The use of bioresonance therapy for the correction of structural functional changes in the brain under stress

E.V. Kudinova
(Scientific and practical "Center for Post-Stress Rehabilitation", Omsk)

SUMMARY

The work examines the structural and functional changes in the head brain under the influence of stressful technogenic factors.
It has been shown experimentally that it is possible to restore altered brain structures using the method of bioresonance therapy.

Key words: bioresonance therapy (BRT), limbic structures,hippocampus, mitochondria.

INTRODUCTION

The problem of evidence-based medicine in experimental confirmation and scientific substantiation of the possibility of biocorrection of structural and functional changes in the body, especially the brain, arising under the influence of a technogenic nature. The specificity of the formation of a stress syndrome is due to which formations of the central nervous system are part of the pathological system [4, 11]. The drugs available today at the disposal of pharmacologists and clinicians used in the treatment of stress syndrome are ineffective. They practically do not reduce the risk of the formation of pathological systems of the brain in response to external influences, they have not only a polyvalent effect, which is not always safe for the body, but also have a symptomatic nature, excluding the intellectual, emotional and behavioral spheres, which prevents the restoration of impaired functions [1] ... To obtain pharmacological preparations adapted to biological organisms with a very strict selectivity of action is an extremely difficult task. The principles of treatment "similis similibus curantur" - like to be treated by like and "contraris contrarius curantur" - the opposite is treated by the opposite formulated by Hippocrates [3]. Treatment with the help of electromagnetic waves is based on the phenomenon of the transfer of information properties to the drug, discovered by R. Voll and M. Glaser-Türk [9]. The greatest effect of drugs is manifested when the body is overexcited and ceases to respond to strong stimuli, the "paradox of super-weak doses" of EMR [12]. The principles of treatment "similis similibus curantur" - like to be treated by like and "contraris contrarius curantur" - the opposite is treated by the opposite formulated by Hippocrates [3]. Treatment with the help of electromagnetic waves is based on the phenomenon of the transfer of information properties to the drug, discovered by R. Voll and M. Glaser-Türk [9]. The greatest effect of drugs is manifested when the body is overexcited and ceases to respond to strong stimuli, the "paradox of super-weak doses" of EMR [12]. The principles of treatment "similis similibus curantur" - like to be treated by like and "contraris contrarius curantur" - the opposite is treated by the opposite formulated by Hippocrates [3]. Treatment with the help of electromagnetic waves is based on the phenomenon of the transfer of information properties to the drug, discovered by R. Voll and M. Glaser-Türk [9]. The greatest effect of drugs is manifested when the body is overexcited and ceases to respond to strong stimuli, the "paradox of super-weak doses" of EMR [12].

MATERIALS AND METHODS

We used animals with a high and low threshold of seizure readiness of the brain, which were kept in standard conditions of the vivarium of the Central Scientific Research Laboratory of the Omsk State Medical Academy. When performing the experiments, all the rules for working with laboratory animals were observed (order of the Ministry of Health of the Russian Federation No. 755 of 12.08.77). The studies were carried out in a chronic experiment on 127 sexually mature white Wistar male rats weighing 170–210 g.

To simulate the stress syndrome, a model of reflex epilepsy under the action of sound stimulation with an intensity of 86 dBA and 102 dBA was used. The selection of animals was carried out according to their sensitivity to the epileptogenic effect of sound stimuli using dosed sound stimulations. Sound stimulations were presented from the first day to 86 dBA (training mode) after completing the groups, the impact was carried out with a strong sound intensity of 102 dB (exhausting mode) and then every third day up to 3 months. The sound exposure was 2 min. The motor response was assessed on a scale of points (L.V. Krushinsky, 1960).

