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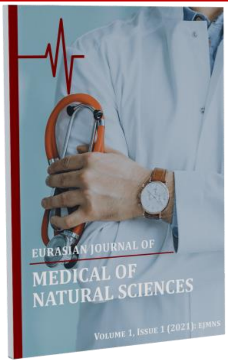

COMPREHENSIVE ASSESSMENT OF MILD AND MODERATE TRAUMATIC BRAIN INJURY BY NEUROIMAGING AND NEUROPSYCHOLOGICAL TESTING

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ABSTRACT

Traumatic brain injury (TBI) remains one of the most pressing problems of modern neurology and neurosurgery, representing an important medical and social problem due to the high prevalence, significant mortality and disability of victims, mainly of young, able-bodied age. According to the World Health Organization, more than 10 million people worldwide suffer from TBI every year, with about 80% of all cases being mild to moderate injuries.

Introduction. Of particular importance is the problem of timely and accurate diagnosis of mild and moderate TBI, since it is these forms of traumatic brain injury that are often characterized by a blurred clinical picture and ambiguity of diagnostic criteria. However, even mild TBI can lead to the development of persistent neurological and cognitive impairments that significantly affect the quality of life of patients and their social adaptation.

Modern neuroimaging methods, including computer and magnetic resonance imaging, functional MRI, and diffusion tensor imaging, open up new possibilities in assessing structural and functional changes in the brain during TBI. However, the isolated use of neuroimaging methods alone does not always allow us to fully assess the extent of brain damage and predict the outcome of injury.

Neuropsychological testing, as an integral part of a comprehensive diagnosis, makes it possible to identify subtle cognitive impairments and emotional-behavioral disorders that may not have clear structural correlates in neuroimaging. The integration of neuroimaging research results and neuropsychological testing data creates the basis for a more accurate assessment of patients' condition and prediction of TBI outcomes.

The socio-economic consequences of mild and moderate TBI are significant: the costs of treatment and rehabilitation, temporary or permanent disability, and the need for social adaptation place a significant burden on the healthcare system and society as a whole. According to experts, the economic damage from TBI and its consequences amounts to several percent of the gross domestic product of developed countries. The development of new neuroimaging technologies and the improvement of neuropsychological diagnostic methods opens up prospects for creating more effective examination algorithms for patients with mild and moderate TBI. The use of modern machine learning and artificial intelligence methods to analyze complex data can significantly improve the accuracy of diagnosis and prediction of injury outcomes. The need to develop standardized protocols for comprehensive examination of patients with mild and moderate TBI, including both neuroimaging and neuropsychological research methods, determines the relevance of this problem and the prospects for further research in this area.

The general structure of neurotrauma is dominated (80-90%) by traumatic brain injury (TBI) of mild to moderate severity. Despite the relatively favorable prognosis for recovery of mental activity, in these cases about 10-15% (according to some data up to 30%) of patients with mild and about 50% of patients with moderate TBI show chronic (persisting for several years after injury) cognitive impairment. However, the patient's quality of life and social readaptation largely depend on the preservation of cognitive functions. Therefore, the role of a neuropsychologist in assessing the severity, structure of the defect and the dynamics of the restoration of cognitive functions (primarily control functions, memory, speech) is extremely important for subsequent rehabilitation. Other important tasks of a neuropsychologist at the TBI clinic include participating in the study of the brain organization of functions to help plan surgery and determine the prognosis of recovery, monitoring the effects of pharmacotherapy and neurosurgery. The solution of the described tasks has both practical and theoretical aspects.

The features of pathology in brain injury determine the specifics of research in this area. Thus, the nature of physical (contact and inertial, causing predominantly local and diffuse pathology, respectively) effects at the time of injury, as well as a cascade of reactive neurophysiological changes after injury, determine the presence of not only local, but also cerebral disorders in patients. Since the symptoms of cerebral disorders are an integral part of the TBI symptom complex, the study of the symptoms of local (focal) brain pathology and specific hemispheric syndromes in patients with TBI requires special approaches.

Focal cortical and subcortical contusions and diffuse axonal injury (DAP) are the most common types of primary brain damage. The cause of focal bruises is most often shock-resistant mechanisms. DAPS occur as a result of rotation, braking, or acceleration mechanisms that cause stretching and damage to axons. The semiovial center, the inner capsule, the corpus callosum, and the brainstem are the most vulnerable to this type of injury.

