Original article

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Changes in the structure of synaptic intercellular contacts in focal brain lesions

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Materials and methods. The results of treatment of 40 cases of supratentorial focal brain lesions (FBL) were retrospectively evaluated. The cases are divided into groups: 30 gliomas of various degrees of malignancy and 5 consequences of traumatic brain injury TBI, 5 epilepsy. All patients underwent surgical interventions. The synaptic plasticity of axo-dendritic and axo-spiny asymmetric synapses of neurons of the VI-VII layers of the frontotemporal cortex was studied by electron microscopy. Morphometric analysis was carried out on a computer image analyzer using the basic software package and STATISTICA 7 program package.

The results. It was found that the density of synapses decreased in glioblastomas (GB) and craniocerebral injury (CCI). Qualitative changes demonstrate the plasticity of synaptic architectonics due to an increase in the number of perforated synaptic contacts. Maximum thickening and diffuse stratification of the postsynaptic density indicates a violation of the functional capacity of the postsynaptic component of contacts. A decrease in the number of synaptic vesicles was revealed in CCI and GB, with their rearrangement, which is probably a manifestation of synaptic dysfunction. The latter proves the irreversibility of destructive local changes and is a prognostically unfavorable criterion. The risk of formation of destructive-degenerative changes in the synaptic apparatus is 7.64 times higher in DA, 3.17 times higher in GB, and 17.31 times higher in CCI compared to cases of epilepsy, with GB significantly increases by 13.5 times compared to DA. Therefore, the assessment of structural features of neuroplasticity should take into account the morphogenesis of the FBL in comparison with clinical data on the dynamics of recovery of functional ability.

Conclusions. In the zones of invasive growth of gliomas of various degrees of malignancy and in CCI and epilepsy, the indicators of synaptic plasticity differ significantly. The density of placement of synapses is lower in GB and CCI. The probability of irreversible destructive-degenerative changes of synapses according to the number of SVs in FBL correlates with the degree of glioma differentiation with a sensitivity of 81.0% and specificity of 76.0%. According to structural changes of intercellular synaptic connections in tumors, significant differences between the GB and DA variants (the sensitivity of the discriminant model is 85.0%, the specificity is 74.0%) have been proved, which is indirect evidence of the increased tumor growth rate, resulting in the destructive effect on the surrounding brain matter. The obtained results are important in assessing the prognosis of the further course of the disease.

Key words: *focal brain lesions; electron microscopy; synapse*

Introduction

The dynamic functioning of the brain is balanced and regulatory weighted in relation to vital activity at the organism level, with the formation of homeostatic neuroplasticity, which, according to some authors, is based on hierarchical synaptic ordering [1] with qualitative and quantitative intercellular rearrangements and situational changes in intercellular connections. One of the functional components of neuroplasticity is synaptic mobility with changes in synaptic structure (the number, length and configuration of their active zones, number of dendritic spines), formation of new synapses, mechanisms for regulating the synaptic transmission efficiency, which ensures adaptive activity of brain functions and has a clear morphological component [2]. Experimental studies have proved that low regenerative property of the brain is not due to internal limitations of the potential of neural progenitor cells, but probably reflects the absence of regulatory signals from the microenvironment, which are necessary for specialized functional neuronal differentiation [3]. One of the morphological and functional aspects of damage to

neurons and the ability of intercellular interactions is disruption of axonal transport due to pathological factors, in particular, hypoxia. As a result, destructive changes in intercellular connections occur, which lead to the development of clinical syndromes. It has been proved that astrocytes, due to the morphogenesis of neurovascular barrier formation, directly affect energy metabolism, and glia provide regulation of neuron activity and modulation of synaptic transmission activity with various extracellular signaling molecules. Different types of glial cells have distinct phenotypic capabilities depending on functional rearrangements and needs (migration, specialization, neuronal degradation). Adaptation to changes occurring in various brain cells and structures is the basis of neuroplasticity [4, 5].

A comparative study of ultrastructural characteristics of the synaptic apparatus will help to form an idea of differences in the structure of intercellular interactions in various types of intracranial pathology, with the selection of probable adverse factors. This proves the relevance of studying structural changes at different levels for different types of brain pathology with the formation of extensive pathological foci.

Purpose: to evaluate changes in the structure of synaptic contacts in various types of focal brain pathology.

Materials and methods

Study participants

The work is based on a retrospective analysis of the results of diagnosis and treatment of 40 patients with focal brain lesions (FBL) in the departments of neurotrauma, intracerebral tumors and functional neurosurgery of the Institute of Neurosurgery named after Acad. A.P. Romodanov, Ukraine in 2015–2020.

Male to female ratio was 2:1. The age of patients at the initial admission ranged from 22 to 64 years.