Comparative analysis of the effect of biocorrection using bioresonance therapy (BRT) on the structural and functional state of the hippocampus and the neuropsychiatric state of experimental animals during the formation of the stress syndrome was carried out on two groups of animals. In animals of group I (n = 63), BRT was not used, and in animals of group II, BRT was carried out according to the standard scheme, using the software and hardware complex "MIRANDA". The main stages of BRT were as follows: 1) testing the state of the brain of animals on the device "MIRANDA" [6]; 2) the formation of the initial data of the information analogue of its own frequency radiation, histological sections of the hippocampus; 3) production of an informational medicinal product, in the inversion mode by transferring the frequency characteristics of the identified pathological zones to a matrix, the matrix was magnetized (structured) water and propolis tincture; 4) carrying out biocorrection using active background radiation of the prepared preparation, which was injected at 0.1 ml 1 time per day.

The device has the following characteristics:

1) the gain of the differential amplifier is 30 dB;

2) the frequency range of processing information bursts in a noise signal within 10-200 kHz;

3) the clock frequency of the shift register - 1.0 ± 0.1 MHz;

4) the intensity of the magnetic field on the surface of the magnetic inductors - 20 ± 1 mT;

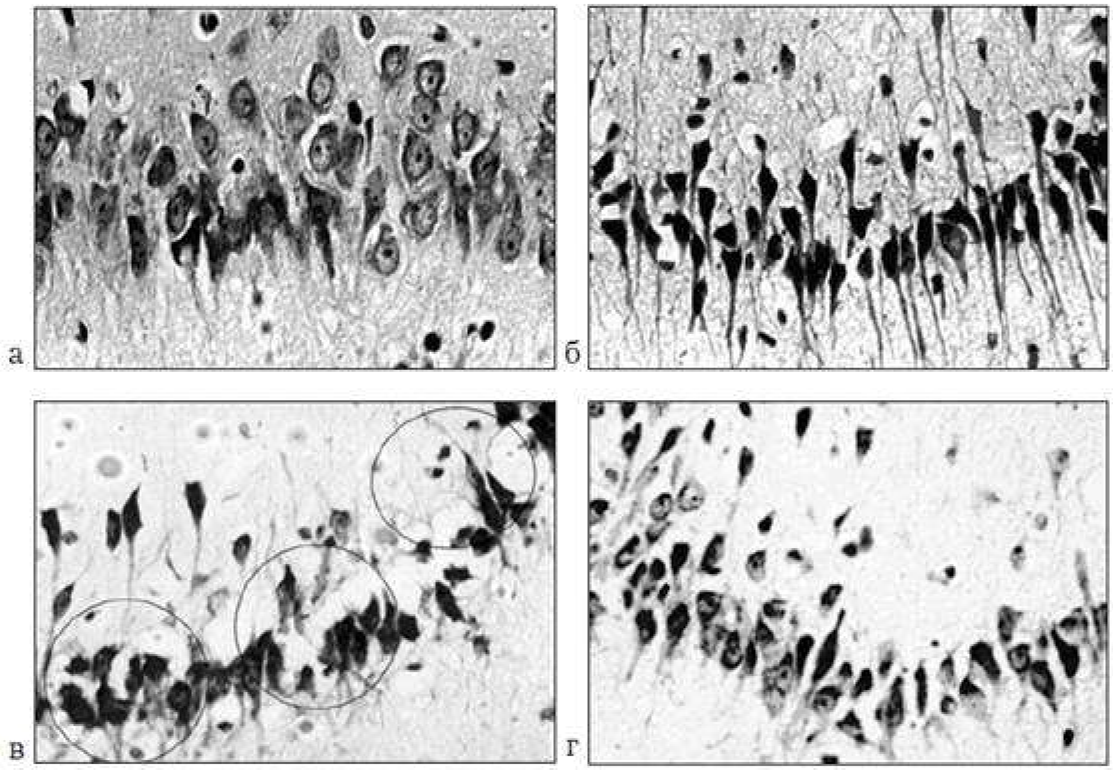
5) type of modulation in the magnetic inductor circuit - pulse-width; 6) the range of change in the frequency of current interruption in the magnetic inductor circuit - from 1.8 to 8.2 Hz; 7) step of regulation of the interruption frequency - 0.1 Hz;

8) duty cycle - from 0.5 to 95% with a step of 5%;

