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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

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გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

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При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

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2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

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Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

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In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

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1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

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6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

REACTIONS OF ASTROCYTES AND MICROGLIA OF THE SENSORIMOTOR CORTEX AT LIGATION OF THE CAROTID ARTERY, SENSITIZATION OF THE BRAIN ANTIGEN AND THEIR COMBINATION

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Today it is widely recognized that a decrease in cerebral blood flow is an important risk factor for the development of neurodegeneration, cognitive impairment and dementia [5, 12,]. The morphological substrate of neurological disorders, the most pronounced are damage to the myelinated nerve fibers of the white matter [24, 14]. In addition, neuronal death in the hippocampus [3] and in the cerebral cortex [26, 27, 22] is observed. These processes are observed against the background of the activation of microglia and astrocytes [6, 3, 25, 27, 29]. The data obtained in the experiments showed that different areas of the brain react differently and at different time intervals [22, 23].

The vast majority of data on pathogenetic mechanisms and cellular reactions in brain tissue during hyperperfusion were obtained on experimental models. Moreover, in most studies, severe cerebral hypoperfusion was simulated, most often reproduced by bilateral simultaneous ligation of the carotid arteries [11, 25]. The rigid model was the model of delayed ligation of the second carotid artery [3]. Only a few studies were performed with soft models of brain hypoperfusion based on bilateral carotid artery stenosis [25, 20] or unilateral carotid artery ligation [22, 31].

As you know, brain tissue is normally separated from the immune system by a blood-brain brain. However, from 5 to 92% of people, according to several authors, in the blood there are antibrain antibodies that can cause brain damage, initiate or enhance neurological manifestations [7, 15].

Our previous studies [10] showed some changes in the cellular composition of the sensorimotor cortex in rats in the long term after ligation of the left carotid artery (after 1 and 3 months). This circumstance was the reason for conducting an immunohistochemical study to identify the details of these changes, and, first of all, in the early stages after circulatory disorders.

The aim of the work is to identify changes in the state of astrocytes and microglia with unilateral ligation of the carotid artery, sensitization with the cerebral antigen and their combination in the sensorimotor cortex in rats.

Materials and methods. Studies were performed on 185 males white Wistar rats weighing 260-290 g. Animals were kept in a vivarium of 3-4 individuals per cage on a standard diet with free access to food and water, and a constant light-darkened regimen. All experiments were carried out according to the "Guide for the Care and Use of Laboratory Animals" [2]. Male rats were used in the experiments, since estrogen levels influence the course of ischemic brain damage [13].

Rats were randomly divided into 6 groups: group K – control, animals (conditionally intact), did not experience any action (n = 10); group PO – pseudo-operated, rats were given access to the left common carotid artery and its mobilization, after which the wound was sutured (n = 35); group LCA – ligation of the common carotid artery (n = 35), rats were accessed and mobilized to the left common carotid artery, a ligature was placed on it, and then the wound was sutured; group Ks, control sensitized (n = 35); group POs, PO with preliminary sensitization (n = 35); groups LCAs, LCA with preliminary sensitization (n = 35). Animals of the groups Ks, POs and LCAs were sensitized 12% before the operation with 20% aqueous-salt extract (antigen) of homologous brain tissue (protein content 0.33-0.5 mg / ml according to Loury) [28]. The rats were injected subcutaneously: on the 1st day - 0.5 ml, on the 2nd day - 1 ml on the 3rd day - 1.5 ml of the extract [28].

All the operation interventions were done under thiopental anesthesia (50 mg / kg). Animal euthanasia was performed using thiopental in overdose (200 mg / kg).

The brain was examined 1, 3, 10, 30, and 90 days after surgery and, accordingly, 12 (1), 15 (3), 22 (10), 42 (30), 102 (90) days after sensitization (surgical intervention). After the introduction of thiopental overdose, the rat skull was quickly opened, the brain was isolated, it was divided into three parts by the frontal section. The middle part was immersed in 10% buffered cold formalin (pH 7.4, 4 ° C) for 24 hours. The samples were compacted into para-lapst and frontal sections 4 μm thick were made, which were stained with Azure II-eosin to assess the general condition of the cerebral cortex

Immunohistochemical reactions were carried out in accordance with the manufacturer's protocols. Primary antibodies were used in the work: rabbit polyclonal to S100 protein (Dako, Denmark), ready for use; rabbit polyclonal to glial fibrillary acidic protein (GFAP) (Dako, Denmark), ready to use; rabbit polyclonal to Iba-1 (Molecular Probes, USA), at a dilution of 1: 750. The reaction products were visualized using an EnVision FLEX detection system (Dako, Denmark) with diaminobenzidine (DAB).