Informed and voluntary written consent to participate in the study was obtained from all patients.

The study was approved by the Committee on Ethics and Bioethics of the Institute of Neurosurgery named after acad. A. P. Romodanov, Ukraine (Minutes №3 date 06.06, 2019).

Inclusion criteria:

- presence of FBL;
- no history of neurosurgical operation;
- instrumental verification of the diagnosis of FBL;
- the patient's performance status is at least 70% on the Karnofsky scale;
- age over 18 years;
- patient's voluntary consent to participate in the study.

Exclusion criteria from the study:

- presence of gross somatic pathology (a state of decompensation);
- absence of multispiral computed tomography (MSCT) and magnetic resonance imaging (MRI) data of the brain;
- the patient's performance status <70% according to Karnofsky;
- age less than 18 years.

40 observations of supratentorial focal brain lesions in adults were selected.

The diagnosis was made on the basis of the analysis of complaints, clinical symptoms, results of instrumental examination. In all observations, the diagnosis was verified by the data of neuroimaging methods and results of morphological examinations.

Characteristics of groups

Cases were divided into groups. The study (I) group included 30 patients with gliomas of various degrees of malignancy. Two experimental groups were formed: Group II - 5 patients with consequences of traumatic brain injury (TBI), including intracerebral foci of contusion and hemorrhages, Group III - 5 patients with pharmacoresistant epilepsy.

Surgery in TBI was performed according to vital indications: the brain matter was examined during the surgical approach (around the contusion area). In epilepsy, indications for surgical intervention were determined by epilepsy diagnostic and treatment group of specialists.

All patients gave informed consent for pathological tissues research removed during surgery and anonymous use of certain personal data.

Study design

All patients underwent complex clinical and neurological (general clinical examinations, assessment of neurological status and its dynamics, examinations of related specialists) and instrumental examination at admission, during examination, treatment and follow-up. The initial condition during hospitalization was assessed according to the Glasgow coma scale [6] and the Karnofsky scale. On admission, MSCT of the brain was performed for all patients, MRI - 83.7%. To control treatment efficacy, patients underwent MRI monitoring (in 69.5% of cases) and MSCT (in 16.4%).

All patients underwent surgical interventions of various types and volume. Postoperative complications, in particular prolonged glioma growth, were recorded in 17 (56%) patients, mainly with malignant gliomas (Grade III and IV).

To objectively assess the presence of ultrastructural changes in brain tumors of macroglial histogenesis, tissue was examined (according to the findings of bioptates in the pathomorphology department): gliomas of various degrees of malignancy - 30, of which diffuse astrocytomas - 10, anaplastic astrocytomas - 10, glioblastomas - 10, TBI with the formation of contusion foci – 5, pharmacoresistant epilepsy – 5.

Synaptic plasticity of axo-dendritic and axo-spiny asymmetric neuronal synapses in the areas of invasive growth of glial tumors of various degrees of malignancy (VI-VII layer of the cerebral cortex of frontotemporal localization) and in other intracranial pathological conditions was studied (TBI, epilepsy).

Statistical analysis

Morphometric analysis was carried out on digital microphotographs obtained using electron microscopes EM-400T (PHILIPS, Netherlands) and PEM-100-01 (SELMI, Ukraine), on a computer image analyzer

This article contains some figures that are displayed in color online but in black and white in the print edition

SAI-01AVN using Kappa opto-electronics GmbH (Germany) software at 17,000 and 22,000 times magnification. In each of the pathological focal lesions, 100 synaptic profiles were analyzed according to the following parameters: the density of synapses on a test area of 100 μm² of the neuropil, the number of synaptic vesicles in the presynaptic terminals of the synapse, the thickness of the postsynaptic density (PSD), synaptic active zone length (AZL). For each nosology, a total area of 500 μm² was analyzed. To analyze synapses of different configurations, they were divided into three main categories: flat, convex and concave. In a concave synapse, the presynaptic terminal protrudes into the postsynaptic element, in a convex synapse, the postsynaptic profile protrudes into the presynaptic element. A perforated synapse was defined as a synapse with AZL interval, as recommended by domestic researchers [7].