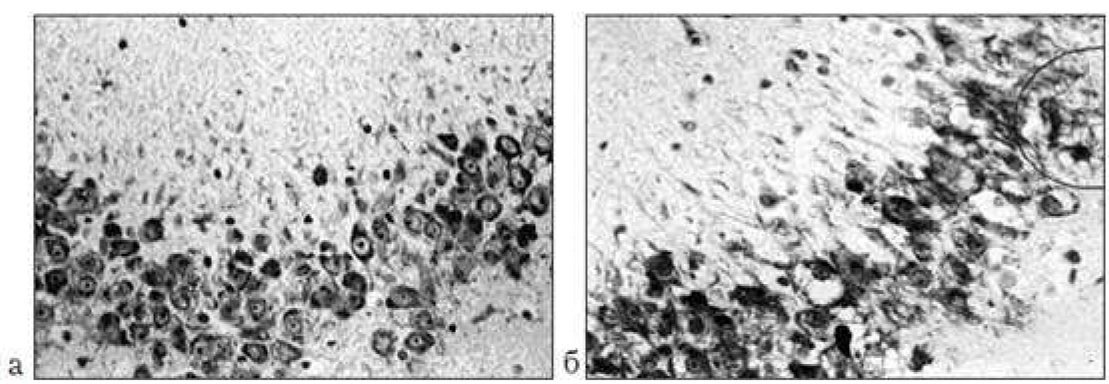
9) modulation frequency - low frequency 240 Hz, high frequency 1.5 GHz.

Material for morphological study was taken from animals of groups I (n = 63) and II (n = 64) after euthanasia under ether anesthesia after 14, 21, 30, 45, 60 and 90 days after 4-, 7-, 10-, 15-, 20- and 30-fold irritations, respectively. After fixation, the material was washed in phosphate buffer, embedded in paraffin, and light-optical preparations were prepared by staining with thionine according to Nissl. For electron microscopy, the hippocampus was isolated, and then pieces of sectors CA1, CA2, CA3, CA4 (5 pieces per case) oriented in the form of pyramids were placed in a 1% solution of osmium tetroxide for 2 hours. After osmosis, the material was washed and embedded in a mixture of epon and araldite (1: 1).

The control was the brain of animals in which, after three times after 48 hours of audiogenic stimulation (86 dBA), a response of 0 points remained (without visual motor excitation) and a group of animals that took ordinary non-magnetized water and epam.



Rice. 1. Sector of the CA field1 hippocampus of white rats at different periods after the start of the experiment (b-d). a - (control) normochromic neurons predominate; b - (without BRT) hyperchromic neurons predominate, nuclei and nucleoli are not determined, the cytoplasm is dark, homogeneous with signs of wrinkling; c - (without BRT) signs of edema-swelling neuropil (porosity, enlightenment), the appearance of neuronal ensembles (O); d - normochromic neurons with clearly verifiable light nuclei predominate, nucleoli and basophilic structured cytoplasm and hyperchromic non-wrinkled neurons. Uv. - x200. paint according to Nissl thionine.



Rice. 2. Sector of the CA field3 hippocampus of white rats on day 90, and - (with BRT) prevail rounded normochromic neurons with clearly identifiable light nuclei,

nucleoli and basophilic structured cytoplasm, neuropil homogeneous without signs of edema-swelling; b - (without BRT) hypochromic and hydropically altered neurons, pronounced signs of edema-swelling of the neuropil and foci of neuronal prolapse (O) (low cell density). Uv. - x200. paint according to Nissl thionine.