Incubation of sections with antibodies was carried out at 22 ° C, with primary for 10 minutes, with secondary for 5 minutes. Slices of rat brain with established positive activity were used as a positive control. Procedures were performed for negative control, but without the use of primary antibodies. Sections intended for densiometry were enclosed in a water-soluble medium Dako Ultramount Aqueous Permanent Mounting Medium (Dako, Denmark) under a coverslip. Other sections were additionally stained with Gill hematoxylin and enclosed in Canadian balsam.

The resulting preparations were studied and photographed with the an Olympus BX51 microscope, an Olympus C3040ZOOM digital camera, and Olympus DP-Soft 3.2 software. Densitometric measurements of S100 expression were performed on a digital image (x200, x400, 1280x960 RGB pixels, lighting mode - photo, standard exposure) using the ImageJ 1.46 image analysis system: (Wayne Rasband (NIH), USA); and counting the number of labeled GFAP and Iba-1 cells (over an area of 430 × 320 μm) in five test fields of the 5th layer of the sensorimotor cortex of the left hemisphere of the brain.

The obtained digital data was processed by standard statistical methods with the calculation of the arithmetic mean. To assess the significance of differences in the average values of indicators between groups, Student t-test was used. The differences were considered statistically significant at $p < 0.05$.

Results and discussion. Performed observations showed that sensorimotor cortex of rat's brain from the control group has that cells with small dense nuclei and thin, moderately branch-

ing processes were detected by GFAP expression. Both in structure and in fact of GFAP expression, they corresponded to astrocytes [8, 9, 30]. In addition, numerous small fibrous and granular GFAP + structures were detected in the neuropil, which can be regarded as fragments of the processes of astrocytes. Around the blood microvasculature, GFAP-labeled the glial limiting membrane were also detected.

With group PO (Fig. 1), 1 and 3 days after the start of the experiment on the part of the operation, the number of GFAP + cells in the cerebral cortex significantly increased compared to K. After 10 days of the experiment, it decreased to control values. After that, on the 30th day of the experiment, their specific number again increased and became significantly higher than group K. After 3 months of the experiment, the number of these cells decreased, but remained significantly higher than in group K. Visually, some of the astrocytes had slightly enlarged bodies and thickened processes. Some thickening of the glial limiting membrane was also sometimes noted.

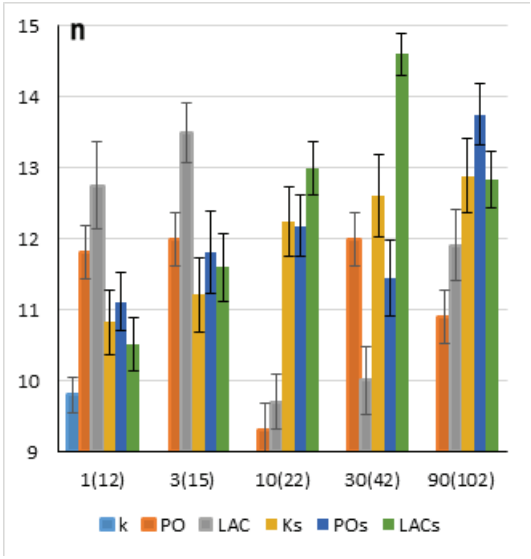

Fig. 1. The number of GFAP+ cells in the fifth layer of the sensorimotor cortex in rats after ligation of the common carotid artery on the left, sensitization with brain antigen, and a combination of these damaging factors. Groups: k - control; PO -; LAC -; Ks -; POs -; LACs -; n is the number of cells in the area of 430x320 mm. (M ± m). 1 (12) -90 (102) day after surgery (day after sensitization)

Under group LCA conditions (Fig. 1), the detection of GFAP in the left hemisphere also showed a significant increase in the number of labeled gliocytes compared with K after 1 and 3, and with PO - 3 days after the start of the experiment. In this case, more often than with PO, an increase in the bodies of astrocytes was observed, a thickening of their processes and perivascular glial membranes.

