to interpret the pathophysiological mechanisms of traumatic brain damage in mild brain trauma as new type of pathological interaction formation between the cerebral cortex and subcortical formations, which enhances brain convulsive sensitivity including the central GABA-, glycine-, choline-, kainate- and monoaminergic neurotransmission participation.

Prospects for further research include a further investigation of animals' brain convulsive sensitivity changes after a mild brain trauma in conditions of chronic convulsive activity to resolve the issue of developing methods of posttraumatic epilepsy effective correction based on this pathological condition pathogenetic mechanisms.

References

1. Kaptalan AO, Lebed OP. Osoblyvosti klinichnoho perebihu posttravmatychnoyi epilepsiyi. Central European Journal for Science and Research. 2021; 1 (67): 61–64 [in Ukrainian]

2. Korshnyak VO. Hostra boyova kontuziyna cherepno-mozkova travma: patohenez, diahnostyka, likuvannya. Kharkiv: FOP Liburkina LM, 2018. 156 p. [in Ukrainian]

3. Stoyanov OM, Pulyk OR, Vastyanov RS. Patohenetychne znachennya tsentral′noyi monoaminerhichnoyi neyroperedachi v mekhanizmakh rozvytku motornykh dysfunktsiy ta nevrolohichnoho defitsytu pislya lehkoyi cherepno-mozkovoyi travmy. Naukovyy visnyk Uzhhorodskoho universytetu. Seriya : Medytsyna. 2015; 1: 100–107. [in Ukrainian]

4. Doganyigit Z, Okan A, Akyuz E, Poshyvak O, Pervak M, Yehorenko O, Godlevsky L. Do roli faktora nekroza pukhlyn-a (TNF-a) ta P-NF-kB v patohenezi pentylenetetrazolovoho kindlinha. Odeskyy medychnyy zhurnal. 2022; 1-2: 15–20. doi: 10.54229/2226-2008-2022-1-2-2 [in Ukrainian].

5. Akyuz E, Lazarowski A, de Cabo C, Godlevsky LS, Shaikh MF, Doganyigit Z. Editorial: Ion-channels in epilepsy. Front Neurol. 2023; 14: 1263539. doi: 10.3389/fneur.2023.1263539.

6. Dang Y, Wang T. Research Progress on the Immune-Inflammatory Mechanisms of Posttraumatic Epilepsy. Cell Mol Neurobiol. 2023; 43(8): 4059–4069. doi: 10.1007/s10571-023-01429-2

7. Evans LP, Woll AW, Wu S, Todd BP, Hehr N, Hedberg-Buenz A et al. Modulation of post-traumatic immune response using the IL-1 receptor antagonist anakinra for improved visual outcomes. J Neurotrauma. 2020; 37(12): 1463–1480. https://doi.org/10.1089/neu.2019.6725

8. Gao Y, Liu N, Chen J, Zheng P, Niu J, Tang S et al. Neuropharmacological insight into preventive intervention in posttraumatic epilepsy based on regulating glutamate homeostasis. CNS Neurosci Ther. 2023; 29(9): 2430–2444. doi: 10.1111/cns.14294

9. Löscher W, Potschka H, Sisodiya SM, Vezzani A. Drug Resistance in Epilepsy: Clinical Impact, Potential Mechanisms, and New Innovative Treatment Options. Pharmacological Reviews. 2020; 72(3): 606–638. doi: https://doi.org/10.1124/pr.120.019539

10. Munakomi S, Cherian I. Newer insights to pathogenesis of traumatic brain injury. Asian J Neurosurg. 2017; 12(3): 362–364. doi: 10.4103/1793-5482.180882

11. Poshyvak O, Pinyazhko O, Godlevsky L, Pervak M, Yehorenko O, Doganyigit Z et al. Immunohistochemical neuroinflammatory markers in the hippocampus of PTZ-kindled rats under conditions of rapamycin and axitinib treatment. ScienceRise: Pharmaceutical Science. 2023; 1(44): 23–31 doi: 10.15587/2519-4852.2023.274703

12. Rauchman SH, Zubair A, Jacob B, Rauchman D, Pinkhasov A, Placantonakis DG, Reiss AB. Traumatic brain injury: Mechanisms, manifestations, and visual sequelae. Front Neurosci. 2023; 17: 1090672. doi: 10.3389/fnins.2023.1090672

13. Stafstrom CE, Carmant L. Seizures and Epilepsy: An Overview for Neuroscientists. Cold Spring Harbor Perspectives in Medicine. 2015; 5 (6): a022426. doi: https://doi.org/10.1101/cshperspect.a022426
14. Vastyanov RS, Stoyanov AN, Krepec YuS, Dzygal AF, Beseda YaV, Puchkova AV. Interleukin-1 receptors antagonist intracerebral administrations anticonvulsive efficacy in conditions of kindling model of epileptogenesis. World of Medicine and Biology. 2020; 74(4): 168–174. doi: 10.26724/2079-8334-2020-4-74-168-174
15. Vezzani A. Brain Inflammation and Seizures: Evolving Concepts and New Findings in the Last 2 Decades. Epilepsy Currents. 2020; 20 (6): 40–43. doi: https://doi.org/10.1177/1535759720948900

Стаття надійшла 18.11.2022 р.