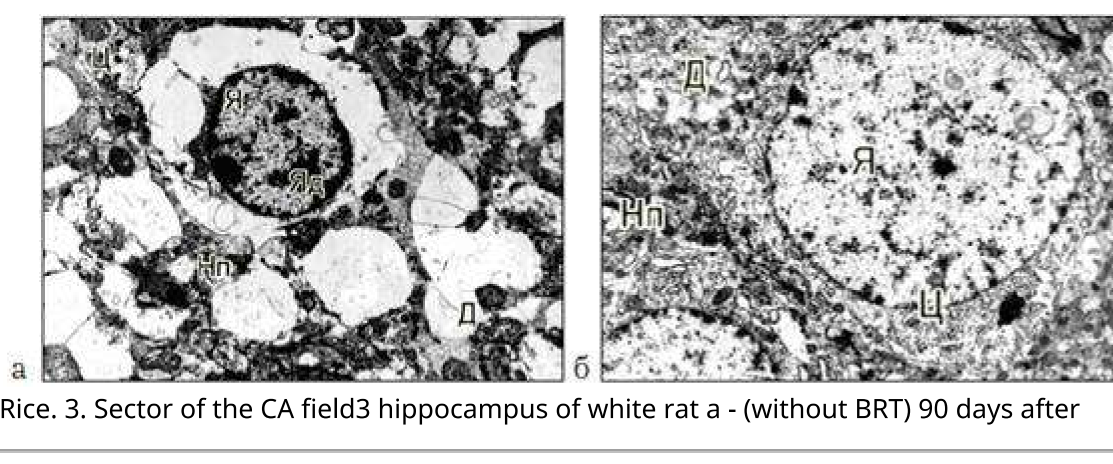
The quantitative data obtained in the work were processed using the methods of statistical analysis generally accepted in biomedical research using the programs "EXCEL" and "Statistica-5" (O. Yu. Rebrova, 2002), in accordance with modern requirements for the analysis of medical data.

RESULTS AND DISCUSSIONIt was experimentally revealed that under the influence of audiogenic stress stimuli, the neural populations of all limbic structures of the brain, amygdala, thalamic nuclei, hypothalamus, but especially the CA3 and CA1 sectors of the hippocampus are reorganized.

Cytoarchitectonics of light-optical material

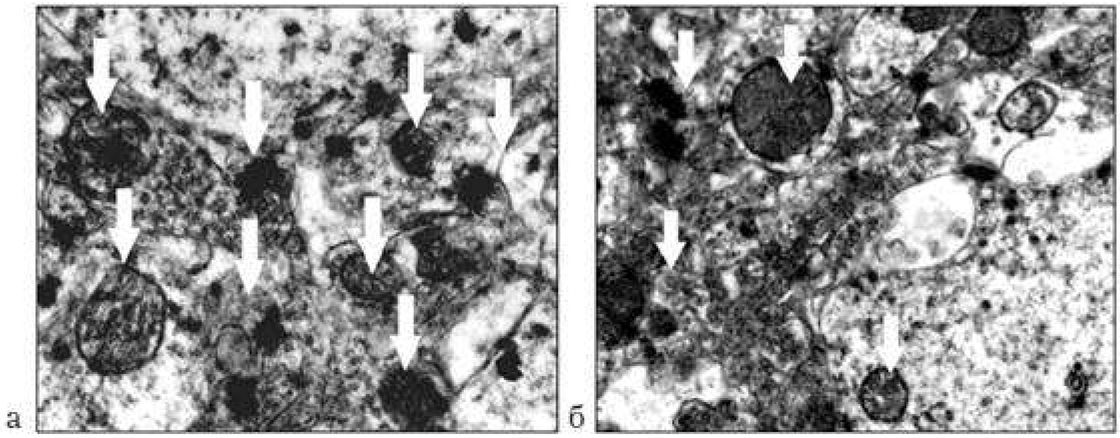
Morphometric analysis of light-optical material significant differences showed in the dynamics of the total numerical density of neurons and the content of the main forms, reactively changed neurons in different sectors of the hippocampal fields of white rats with repeated stimuli.

Analysis of variance (Kruskal-Wallis ANOVA) in rats of group I in all fields of the hippocampus showed statistically significant changes in all the studied parameters, and in group II - in all parameters except for the number density of hypochromic neurons in the sector of the field CA1. The degree of structural and functional changes was significantly different depending on the sectors of the hippocampus and the use of BRT. In all hippocampal fields of animals of this group, paired comparison of terms with group I using the Kolmogorov-Smirnov test revealed a statistically significantly higher total number density of neurons and a lower content of reactively changed neurons. A completely different dynamics of the total number density of neurons and the content of reactively changed cells was characteristic of the hippocampus of white rats of group II.