Sensitization by brain antigen (Ks) led (Fig. 1) to a significant increase in the number of GFAP + cells in the studied cortical area 12 days after the start of antigen administration and gradually increased until the end of the third month of observation. Moreover, the severity of these changes was greater than with group LCA. This also applied to the increase in the size of labeled hypertrophic astrocytes with thickened processes were more common. Also, an uneven thickening of glial limiting membranes was more often observed. However, the latter sometimes showed discontinuity.

The pseudo operation performed in sensitized animals did not lead to a significant change in the number of astrocytes compared with the group Ks (Fig. 1).

At LCAs (Fig. 1) showed a gradual uniform increase in the number of GFAP + cells compared to group K from the first to 30 days and a slight decrease by 90 days after the operation. But, in comparison with LCA on the 1st and 3rd day after the operation, their number was significantly lower, and on the 10th and 30th it became significantly larger, followed by a slight decrease by 90 days. Compared to group Ks, the increase was slower, and on day 30 of the experiment it became reliably large, and by 90 the indices in these groups were practically compared.

A densitometric evaluation of S100 expression showed (Fig. 2) that its significant changes were not observed in any of the groups. However, the tendency was observed that at group Ks one day after the operation, it was lower than in the control and subsequently, up to 30 days, it gradually increased. There was also a tendency to increase S100 expression in group LCAs from 1 to 3 days, which persisted up to 30 days. In this case, significant differences were noted between Ks and LCAs groups after 1 (12) and 3 (12) days of the experiment. Visually, the expression of S100 in group K looked like diffuse, small, often merging flakes in the neuropil. At the same time, it was practically impossible to identify the bodies and processes of individual astrocytes. With group LCAs against a background that did not visually differ from other groups, it was sometimes possible to distinguish individual cells whose bodies and processes were somewhat more intensely labeled.

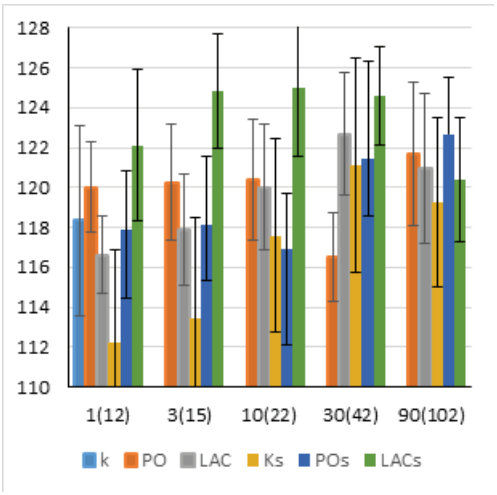

Fig. 2. - Densitometric evaluation of S100 expression in the fifth layer of the sensorimotor cortex in rats after ligation of the common pubic artery on the left, sensitization with brain antigen, and a combination of these damaging factors (conventional units, M ± m). Groups: k - control; PO -; LAC -; Ks -; POs -; LACs -; 1 (12) -90 (102) a day after surgery (a day after sensitization)

Evaluation of the number of detected Iba1+ cells in the sensorimotor cortex showed (Fig. 3) that, with group PO, their number does not change significantly during the experiment.

With group LCA, their specific number after 1 and 3 days after the operation becomes significantly larger than in K, and after 3 days - than with group PO (Fig. 3). Visually, an increase in some labeled cells was noted due to the volume of their bodies and thickening of the processes. Subsequently, their number decreased to the level of control values.

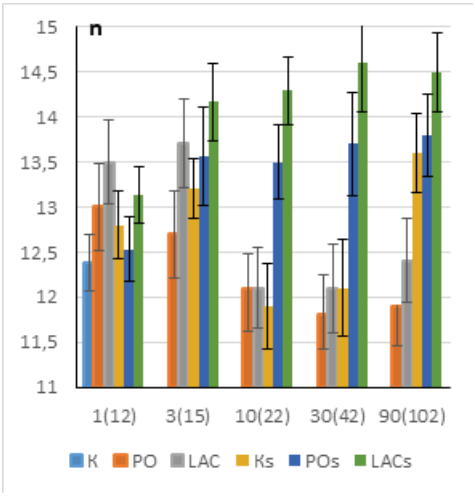

Fig. 3. The number of Iba1+ cells in the fifth layer of the sensorimotor cortex in rats after cerebrovascular accident and its reproduction after preliminary sensitization. n is the number of cells in the area of 430x320 mm (M ± m). Groups: k - control; PO -; LAC -; Ks -; POs -; LACs -; 1 (12) -90 (102) days after surgery (day after sensitization)