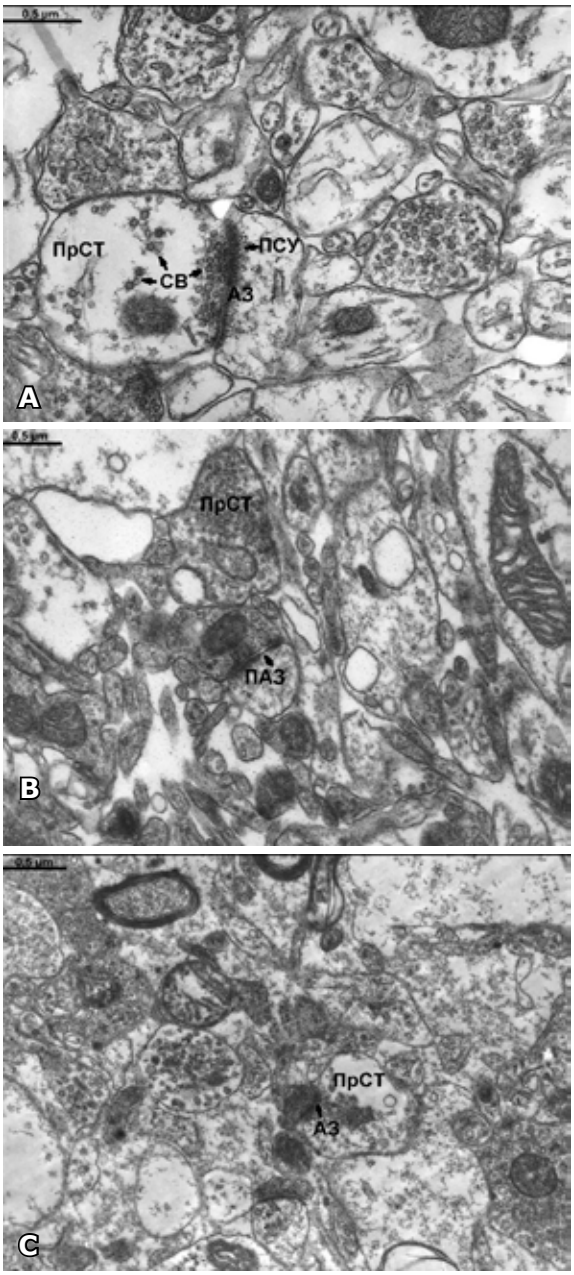

Fig. 1. Synapses in various pathological conditions:
A - TBI. Flat non-perforated synapse. Decrease in the number of synaptic vesicles (SVs, arrows) and their redistribution in the presynaptic terminal (PrST);
B - Epilepsy. Convex perforated synapses (PAZ - perforated active zone). The presynaptic terminal is filled with synaptic vesicles;
C - DA. Convex non-perforated synapses (AZ - active zone). Scale – 0.5 μm

The normality of data distribution was checked using the Shapiro–Wilk test. Since the test did not confirm that the distribution law was normal for a third of the cases, nonparametric Kruskal-Wallis rank discriminant analysis and pairwise comparisons of groups in the Kruskal-Wallis test dialog were used for multiple intergroup comparisons of mean values, which is equivalent to multiple comparisons using the Mann-Whitney U-test [8].

Parametric methods of MANOVA variation statistics and a licensed software package were used for statistical processing of the data obtained. Predicting the probability of the risk of damage to the synaptic apparatus in intracranial pathologies was carried out by logistic regression analysis with the calculation of the odds ratio (OR) with a 95% confidence interval (CI). Statistical significance (p) was assessed by Pearson's chi-square test. Discriminant analysis was used to objectify the presence of differences between the studied groups [9].

Results and discussion

The synaptic plasticity of axo-dendritic and axo-spiny asymmetric synapses of neurons in the zones of invasive growth of glial tumors of various degrees of malignancy (VI-VII layer of the cerebral cortex of the frontotemporal localization) and in other intracranial pathological conditions (TBI, epilepsy) as a manifestation of mediated signs of hypoxia was studied.

It was found that synaptic density per 100 μm² of neuropil was statistically significantly decreased only in the TBI group (Kruskal-Wallis test; p=0.02 compared to the epilepsy group). The synaptic density in the groups with diffuse astrocytomas (DA) and anaplastic astrocytomas (AA) were almost indistinguishable. In the group of patients with epilepsy, this indicator slightly increased (Kruskal-Wallis test; p=0.002 compared to the TBI group). The plasticity of synapse architectonics in pathological conditions was largely preserved, in particular, due to an increase in the number of perforated synaptic contacts in epilepsy, DA and AA ***(Fig. 1, Table 1).***

The changes in presynaptic terminals detected in FBL indicate the dysfunction of mechanisms of synaptic vesicles approaching the presynaptic membrane ***(Fig. 2A,B,C)***, are an indicator of changes of mediator release, negatively affect synaptic transmission and cause functional asynapsis: morphologically, the synapse still exists, but does not function ***(Fig. 2G)***.