Rice. 3. Sector of the CA field3 hippocampus of white rat a - (without BRT) 90 days after

audiogenic irritation. Severe manifestations of edema-swelling; b - (with BRT) local destruction and swelling of the cytoplasm (*), moderate expansion of the endoplasmic reticulum, ultrastructural preservation of the nucleus and organelles of the cytoplasm. D - dendrite, Np - neuropil, C - cytoplasm, I - neuron nucleus. Uv. 16300.



Rice. 4. Neuropil of the CA field sector1 white rat hippocampus 90 days after audiogenic irritation. a - (without BRT) focal edema-swelling of the neuropil, destruction of cristae in some mitochondria, mitochondria (arrow); b - (with BRT) slight edema-swelling of the neuropil, mitochondria without a sign of damage, mitochondria (arrow).
Uv. 18500.

In the CA1 field, the neuroprotective effect of BRT manifested itself by the end of the experiment (90 days) by preserving 30% of neurons, in the CA2 field - 11.1% of neurons and in the CA4 field - 18.2% of neurons (respectively, $p < 0.05$, $p < 0.05$ and $p < 0.025$). In field CA3, differences in the total numerical density of neurons were detected only 21 days after the start of the experiment and amounted to 25.0% ($p < 0.001$). When paired comparison in terms in the CA1 field of the hippocampus of animals of group II, the content of hypochromic neurons was twice as high as in group I, only after 21 days of the experiment. The content of non-wrinkled hyperchromic neurons did not differ statistically significantly for any period, and the content of wrinkled neurons did not differ 2–3 times ($p < 0.001$) was superior to that in group I.

In field CA2 of the hippocampus of animals of group II, the content of hypochromic neurons did not differ, and the content of non-wrinkled and wrinkled hyperchromic neurons significantly exceeded that in group I. The maximum difference (5 times, $p < 0.001$) by the content of non-wrinkled hyperchromic neurons was noted 30 days after the start of the experiment, and by the content of wrinkled hyperchromic neurons (3 times, $p < 0.001$) - 14 days after the start of the experiment.

In field CA3 of the hippocampus of animals of group II, the content of hypochromic neurons did not differ, and the content of non-wrinkled and wrinkled hyperchromic neurons, as in field CA2, exceeded that in group I. However, the degree of difference was lower, and the peak of the maximum differences fell on other terms. Maximum difference (2.5 times,$p < 0.001$) according to the content of non-wrinkled hyperchromic neurons was noted after 60 days, and according to the content of wrinkled hyperchromic neurons (3 times, $p < 0.01$) - after 21 and 90 days.

The neuroprotective effect in field CA1 manifested itself by the end of the experiment (60–90 days) by preserving 68% of neurons, in field CA2 - 74.8% of neurons and in field CA4 - 81.5% of neurons (respectively, $p < 0.05$, $p < 0.05$ and $p < 0.025$), in the CA3 field 53.0% ($p < 0.001$).

In sector CA3, there is a significant loss of neurons and a long-term preservation of a high content of reactively altered cells. When using bioresonance therapy in the CA3 sector of the hippocampus, a rather significant (32.4%) decrease in the total number of neurons was noted, but, as in the CA2 sector, this occurred against the background of a low content of reactively changed cells.

Cytoarchitectonics of electron microscopic materialBiocorrection has a positive effect on the synaptoarchitectonics and mitochondria of the hippocampus.

Intact mitochondria occupied a large area in the pre-postsynaptic zones of the synapse. At the same time, the number of synaptic mitochondria increased and this was due to small, probably newly formed, round mitochondria with a dense matrix. The total number of mitochondria in the CA1 sector of the field increased by 3.8 times ($p < 0.005$), sector of the field CA3 2.9 times ($p < 0.001$), sector of field CA2 by 1.1 times, sector of field CA4 by 1.4 times ($p < 0.001$).