After 12 and 15 days after sensitization with the brain antigen (Fig. 3), there was a slight, not significant, increase in the number of labeled microglia cells in the sensorimotor cortex, after which it decreased by 22 and 42 days of observation. However, after 102 days, the number of these cells in the Ks group turned out to be significantly larger than in group K. In the PO group, unlike the indicators in the Ks group, the number of these cells increased by 3 (15) days of the experiment and remained at this level until the end of the observations.

With LCAs group (Fig. 3) showed a statistically significant increase in the number of microgliocytes compared to K group from the first day after the operation, which increased slightly by the 30th day of the experiment. Moreover, on 10 (22) and 30 (42) days, it was significantly larger than with POs group. In this group, there was also a tendency toward an increase in the size of part of the microglia cells and a thickening of their processes.

When comparing the data obtained with LCA and PSAs groups, it was revealed that in the last 10 (22) days of the experiment, the number of Iba1+ cells was significantly larger. At the same time, there was no distinct tendency towards its decrease.

Thus, the studies showed that such relatively small disorders in the brain that occur during unilateral ligation of the carotid artery cause reactions from astrocytes and microglia. Moreover, even such manipulations as immobilization of the carotid artery (in our case, group PO) can cause episodic significant increases in the number of these glial cells. The use of immunohistochemical markers allows us to identify these changes more fully and earlier than using general histological methods [10].

With LCA group, a more pronounced reaction of astrocytic glia, in comparison with microglia, is noteworthy. If a significant increase in the number of cells of the latter was observed only after 1 and 3 days, then the number of astrocytes was found to be increased after 3 months of the experiment. Moreover, the dynamics of the latter was uneven, and was characterized by a decrease in this indicator on 10 and 30 days after the operation. This may indicate different mechanisms for increasing the number of astrocytes expressing GFAP. It can be assumed that not all cells of this type normally express GFAP, and impaired hemocirculation leads to their activation, which leads to the manifestation of these properties. The growth in the number of astrocytes after one month of the experiment, it must be assumed is already connected with a real increase in their number due to proliferation [28].

It should also be noted that despite the fact that the amount of microglia from 10 days of the experiment did not significantly differ from the control, a certain part of these cells could be considered as reactively [4,17,29]. The latter was manifested by an increase in cell bodies, a decrease in the number, but a thickening of the processes. Considering that a number of authors indicate that the microglia reaction precedes changes in astrocytes, in our case it can be assumed that microglia cell hyperplasia is accompanied by an increase in the production of pro-inflammatory factors [20, 25] without a significant increase in its number. On the other hand, given that astrocytes are intimately associated with blood vessels [18], it can be assumed that this determines their more pronounced reaction with relatively small circulatory disorders in the sensorimotor cortex with LCA.

In our observations, in general, it was not possible to identify a significant increase in S100 expression in the sensorimotor cortex, although a tendency to its growth was noted. However, its increase in some parts of the cells, which made them noticeable against the background of more or less uniform expression in the sensorimotor cortex, nevertheless coincides with the data of other observations [3,27]

Despite the presence of a blood-brain barrier, in the blood from 5 to 92% of the examined people who had no history of cerebrovascular accidents, antibodies to tissue components of the brain are detected [7,15]. Our sensitization of rats with a brain antigen performed by us to model this phenomenon was not accompanied by clear signs of neurological deficit. However, significant increases in blood levels of anti-brain antibodies and circulating immune complexes were noted [1]. It should be noted that they also increased with LCA, but to a much lesser extent [1]. Morphologically in the sensorimotor cortex, sensitization led to an increase in the number of reactively named neurons during the first month of observation and to a slight increase in the number of gliocytes after one and three months of observation [10].

Our studies revealed a reliable, gradually increasing increase in the number of GFAP + cells in the sensorimotor cortex after sensitization with the brain antigen. In rats of this group, as in PSA, the increase in astroglia was greater than microglia. A comparison of these results with those of LCA showed their significantly greater value during the first month of the experiment. Assessment of the number of microglia cells in Ks showed a gradual increase in their number, which became reliably large compared to K group only three months after sensitization. As for the assessment of S100 protein expression, no significant quantitative changes were observed in the LCA group.