DOI 10.26724/2079-8334-2023-4-86-222-226
UDC 612.273.2+616.155.32+616.423.428]-091

T.S. Sultanova, E.C. Akbarov, S.M. Yagubova
Azerbaijan Medical University, Baku, Azerbaijan

THE EFFECT OF HYPOXIA ON THE MORPHOLOGICAL AND FUNCTIONAL QUALITIES OF THE INTERALVEOLAR CAPILLARIES OF THE LUNGS AFTER ACUTE PHYSICAL LOAD IN THE EXPERIMENT

e-mail: syagubova.71@gmail.com

The purpose the study was a comprehensive study of the structural restructuring of the respiratory section of the lungs during physical exertion in the experiment, the determination of the morphological equivalent of acute fatigue of the air-blood barrier. The study was performed on 30 laboratory-outbred male rats weighing 120.0–150.0 g. Histological and electron-microscopic methods were used. Experimental findings once again prove that alveolar hyperventilation affects respiratory alveolocytes and the endothelium of interalveolar capillaries, predetermining the further course of the pathological process in the aero-hematic barrier. Analysis of the available factual data on the submicroscopic reorganization of the endothelium in the early stages of hypoxia will allow us to agree with the opinion about deep violations of the pulmonary capillaries during acute limiting physical activity. An increase in the permeability of the alveolar-capillary membrane, pulmonary vascular resistance, and a violation of the mechanics of breathing with the development of alveolar hypoxia is currently recognized as the main pathogenic factors of hypoxemia and damage to the lung parenchyma.

Key words: physical load, interalveolar capillaries, hypoxia, acidosis.

Т.С. Султанова, Е.Ч. Акбаров, С.М. Ягубова

ВПЛИВ ГІПОКСІЇ НА МОРФОФУНКЦІОНАЛЬНІ ЯКОСТІ МІЖАЛЬВЕОЛЯРНИХ КАПІЛЯРІВ ЛЕГЕНЬ ПІСЛЯ ГОСТРОГО ФІЗИЧНОГО НАВАНТАЖЕННЯ В ЕКСПЕРИМЕНТІ

Метою дослідження було комплексне вивчення структурної перебудови респіраторного відділу легень при фізичному навантаженні в експерименті, визначення морфологічного еквівалента гострої втоми аерогематичного бар'єру. Дослідження виконано на 30 лабораторних безпородних щурах-самцях масою 120,0–150,0 г. Використовували гістологічні та електронно-мікроскопічні методи. Результати експерименту ще раз доводять, що альвеолярна гіпервентиляція вражає дихальні альвеолоцити та ендотелій міжальвеолярних капілярів, зумовлюючи подальший перебіг патологічного процесу в аерогематичному бар'єрі. Аналіз наявних фактичних даних щодо субмікроскопічної реорганізації ендотелію на ранніх стадіях гіпоксії дозволить погодитися з думкою про глибокі порушення легеневих капілярів при гострому обмеженні фізичного навантаження. Основними патогенними факторами гіпоксемії та ушкодження паренхіми легень у цей час визнано підвищення проникності альвеолярно-капілярної мембрани, легеневого судинного опору та порушення механіки дихання з розвитком альвеолярної гіпоксії.

Ключові слова: фізичне навантаження, міжальвеолярні капіляри, гіпоксія, ацидоз.

The respiratory system includes the airways, the respiratory section, and the motor apparatus. Each of them is an independent section with a special structure, function, and regulation, the study of which is devoted to numerous monographs, manuals, and reviews [1, 2, 7, 11, 14].

We will turn to some parts of this system, in particular the respiratory department, which provides blood transport and gas exchange through the alveolar-capillary membrane.

These processes are commonly referred to as ventilation, perfusion, and diffusion. However, before oxygen molecules acquire the ability to be involved in the terminal oxidation reaction in mitochondria and interact with ionized hydrogen, they have to overcome the system of semipermeable biological membranes that transport oxygen from the alveolar air to the mitochondrial matrix.

The lungs are not just a reservoir of blood; the capacity of the lungs' arterial, capillary, and venous beds is regulated by both extrapulmonary and local factors. Local reflective reactions are stimulated by hypoxia and acidosis, which can directly affect the vascular system.

There are many controversial issues, the study of which requires the use of a comprehensive methodological approach to analyze morphological changes at the level of hepatoparenchymal barriers and ultrastructure.