The high density of mitochondria in the neuropil was often combined with a large number of small synaptic contacts. This was especially typical for animals with bioinformatic effects.

So, after 24 audiogenic influences (90th day of the experiment) in the hippocampus of animals of group II, the content of destructively altered synaptic terminals was 22% less ($\chi_2 = 9.520$, df = 1, $p = 0.002$) than in the hippocampus of animals of group I. Moreover, the total number density of synapses in the hippocampus of animals of group II exceeded that in animals of group I by 15% (Kolmogorov-Smirnov test, $p < 0.01$).

Compensatory and induced audiogenic irritation the reorganization of interneuronal synapses was accompanied by changes in the mitochondria of the neuropil and the zone of synaptic contact. In all fields of the hippocampus of animals of both groups, the area and number of mitochondria per unit area of the neuropil changed, first of all. The mitochondrial area of the CA1 field sector increased 4.2 times ($p < 0.005$), the sector of the CA3 field by 5.8 times ($p < 0.001$), sector of the CA2 field 2.9 times ($p < 0.001$), sector of the CA4 field by 4.5 times ($p < 0.001$). It should be noted that biocorrection had a beneficial effect on mitochondria. In animals of the group with bioinformatics influence, this is evidenced by the fact that ultrastructurally intact mitochondria were often revealed during the audiogenic stress syndrome against the background of pronounced destruction and edema-swelling of the neuropil.

The results of morphometric analysis indicate the existence statistically significant positive influence biocorrection on cytoarchitectonics of all studied sectors of the hippocampus in animals. The neuroprotective effect of BRT is most pronounced in the CA1 field, and to the least extent in the CA2 field. It is likely that the different responses of the pyramidal neurons of the studied sectors of the hippocampal fields to biocorrection are explained by the peculiarities of their structural and functional organization.

Thus, the results of an electron microscopic study indicate that the formation of an audiogenic stress syndrome is accompanied by pronounced destruction and reorganization of interneuronal synapses in animals of both groups. With the drug, the severity of destructive processes in the neuropil decreases, thereby contributing to the preservation of interneuronal relationships and greater stability of the neural networks of the hippocampus.

Consequently, under conditions of using biocorrection with a smaller deficit of neurons and synapses, the reparative replacement of a significant population of damaged hippocampal synapses through mechanisms of neosynaptogenesis occurs to a lesser extent, and the activation of preserved synapses is compensatory in nature, is aimed at maintaining the activity of already existing neuronal circuits of the functional systems of the brain and prevents the formation of pathological systems of the brain that are formed during stress syndrome.

Psychoneurological status

Post-stress states were manifested by pronounced wavelike changes in the indicators of the orientational-exploratory and emotional components of animal behavior. Testing of animals 1 day after stress revealed a decrease in indicators of orientation-exploratory activity by 42.9% ($P < 0.05$) compared with control. 3 days after stress, the structure of the behavior of the rats changed in the group without BRT. The animals were excited and showed high physical activity. Behavior was activated by increasing both horizontal and vertical components. The duration of the latent period decreased by 30.6% ($P < 0.01$) compared to the previous period. This increase in motor activity testified to the state of arousal of the animal and the maintenance of a high level of emotional tension.

In addition to the increase in the severity of the epileptic, the somatic status and behavioral reactions suffered. There was an increased aggressiveness of animals, vocalization in the post-paroxysmal period, posterior paraplegia often developed with dysfunction of the pelvic organs. With 30-fold presentation of dosed EMR (1 time in 3 days) sexually mature initially highly sensitive (ADR 0 points - no visible audiogenic motor excitation) to the epileptogenic effect of dosed sound stimuli in Wistar rats (group II) against the background of bioresonance therapy, the threshold of seizure activity of the brain did not decrease in all animals. In sexually mature, initially highly sensitive Wistar rats with a high sensitivity to the epileptogenic effect of sound irritations, the use of bioresonance therapy leads to a complete or partial decrease in sensitivity and reactivity to sound stimuli. The cessation of epileptiform convulsive paroxysms in 72.7% of initially low-threshold highly sensitive animals to the epileptogenic effect of sound stimuli and audiogenic motor excitation - in 45.4%.