The combination of software and sensitization also did not reveal significant changes in S100 expression. The increase in the number of labeled astrocytes was not significantly different from Ks group. The number of microglia cells significantly increased both in comparison with K and Ks groups.

Sensitization significantly stimulated an increase in the number of both astrocytes and microglia in the sensorimotor cortex. At certain stages of observation, they were significantly higher than those for Ks and, in the vast majority, for LCA. Also, in these animals, a significant increase in S100 expression was observed after 3 (15) days of the experiment compared with Ks, although such a point increase does not seem to be generally convincing.

A comparison of the levels of changes in the studied parameters with a combination of sensitization and LCA suggests that sensitization plays a more significant role in them.

In general, the observed reactions suggest that with discirculatory disturbances in the brain in rats, revealed changes in astrocytes and microglia tend to reverse. This can be explained by the fact that the animals used in the experiment were practically healthy and had high compensatory-adaptive potencies. In humans, a similar reverse development of glial reactions cannot be expected, since cerebral hypopefusion / dyscirculation develops against the background of changes in the vascular bed, which, as a rule, also progress [21]. Accordingly, similar changes in human glia of the brain will act as secondary factors contributing to neurodegenerative processes [16,19].

Conclusion. Relatively small hemocirculation disorders in the brain with unilateral ligation of the carotid artery can cause activation of astrocytes and microglia. In this case, the reaction of astrocytes detected by the expression of GFAP is more pronounced than Iba 1 + cells. Perhaps this is due to the close contact of astrocytes with blood vessels. A significant role in glia changes is played by sensitization by cerebral antigens, which develops with impaired hemocirculation in the brain and potentiates the damage caused by it. When extrapolated to humans, it can be assumed that sensitization can make a significant contribution to the development of brain damage in conditions associated with hypoperfusion.

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SUMMARY

REACTIONS OF ASTROCYTES AND MICROGLIA OF THE SENSORIMOTOR CORTEX AT LIGATION OF THE CAROTID ARTERY, SENSITIZATION OF THE BRAIN ANTIGEN AND THEIR COMBINATION

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The aim of the work is to identify changes in the state of astrocytes and microglia with unilateral ligation of the carotid artery, sensitization with the cerebral antigen and their combination in the sensorimotor cortex in rats.

Studies were performed on 185 male Wistar white rats weighing 260-290 g. The brain was examined 1, 3, 10, 30 and 90 days after surgery and, respectively, 12 (1), 15 (3), 22 (10), 42 (30), 102 (90) days after sensitization (surgical intervention).

Immunohistochemical reactions were carried out in accordance with the manufacturer's protocols. Primary antibodies were used in the work: S100 (Dako, Denmark); GFAP (Dako, Denmark), Iba-1. Densitometric measurements of S100 expression were performed using ImageJ 1.46 and counting the number of labeled GFAP and Iba-1 cells. Statistical processing was performed using t-student test.

In general, the observed reactions suggest that with discirculatory disturbances in the brain in rats, the detected changes in astrocytes and microglia tend to reverse. This can be explained by the fact that the animals used in the experiment were practically healthy and had high compensatory-adaptive potencies. In humans, a similar reverse development of glial reactions cannot be expected, since cerebral hypopefusion / dyscirculation develops against the background of changes in the vascular bed, which, as a rule, also progress. Accordingly, similar changes in human glia of the brain will act as secondary factors contributing to neurodegenerative processes.

Comparatively small hemocirculation disorders in the brain with unilateral ligation of the carotid artery can cause activation of astrocytes and microglia. In this case, the reaction of astrocytes detected by the expression of GFAP is more pronounced than Iba 1 + cells. Perhaps this is due to the close contact of astrocytes with blood vessels. A significant role in glia changes is played by sensitization by cerebral antigens, which develops with impaired hemocirculation in the brain and potentiates the damage caused by it. When extrapolated to humans, it can be assumed that sensitization can make a significant contribution to the development of brain damage in conditions associated with hypoperfusion.

Keywords: carotid ligation, discirculatory disorders, S100, GFAP, Iba-1.