A statistically significant decrease in the number of synaptic vesicles was observed in the TBI and GB groups, as well as their rearrangement inside the terminals ***(Table 2A, Fig. 3A)*** and a decrease in active zone length of the synapse in the AA group ***(Table 2B, Fig. 3B)*** may indicate disruption of the recycling process of synaptic vesicles and reflect manifestations of synaptic

Table 1. Ratio of synapses of different configurations (n=500)

Nosology	Density per 100 μm² *	Convex	Flat	Concave	Perforated
DA	18 (17;19)	50	33	0	17
AA	14 (13;15)	57	22	0	21
GB	19 (17;21)	32	68	0	0
EPI	22 (18;23)	38	24	19	19
TBI	8 (7; 9)	25	38	37	0

Note: Median and interquartile range are given; DA - diffuse astrocytoma; AA – anaplastic astrocytoma; GB - glioblastoma; EPI – epilepsy; TBI – traumatic brain injury.

dysfunction after mediated ischemic impact. Maximum thickening and diffuse stratification of the PSD, present in cases of GB and TBI ***(Table 2C, Fig. 3C)***, indicate a disruption of the receptor function of the postsynaptic component of contacts in such cases.

For discriminant analysis, 4 morphometric indicators were used, which characterized the plasticity of synapse architectonics in the zone of invasive spread of glial tumors. Two discriminant functions were required to detect differences between study groups. The results of the analysis of discriminant functions for study groups depending on the degree of tumor malignancy (DA Grade II — GB Grade IV) are presented ***(Fig. 4)***. As evidenced by the analysis, discrimination between groups according to the nosology was highly significant. Analysis of the contribution of each variable to the total discrimination depending on the nosology in the DA-GB study groups by Wilks' lambda revealed the greatest contribution of the variable «the number of synaptic vesicles in presynaptic terminal» ***(Table 3)***.

Based on the morphological criteria of changes in the structure of synapse, we managed to statistically