Severe violations of behavioral and emotional reactions develop in animals with an initial audiogenic motor response of 2–4 points (epileptiform convulsive paroxysms). At the same time, the ability to learn decreases, the preservation of the long-term memory engram is shortened, the general motor activity of animals increases, and protective-phobic behavior is activated. In other animals, the proportion and severity of audiogenic epileptiform convulsive paroxysms and audiogenic motor excitation decreases. Long-term memory improves in all animals of group II with different thresholds of brain convulsive readiness. Longer preservation of the long-term memory engram is observed in high-threshold animals with an audiogenic motor response not exceeding 1 point (audiogenic motor excitation, not transforming into epileptiform convulsive paroxysm). Protective-phobic reactions are largely normalized. The effect of BRT during multiple threshold sound stimuli depends on the initial threshold of seizure readiness of the brain and the severity of the audiogenic motor response during sound stimuli.

Thus, the data obtained indicate a deep restructuring of the neuronal networks of the limbic structures of the brain, both quantitative and qualitative. These changes have a certain time dependence on audiogenic stimuli, changing the neuropsychiatric status of experimental animals. Biocorrection has a positive effect even with multiple ARs and depends on the initial threshold of seizure activity of the brain and the severity of the audiogenic motor reaction during sound stimuli, which does not transform into epileptiform seizure paroxysms. Protective-phobic reactions are largely normalized, the orientation (vertical, stance) is preserved and the exploratory (horizontal, mink) motor activity is restored to normal.

Currently, a compromise is proposed: the formation of a pathological focus can occur only in certain brain structures, whose neurons are capable of developing paroxysmal polarization shifts, and the neural network allows synchronizing the bursting activity of these neurons [13]. The limbic system, as a single integral functional system, includes structures that are fundamentally different in terms of their structure, supporting and enhancing the circulation of excitatory impulses of the brain, especially the hippocampus, which has various connections with all brain analyzers [2]. Normally, the physiological role of the hippocampus should be reduced to a certain increase in short-period fluctuations, contributing to the expansion of their adaptive capabilities, Recent studies make it possible to raise the question of the existence of chronotropic properties in a given brain structure. They are manifested in the interest of the hippocampus in internal timing, as well as in the organization of biological rhythms [1]. Any afferent impulses cause a high response of efferent neurons, in which pathologically active neural networks can form from neurons with paroxysmal activity [10, 13]. Therefore, when hyperactive neurons and foci of pathologically enhanced excitation appear in it, the hippocampus becomes the center of the formation of the pathological system of the brain (G.N. Kryzhanovsky, 1997). But, being by its nature a part of the brain that facilitates the deployment of a stress response (A.G. Koreli, 1989), the hippocampus has a regulatory effect on the balance of the inhibitory and excitatory systems of the brain. Therefore, it can be assumed that as a result of the formation of group neuronal ensembles with increased information content of neurons and pathological reverberation of excitation in the hippocampus in the CA1 field, dominant pacemaker zones appear, which are involved in the formation of pathological brain systems that trigger the development of stress syndrome.

CONCLUSIONS

It has been experimentally proven that under stress there is a reorganization of the limbic structures of the brain, especially the hippocampus. Changes of a diffuse-focal nature, reorganization of the hippocampal field CA3 sector contributes to the appearance of neuronal ensembles in the CA1 field sector with the formation of a dominant pacemaker zone in it, which changes the integrative triggering activity of the whole brain. The possibility of restoring the structural and functional state of the hippocampus has been shown; when a generalized focus of dominant excitation is eliminated with the help of BRT, the development of stress syndrome is prevented, opening up broad prospects for the treatment and prevention of a number of diseases.

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Author's address
Ph.D. E.V. Kudinova
Scientific and practical "Post-stress rehabilitation center" (Omsk)
kudinova_kleo@mail.ru

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