РЕЗЮМЕ

РЕАКЦИИ АСТРОЦИТОВ И МИКРОГЛИИ СЕНСОМОТОРНОЙ КОРЫ ПРИ ПЕРЕВЯЗКЕ СОННОЙ АРТЕРИИ, СЕНСИБИЛИЗАЦИИ МОЗГОВЫМ АНТИГЕНОМ И ИХ КОМБИНАЦИИ

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Цель исследования - определить изменения состояния астроцитов и микроглии при односторонней перевязке сонной артерии, сенсибилизации мозговым антигеном и их комбинации в сенсомоторной коре у крыс.

Исследования проведены на 185 самцах белых крыс линии Вистар весом 260-290 г. Головной мозг исследовали спустя 1, 3, 10, 30 и 90 суток после оперативного вмешательства и, соответственно, спустя 12 (1), 15 (3), 22 (10), 42 (30), 102 (90) дней после сенсибилизации (оперативного вмешательства).

Иммуногистохимические реакции проводили в соответствии с протоколами производителя. В исследовании использованы первичные антитела: S100 (Dako, Denmark); GFAP (Dako, Denmark), Iba-1. Проведены денситометрические измерения экспрессии S100 при помощи Image J1,46 и подсчет количества меченых GFAP и Iba-1 клеток. Статистическую обработку проводили при помощи t-критерия Стьюдента.

Наблюдаемые реакции позволяют судить, что при дисциркуляторных нарушениях в мозге у крыс выявленные изменения астроцитов и микроглии проявляют тенденцию к обратному развитию. Это можно объяснить тем, что животные, используемые в эксперименте, были практически здоровы и обладали высоким компенсаторно-приспособительным потенциалом. У человека нельзя ожидать подобного обратного развития глиальных реакций, поскольку гипоперфузия мозга/дисциркуляция развивается на фоне изменений сосудистого русла, которые, как правило, еще и прогрессируют. Соответственно, аналогичные изменения глии мозга у человека выступают как вторичные факторы, способствующие нейродегенеративным процессам.

Сравнительно небольшие нарушения гемоциркуляции в мозге при односторонней перевязке сонной артерии способны вызвать активацию астроцитов и микроглии. При этом реакция астроцитов, выявляемая по экспрессии GFAP, более выражена, чем Iba 1+-клеток, что, по всей вероятности, связано с тесным контактом астроцитов с кровенос-

ными сосудами. Значимую роль в изменениях глии играет сенсибилизация мозговыми антигенами, развивающаяся при нарушениях гемоциркуляции в мозге и усиливающая повреждения, вызванные ею. При экстраполяции на человека следует полагать, что сенсибилизация может вносить существенный вклад в развитие повреждений мозга при состояниях, связанных с гипоперфузией.

რეზიუმე

სენსომოტორული ქერქის ასტროციტებისა და მიკროგლიის რეაქცია საძილე არტერიის გადაკვანძვის, ტვინის ანტიგენით სენსიბილიზაციის და მათი კომბინაციის დროს

ლ. იარემენკო, ა. გრაბოვოი, გ. ჩერკასოვი, ტ. ლახტადირი, ს. შეჰელევი

ა. ბოგომოლცის სახ. ეროვნული სამედიცინო უნივერსიტეტი, კიევი, უკრაინა

კვლევის მიზანს წარმოადგენდა ვირთაგვების სენსომოტორულ ქერქში ასტროციტების და მიკროგლიის მდგომარეობის ცვლილებების შეფასება საძილე არტერიის ცალმხრივი გადაკვანძვის, ტვინის ანტიგენით სენსიბილიზაციის და მათი კომბინაციის დროს.

კვლევა ჩატარდა Wistar-ის ხაზის 260-290 გრ მასის 185 თეთრ მამრ ვირთაგვაზე. თავის ტვინის კვლევა განხორციელდა ოპერაციული ჩარევიდან 1, 3, 10, 30 და 90 დღის შემდეგ და, შესაბამისად, სენსიბილიზაციიდან 12 (1), 15 (3), 22 (10), 42 (30), 102 (90) დღის შემდეგ.

