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Changes In the Morphology of Neurons of The Parietal Cortex and Hippocampus of Rats in The Dynamics of Step Subtotal Cerebral Ischemia

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Abstract

The study of the brain in norm and pathology is an urgent and promising direction of modern science and, in this regard, a frequent topic of dissertation research. Cerebral ischemia leads to a number of general and local metabolic and functional disorders, the pathogenesis of which is complex, multifaceted and largely. The aim was to change the morphology of neurons in the parietal cortex and hippocampus of rats in the dynamics of stepwise subtotal cerebral ischemia. With stepwise bilateral ligation of both common carotid arteries with an interval of 7 days, negative changes were least pronounced, especially in the hippocampus. The longer the interval between dressings, the more effectively neurons adapt to lack of oxygen, which makes it possible to further study in more detail the dynamics of the mechanisms of damage development and adaptive changes in the brain.

Keywords: *neurons; parietal cortex; hippocampus; cerebral ischemia*

Introduction

The study of the brain in norm and pathology is an urgent and promising direction of modern science and, in this regard, a frequent topic of dissertation research. Cerebral ischemia leads to a number of general and local metabolic and functional disorders, the pathogenesis of which is complex, multifaceted and largely unclear [1-14].

The aim was to change the morphology of neurons in the parietal cortex and hippocampus of rats in the dynamics of stepwise subtotal cerebral ischemia

Methods

The experiments were performed on 40 male mongrel white rats weighing 260 ± 20 g in compliance with the requirements of the Directive of the European Parliament and of the Council No. 2010/63/EU of 22.09.2010 on the protection of animals used for scientific purposes.

The choice of experimental animals is due to the similarity of the angioarchitectonics of the rat and human brains. Modeling of cerebral ischemia (CI) was performed under intravenous thiopental anesthesia (40-50 mg/kg).

The studies used models of step subtotal (SSCI) cerebral ischemia.

Stepwise subtotal CI (SSCI) was performed by sequentially dressing the CCA at intervals of 1 day (subgroup 1), 3 days (subgroup 2) or 7 days (subgroup 3). The material was taken 1 hour (n=6) and 1 day (n=6) after the dressing of the second CCA in each of the groups.

Morphological study of the size and shape of the pericaryons of neurons, determination of the number of neurons with varying degrees of cytoplasmic chromatophilia was carried out [2-4].

To prevent systematic measurement errors, brain samples from the compared control and experimental animals were processed under the same conditions.

As a result of morphometric and cytophotometric studies, quantitative continuous data were obtained, which were processed using the licensed computer program Statistica 10.0 for Windows (StatSoft, Inc., USA).

Since the experiment used small samples that had an abnormal distribution, the analysis was carried out using nonparametric statistics. The data is presented in the form of Me (LQ; UQ), where Me - the median, LQ - the value of the lower quartile; UQ - the value of the upper quartile. The differences between the groups were considered significant at p<0>

Results

There were no changes in the morphology of neurons within one subgroup after 1 hour and 1 day after ligation of the second CCA in all groups.

In the parietal cortex, compared with the value of the indicator in the control group, the S of pericaryons of neurons in the 1st subgroup decreased by 48% one hour after the second ligation (p<0>

At the same time, the area of pericaryons of neurons in the 2nd subgroup was less by 10% (p<0>

Compared with subgroup 1, S of neurons in the 3rd subgroup was 26% less (p<0>

Compared with the control, the form factor of neuronal pericarions in subgroup 1 decreased by 11% (p<0>

In subgroup 2, the form factor was 12.5% less than in subgroup 1 (p<0>

Compared with the value in the 1st subgroup, in subgroup 3, 1 hour after dressing, the form factor did not change, and after 1 day it decreased by 12.5% (p<0>

In the 3rd subgroup, the form factor was 12.5% less after an hour than in the 2nd subgroup (p<0>

The neuronal pericaryon elongation factor increased in the 1st subgroup by 8% (p<0>