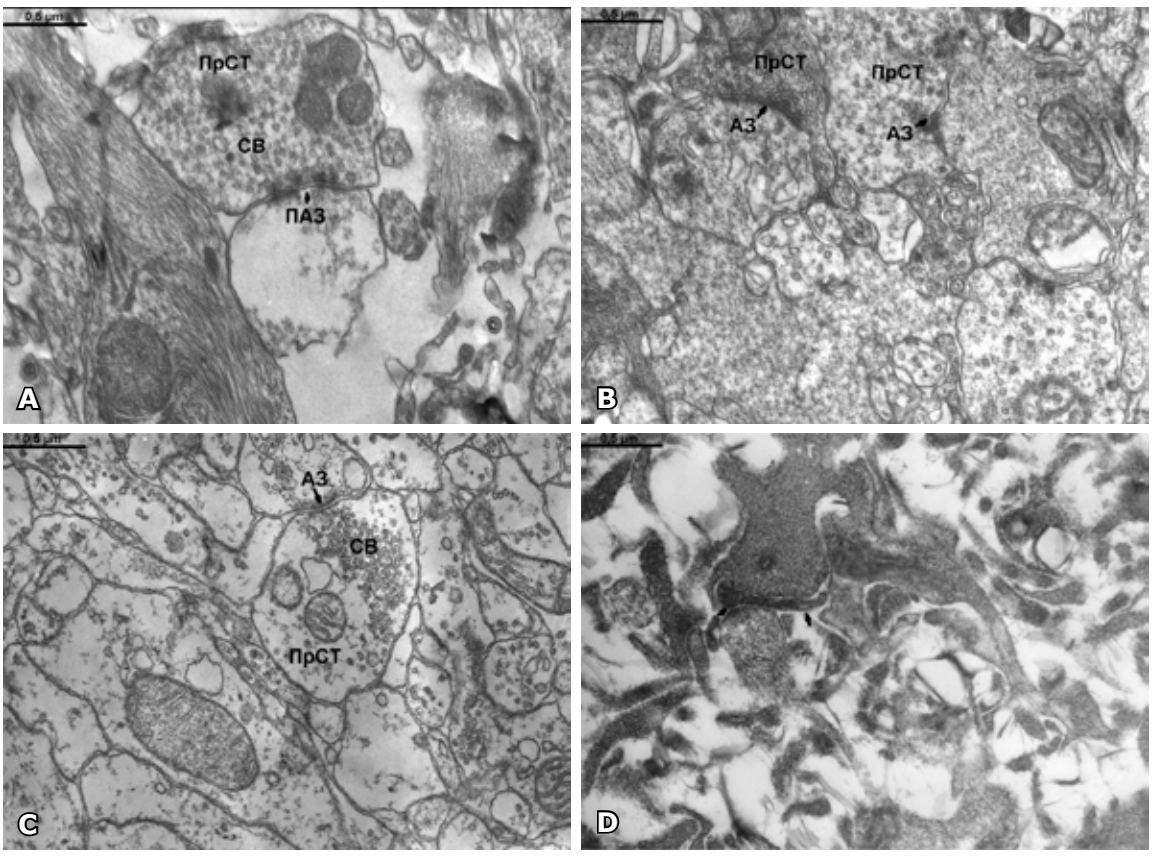

Fig. 2. Synapses of different configurations: A – DA. Perforated (arrow) flat synapse on the background of neuropil edema; B – AA. Convex non-perforated synapses; C – GB. A decrease in the number of SVs on the background of swelling of synaptic terminals; D - EPI. The process of the tumor astrocyte invades between presynaptic and postsynaptic terminals (arrow), blocking synaptic transmission. Scale – 0.5 μm

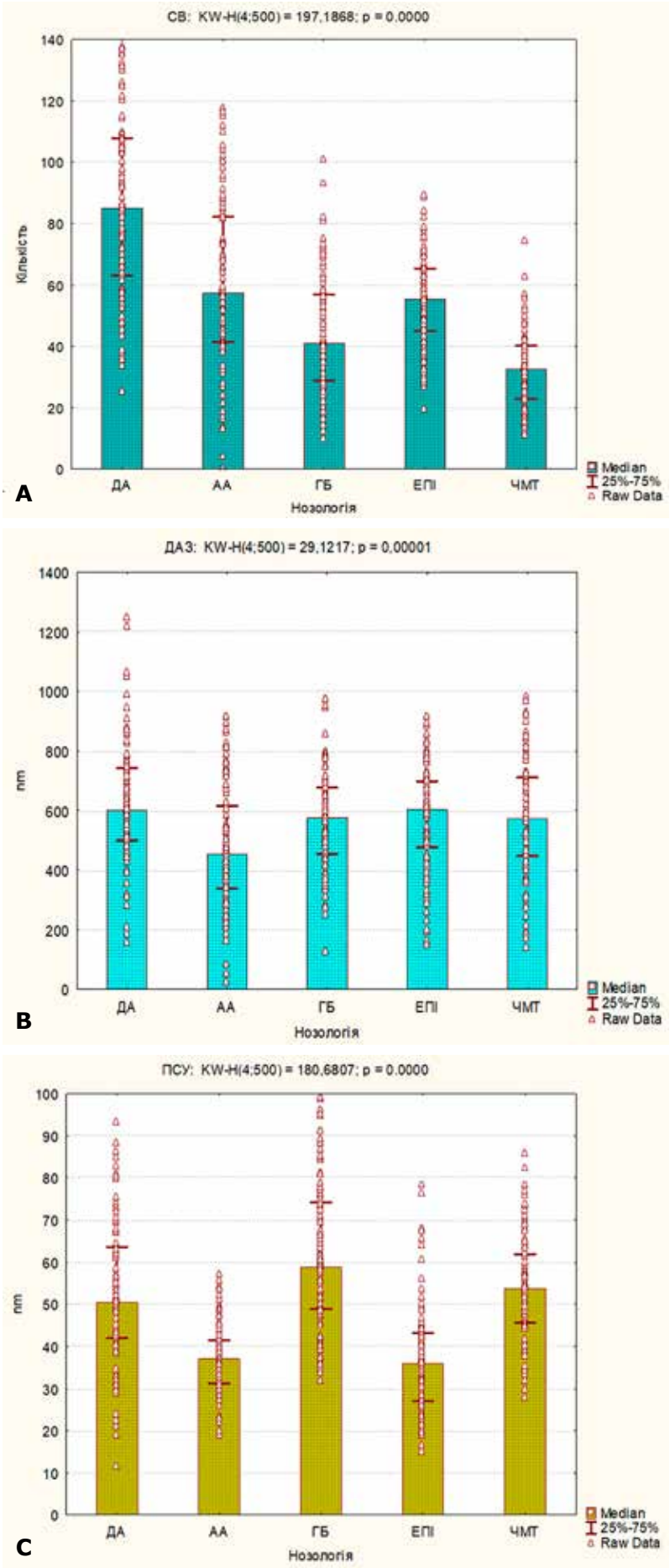

Fig. 3. Differences in quantitative indicators of synapses between study groups (Kruskal-Wallis test): A - the number of synaptic vesicles in the presynaptic terminal; B – active zone length of the synapse, nm; C – postsynaptic density, nm