იმუნოჰისტოქიმიური რეაქციები ჩატარდა მწარმოებლის პროტოკოლების შესაბამისად. კვლევაში გამოყენებული იყო პირველადი ანტისხეულები: S100 (Dako, Denmark), GFAP (Dako, Denmark), Iba-1. ჩატარებულია S100-ის ექსპრესიის დენსიტომეტრიული გაზომვა Image J1,46-ის გამოყენებით და განსაზღვრულია ნიშანდებული GFAP და Iba-1 უჯრედების რაოდენობა. შედეგები სტატისტიკურად დამუშავდა სტიუდენტის t-კრიტერიუმის გამოყენებით.

განვითარებული რეაქციები მიუთითებს, რომ ვირთაგვების თავის ტვინის დისცირკულაციური დარღვევების დროს ასტროციტებისა და მიკროგლიის ცვლილებებს ახასიათებს უკუგანვითარების ტენდენცია. ეს შეიძლება აიხსნას იმით, რომ ექსპერიმენტში გამოყენებული ცხოველები იყო პრაქტიკულად ჯანმრთელი, მაღალი კომპენსაციურ-შემგუებლობითი პოტენციალით. ადამიანის ორგანიზმში გლიის რეაქციის ასეთი უკუგანვითარებითი ხასიათი მოსალოდნელი არ არის, რადგანაც ტვინის ჰიპოპერფუზია/დისცირკულაცია ვითარდება სისხლძარღვოვანი კალაპოტის ცვლილებების ფონზე, რომელიც, როგორც წესი, ამავე დროს პროგრესირებს კიდეც. შესაბამისად, ადამიანის ტვინის გლიის ცვლილებები ნეიროდეგენერაციული პროცესების ხელშემწყობ მეორად ფაქტორს წარმოადგენს.

ტვინში ჰემოცირკულაციის შედარებით მცირე დარღვევებმა საძილე არტერიის ცალმხრივი გადაკვანძვის დროს შეიძლება გამოიწვიოს ასტროციტების და მიკროგლიის აქტივაცია. ამასთან, ასტროციტების რეაქცია, გამოვლენილი GFAP-ის ექსპრესიით უფრო გამოხატულია, ვიდრე Iba 1+-უჯრედებისა. შესაძლოა, ეს დაკავშირებულია ასტროციტების მჭიდრო კონტაქტთან სისხლძარღვებთან. გლიის ცვლილებებში მნიშვნელოვან როლს ასრულებს სენსიბილიზაცია ტვინის ანტიგენებით, რომელიც ვითარდება ტვინის ჰემოცირკულაციის დარღვევის დროს და აძლიერებს მის მიერ გამოწვეულ დაზიანებებს. ადამიანის ორგანიზმზე ექსტრაპოლაციის დროს უნდა ვივარაუდოთ, რომ შესაძლოა სენსიბილიზაციამ მნიშვნელოვანი წვლილი შეიტანოს ტვინის დაზიანების განვითარებაში ჰიპოპერფუზიასთან დაკავშირებული მდგომარეობების დროს.

THE PHYSIOLOGICAL BASIS FOR ASSESSMENT OF HAEMODYNAMIC PARAMETERS BY MEANS OF ARTERIAL PRESSURE PULSE WAVEFORM ANALYSIS IN PERIPHERAL ARTERIES

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Online control of the major haemodynamic parameters – systemic arterial pressure (SAP) and cardiac output (CO) is an actual problem both in the intensive care and open-chest surgery. The common obstacle in the implication of various clinical approaches for measuring and monitoring of these parameters is the problem of combination of precision, practical simplicity and minimal damage. This can be provided by means of non-invasive pulse waveform analysis in peripheral arteries with further reconstruction of the pressure and flow pulse waveforms in the major arterial vessels [12, 20, 31, 33]. This methodology was suggested long ago [16, 7, 25], but its practical implementation remained limited for decades by the absence of suitable computer software. Progress in computer programming has made this methodology accessible both in clinical practice and experimental research.

Correlation between simultaneous and corresponded periodical processes in the cardiovascular system that follow pulsatile heart performance can be expressed in terms of transfer functions – differential operators that describe such correlations [2, 9, 11, 20, 21, 22, 26, 32, 33, 34, 43]. According to common views [4, 6, 7, 13, 14, 29, 45] this approach is effective only under steady-state conditions in the cardiovascular system. Physiological responses evoked by changes in circulation blood volume (CBV), action of vasoactive agents, surgical manipulations and various pathological states critically increase technical and calculating errors of such estimations [19, 28, 37, 38, 39,