The elongation factor of pericaryons of neurons was in the 2nd subgroup greater than in the 1st, by 7% (p<0>

In subgroup 3, the elongation factor after 1 hour was greater than in subgroup 2 by 7% (p<0>

In the hippocampus, the area of pericaryons of neurons in the 1st subgroup SSCI decreased by 28% (p<0>

In the 2nd subgroup, there was a decrease in S by 17% (p<0>

Compared with subgroup 1, in the 3rd subgroup, the area of neurons decreased by 27% (p<0>

The area in the 3rd subgroup an hour later was 12% less than in subgroup 2 (p<0>

The form factor in the 1st subgroup an hour and a day after the second dressing decreased by 11% compared to the control (p<0>

In the 2nd subgroup, it was 12.5% less (p<0>

Compared with subgroup 1, in subgroup 3, the form factor decreased by 12.5

Discussion

With a lack of oxygen in the brain, structural restructuring begins. There is a deformation of the pericaryons associated with a violation of the water balance of the cell [4,5].

The study found that stepwise bilateral ligation of CCA with an interval of 1 and 3 days leads to irreversible damage to the neurons of the parietal cortex and hippocampus of rats, which manifests itself in a decrease in their size, deformation of pericaryons, an increased number of shrunken neurons and shadow cells, most of these disorders were expressed in subgroup 3. When both CCA were ligated with an interval of 7 days, there were fewer negative changes, especially in the hippocampus: the size of the pericaryons of neurons and the ratio of neurons according to the degree of chromatophilia of the cytoplasm did not differ so much from the indicators in the control group [4]. According to the literature data, 7 days after hypoxia caused by ligation, due to the development of adaptive mechanisms, there is a tendency to improve microcirculation: the patency of capillaries is restored, their number and diameter increase, which leads to an increase in the intensity of cerebral blood flow. Improving cerebral circulation is one of the important effects of adaptation to hypoxia. It is based on an increase in vascular density [10-14].

This neovascularization is explained by the production of NO and activation of hypoxia-induced transcription factor (HIF-1). This factor regulates the adaptive responses of the cell to changes in tissue oxygenation, improves oxygen delivery due to stimulation of erythropoiesis, angiogenesis, humoral and metabolic processes (activation of glucose transport, increased glycolytic production of ATP, ion transport) and cell proliferation. In addition to HIF, other hypoxia–sensitive transcription factors have recently been discovered-metallotranscription factor (metaltranscription factor–1 - MTF-1), nuclear factor kappa B (NF–kB - nuclear factor kappa kB), c-Fos and c-Jun, etc..When the brain adapts to hypoxia, the immunoreactivity to NF-kB and phosphorylated CREB (c-AMP response element binding protein) increases, especially in the hippocampus [2-10].

The activity of the key enzyme of the respiratory chain NADPH-cytochrome C-oxidoreductase increases in neurons. Its affinity for NADPH decreases, which increases the resistance of mitochondria to oxygen. With a decrease in the intensity of oxidative processes, a more efficient work of the respiratory chain was noted – a "paradoxical effect" of adaptation

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to hypoxia. There is a clear inverse relationship between the phylogenetic age of the cortex and the severity of its adaptive variability, which explains the better state of hippocampal neurons in CI compared to the parietal cortex [7,11-14].

Thus, with stepwise bilateral ligation of both common carotid arteries with an interval of 7 days, negative changes were least pronounced, especially in the hippocampus. The longer the interval between dressings, the more effectively neurons adapt to lack of oxygen, which makes it possible to further study in more detail the dynamics of the mechanisms of damage development and adaptive changes in the brain.

The conducted studies have shown the dependence of the severity of brain damage on the interval between the cessation of blood flow for one and both CCA. Adaptation took place better with a 7-day interval between dressings, while with a dressing with an interval of 1 day, the degree of morphological changes was maximal, which indicates insufficient resources for the implementation of adaptation mechanisms.

Conflict of interest

The authors declares that they have no competing interests

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