Table 2A. Number of synaptic vesicles in the presynaptic terminal

SV	DA 85 (63; 108)*	AA 57 (42; 82)*	GB 41 (29; 57)*	EPI 55 (45; 65)*	TBI 33 (23; 40)*
DA		P<0,0001	P<0,0001	P<0,0001	P<0,0001
AA	P<0,0001		P<0,0001	p=1,0	P<0,0001
GB	p<0,0001	P<0,0001		p=0,002	p=0,002
EPI	P<0,0001	p=1,0	p=0,002		P<0,0001
TBI	P<0,0001	P<0,0001	p=0,002	P<0,0001	

Table 2B. Active zone length of the synapse, nm

AZL	DA 601 (500; 742)*	AA 456 (338; 617)*	GB 576 (456; 677)*	EPI 603 (476; 698)*	TBI 573 (448; 711)*
DA		p<0,0001	p=0,78	p=1,0	p=1,0
AA	p<0,0001		p=0,008	p=0,002	0,002
GB	p=0,78	p=0,008		p=1,0	p=1,0
EPI	p=1,0	p=0,002	p=1,0		p=1,0
TBI	p=1,0	p=0,002	p=1,0	p=1,0	

Table 2C. Postsynaptic density, nm

PSD	DA 50 (42; 64)*	AA 37 (31; 41)*	GB 59 (49; 74)*	EPI 36 (27; 43)*	TBI 54 (46; 62)*
DA		p<0,0001	p=0,009	p<0,0001	p=1,0
AA	p<0,0001		p<0,0001	p=1,0	p<0,0001
GB	p=0,009	p<0,0001		p<0,0001	p=0,51
EPI	p<0,0001	p=1,0	p<0,0001		p=0,0001
TBI	p=1,0	p<0,0001	p=0,51	p<0,0001	

*Note: * Median and interquartile range are given; DA - diffuse astrocytomas; AA - anaplastic astrocytomas; GB - glioblastoma; EPI - epilepsy; TBI – traumatic brain injury.*

significantly distinguish between GB and DA, removing from the discriminant model the nosology of AA with low discrimination sensitivity ***(Table 4)***, by applying a multiple discriminant analysis using two study groups and three morphometric indicators in the zone of tumor invasion. The data distribution was carried out with the statistical model sensitivity at the level of 80% (p<0.0001).

The probability of destructive and degenerative changes in synaptic apparatus sructure in gliomas in the early postoperative period depending on the degree of tumor malignancy (DA and GB) was calculated using logistic regression analysis with sensitivity of 81.0% (95% CI - 72.2–87.5%) and specificity of 76.0% (95% CI – 66.8–83.3%) ***(Table 5)***. This makes it possible to consider the structural changes of synapses as a prognostic criterion of the course — the severity of destructive influence of gliomas and local asynapsis.

The selection of features significantly associated with the risk of formation of structural signs of destructive and degenerative changes of the synaptic apparatus in FBL by applying the method of constructing multivariate logistic regression models was carried out. One significant feature was identified - the number of synaptic vesicles in presynaptic terminals ***(Table 6)***.

Consequently, the risk of destructive and degenerative changes of the synaptic apparatus in DA is statistically significant which is 7.64 times higher compared to cases of epilepsy, in GB - 3.17 times, in TBI - in 17.31 times, in GB compared to DA - in 13.5 times ***(Table 7)***. The morphometric data obtained by us prove that when assessing the structural features of neuroplasticity, one should take into account the pathogenesis of the pathological process, the specificity of the brain damage zone, the effect of exogenous and endogenous influences in comparison with personalized clinical data regarding the risks of compensatory-adaptive dominance and destructive-degenerative processes in the central nervous system (CNS) and the dynamics of functional ability recovery.

Neuroplasticity implies consolidation of changes that have arisen and is the pathogenetic mechanism of compensatory functioning of the nervous system regarding the consolidation of broken and functionally capable intercellular connections of the individual system [10]. In the central nervous system, the processes of neuroplasticity are constant and at different levels, involving functionally specialized neuronal modules in different parts of the central nervous system. Adverse and pathological conditions distort

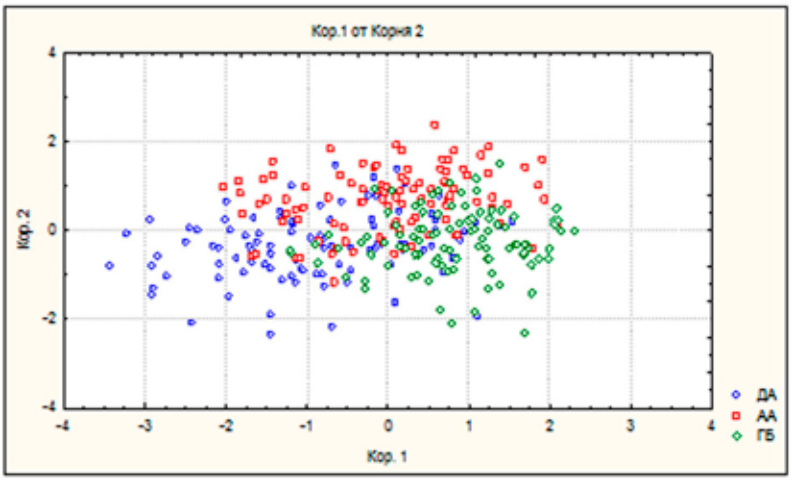

Fig. 4. Scatter plot of discriminant functions in a subgroup of gliomas depending on the degree of tumor malignancy (DA Grade II - GB Grade IV)

Table 3. Results of discriminant functions analysis for morphometric parameters of synaptic plasticity (MANOVA) (model variables - 3, λ - 0.57, Approx. F (2,19) =73.4, p<0.0001)

	Wilks' lambda	**F-remove (2,295)**	**Statistical significance level, p**
Number of SVs	0,78	64,37	<0,0001
PSD, nm	0,621	20,94	<0,0001
SAZ nm	0,59	12,6	<0,0001

Table 4. Classification matrix of multiple factor analysis of intergroup differences according to indicators of synapse structure between diffuse astrocytomas and glioblastomas (discriminant function)

	Percentage of correct classifications	**DA**	**GB**
DA	74	74	26
GB	85	15	85
Total	80	89	111

* Sensitivity of the discriminant model was 85% (95% CI – 76.7–90.7%), specificity – 74% (95% CI – 64.6–81.6%). The overall predictive significance was 80%.

Table 5. Logistic regression analysis classification matrix of intergroup differences according to indicators of synapses between diffuse astrocytomas and glioblastomas

	Percentage of correct classifications	**DA**	**GB**
DA	76	74	26
GB	81	15	85

Table. 6. Criteria for predicting the risk of destructive and degenerative changes in the synaptic apparatus in focal brain lesions by the method of multivariate logistic regression models

	Beta	**Std.Err.**	**Level of statistical significance, p**
PSD DA	-0,023	0,037	0,542
AZL DA	0,036	0,037	0,336
Number of SVs	-0,568	0,037	<0,0001

Table 7. Risk factors for destructive and degenerative changes of the synaptic apparatus in focal brain lesions

Study group/ factorial feature «Number of SVs»	**Odds ratio (95% CI)**	**Level of statistical significance, p**
DA	7,64 (4,041–14,44)	**< 0,0001**
AA	1,22 (0,701–2,13)	0,045
GB	3,17 (1,78–5,65)	**< 0,0001**
TBI	17,31 (8,559–35,01)	**< 0,0001**
EPI	1	
DA	1	
GB	13,5(6,85–26,60)	**<0,0001**

compensatory and plasticity and cause the emergence and consolidation of pathological changes, and therefore have a morphogenetic component. Different parts of the CNS have different neuroplastic potential. It has been proved that the cerebral cortex is the most plastic with a variety of cellular modules. The organization of higher specialized functional cortical representations and collateral parallel and reciprocal neural networks of zones of functional overlap (cognitive, complex motor acts, speech) are of certain importance [11].

Asynapsis, predominantly functional, is believed to underlie the clinical manifestations of TBI, in particular cerebral concussion. The morphological substrate of a cerebral concussion is colloidal imbalance in neurons, which leads to swelling of synapses and block of afferent and efferent nerve impulses. In severe cases, there is a violation of the ultrastructure of axial cylinders of neurons, which causes dislocation changes with axonotomy and the formation of irreversible changes in the leading pathways at different levels: refraction and rupture of axons with the exit of axoplasm from a neuron with the formation of microglial nodules and axons with focal demyelination (axonal damage) [12]. In the case of progression and invasive spread of gliomas, such structural changes are longer and, in our opinion, have individual metabolic characteristics.

The limbic system and motor cortex of the cerebral hemispheres have been proved to have the highest plasticity potential [13-15]. Methods of studying neuroplasticity include MRI, positron emission and single photon emission tomography, electrophysiological studies, transcranial magnetic stimulation, morphological (histological and ultrastructural) methods [16, 17]. In clinical practice, electroencephalography, the method of evoked potentials, in particular cognitive evoked potentials, somato-sensory evoked potentials, and functional MRI are used to assess neuroplasticity [18,19]. Each of the methods has advantages and disadvantages, they complement each other's results and allow assessing the patient's condition as a whole. High-frequency electrical stimulation of deep brain gray matter nuclei is able to modulate the function of the cortico-subcortical tracts, improving motor, cognitive and behavioral functions in Parkinson's disease, dystonia, essential tremor, pharmacoresistant epilepsy, etc. [20].

As evidenced by clinical experience, in the case of FBL a significant volume of resumption of functioning only due to activation of «spare» representations is insufficient. It has been proved that the neuroplastic potential is different in different parts of the brain: the cerebral cortex is the most plastic zone due to the heterogeneity of the cell population and the peculiarities of intercellular contacts and connections [21]. Therefore, the study of possible activation and involvement of various zones of a personalized functional neural network, both around the pathological center (perifocal zone) and in remote areas, is an urgent but extremely difficult problem. Treatment of patients with cerebrovascular and post-traumatic aphasias is associated with difficulties [13,22]. The possibility of a limited capacity of neuroplasticity in these cases of special modality-specific functions is assumed. Morphological studies make it possible to calculate and predict the risk of loss of functions and limit the phenomenon of neuroplasticity. This is fundamentally important for substantiating rehabilitation measures and social adaptation programs for such patients.

According to modern concepts, both true recovery and compensation of impaired functions in brain damage are based on mechanisms of neuroplasticity. As noted by clinicians, the rehabilitation potential of renewal of higher mental functions is determined by the features of the development and course of the disease, structural and functional characteristics of brain matter and vascular system, the features of sanogenesis, and compensation possibilities. An important role is played by the individual resource of plasticity [23]. Studying morphological changes in relation to the implementation of mechanisms underlying neuroplasticity at the macro-, micro-, and ultrastructural levels, it is possible to single out unfarorable factors of irreversible destructive changes and assess the probability of activity and rate of recovery of lost functions as a neuroplasticity phenomenon. Methods of assessing the morphogenesis of neuroplasticity (clinical, neuroimaging, electrophysiological, biochemical) require a dynamic evaluation, and morphological methods require a mandatory clinical-instrumental comparison.

It has been established that TBI is an important factor in cognitive impairment. A 10-year meta-analysis demonstrated, using a significant clinical dataset, that the risk of developing Alzheimer's disease is 60% higher after TBI. [24]. A fundamental study of patients confirmed the importance of TBI as a risk factor for developing Alzheimer's disease [25]. Separate studies indicate the probability of mild TBI as a risk factor for the development of neurodegenerative changes in the brain [26]. Therefore, when studying the structural characteristics and morphogenesis of neuroplasticity, one should take into account the type of pathology, the specificity of the functional area of the brain, the dominance of hemispheres, the effectiveness of physical and mental state with a complex diagnostic dynamic approach to identify statistically significant criteria for predicting the course of the disease and the possibility of functional recovery. The concept of neuroplasticity and the state of synaptic homeostasis requires further development and multidisciplinary well-coordinated syntonic interaction.

Thus, the study of the links of morphogenesis and pathogenesis in relation to the mechanisms of neuroplasticity will help improve treatment strategies and substantiate the feasibility of using the latest intraoperative monitoring technologies to restore lost functions in patients with FBL. The concept of neuroplasticity due to the adaptive transformation of the synaptic system plays a key role in predicting the functional recovery and decent quality of life in FBL due to the polyfunctional mechanism of neuroplasticity under the condition of careful preoperative planning of volumes and methods of influence in the surgical treatment of intracerebral pathological processes.

Conclusions

1. Axo-dendritic and axo-spiny asymmetric synapses of neurons in the zones of invasive spread of glial tumors of various degrees of malignancy in TBI and epilepsy are statistically significantly different.

2. The density of synapses on an area of 100 μm^2 of the neuropil differs statistically significantly in GB and TBI. Gliomas II and III degrees of malignancy are almost identical in terms of morphometric parameters.

3. The risk of destructive and degenerative changes of the synaptic apparatus increased significantly in DA by 7.64 times compared to cases of epilepsy, in GB – by 3.17 times, in TBI – by 17.31 times, in GB compared to DA – by 13 ,5 times.

4. Using the method of logistic regression analysis, the probability of increase and severity of destructive and degenerative changes in the synaptic apparatus was estimated by the number of synaptic vesicles in the preterminals of the synapse in intracranial pathologies in the early postoperative period, depending on the degree of glioma differentiation (DA/GB) with sensitivity of 81.0% (95% CI – 72.2–87.5%) and specificity of 76.0% (95% CI – 66.8–83.3%).

5. Statistically significant differences between glioma variants (glioblastomas and diffuse astrocytomas) have been proved using multivariate discriminant analysis on structural changes of intercellular synaptic connections in the area of invasive tumor spread (sensitivity of the discriminant model – 85.0% (95% CI – 76.7)) -90.7%), specificity — 74.0% (95% CI — 64.6–81.6%)), which is indirect evidence of tumor growth rate and its destructive effect on the surrounding brain matter.

Disclosure

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

The written informed consent was obtained from each patient.

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