Anatomical features of certain areas of the brain (frontal areas, corpus callosum, deep median structures, including the basal ganglia and anterolateral regions, as well as the temporal regions and the hippocampus) contribute to their particular vulnerability to TBI. This leads to the presence of "nuclear" symptoms present in the picture of almost any TBI (impaired control functions, attention, memory, neurodynamics, and speech disorders). However, due to the individual combination of numerous factors (the nature and severity of the injury, the patient's premorbidity, genetic profile, etc.), it is difficult to identify a single neuropsychological syndrome in brain injury. Moreover, almost any pattern of cognitive impairment can be detected in this category of patients.

It is difficult in most cases to accurately diagnose the degree of microstructural axonal damage at an early stage after injury by means of routine CT or MRI, since these studies do not always allow visualizing the disorders that have occurred. Most researchers recognize the rather high informative value of diffuse tensor examination (DT-I) in MRI. The method of diffuse tensor MRI (DT-MRI) makes it possible to evaluate the diffusion characteristics of the medium under study and the direction of water diffusion (anisotropy) and, thus, provides information about the degree of preservation of white matter tracts. Diffusion anisotropy is heterogeneous in different areas of the white matter and reflects differences in fiber myelination, diameter, and orientation. Fractional anisotropy (FA) characterizes the spatial orientation of fibers and indicates the size of the excess of diffusion along one direction compared to others and is used as a quantitative indicator of the degree of diffusion anisotropy. Pathological processes that change the microstructure of white matter, such as rupture, disorganization and separation of fibers, combined with rupture of myelin, retraction of neurons, increase or decrease in extracellular space, affect the indicators of diffusion and anisotropy.

The most informative and most commonly used indicators in the CT study are FA and average diffusivity (SD). Water diffusivity provides important information for determining the mechanisms of changes in white matter after damage to myelin or loss of axons. FA decreases in most brain tracts after TBI. Thus, according to long-term catamnestic studies, diffuse atrophy of the corpus callosum, which is most vulnerable to traumatic effects, is noted.

The application of the most promising approach to date to the study of functional brain changes in TBI by recording brain activity (using fMRI) during the performance of cognitive tasks requires consideration of a number of emerging problems. Thus, head movements during fMRI recording may coincide with the expected brain response to a stimulus and be misinterpreted as brain activation corresponding to the activity under study.

In fMRI studies, when analyzing the activation of "areas of interest" pre-determined by the researcher, it should be borne in mind that cognitive activity is carried out with the participation of a functional system of several brain regions working in concert, rather than a single brain region chosen by the researcher. Analysis of the trajectories of brain activation (path analysis, partial least squares) allows us to determine the degree and direction of the relationship between brain structures and assess the functioning of brain networks [29]. In this situation, the concepts developed in neuropsychology about the systemic structure of higher mental functions and their connection with the work of certain brain departments are of great importance.

The choice of experimental design during fMRI studies depends on the nature of the research task. If a detailed analysis of cognitive processes is necessary, the event-related reaction paradigm is the most appropriate (it allows you to identify individual patterns of short-term brain activation in response to single stimuli from a general hemodynamic reaction), which has a high spatial and temporal resolution, allowing you to record episodes of short-term activation and compare it with the quality of activity, as well as to record the activation of areas, included in one functional system. The block design, which allows you to get an indicator of average brain activation when performing a task over a certain time period, has become widespread due to its simplicity and brevity.

To increase the reliability of fMRI data, additional factors affecting brain activation must be taken into account. Thus, it is known that an increase in cognitive load can change both the degree and localization of brain activation. For example, an increase in the volume of the same type of load on working memory in healthy subjects causes an increase in right-hemisphere activation, while under normal conditions, performing a working memory test is associated with frontal activation. Patients with TBI in a similar situation show an activation pattern similar to the norm due to increased activation. When conducting research on the dynamics of recovery after injury, it is important to take into account that the novelty of the stimulus affects the degree and localization of brain activation (the more familiar the stimulus, the less it causes activation). The emotional state of the subject also affects the features of brain activation. Indeed, structures such as the amygdala, the anterior cingular cortex, and the frontal lobes are involved in both cognitive and emotional processes.

Due to the high variability of brain activation patterns during cognitive activity in normal and even greater extent in patients with TBI, random effects analysis is more informative when analyzing the obtained fMRI data, which allows us to obtain a picture of the most common foci of activation in the study group of patients instead of the "average" activation pattern when using the analysis. fixed effect analysis.

Various factors influence the correctness of activation assessment in neuroimaging studies. Thus, it is necessary to take into account that the heterogeneity of disorders and the appearance of some of them only over time, as well as the variation in time from the moment of injury to the study, affect the results obtained. fMRI, being one of the most common methods (due to its high resolution, relative accessibility, and lack of radiation exposure), is not sensitive enough in certain situations, and is also susceptible to artifacts in the visualization of the ventral frontal and temporal regions.

Early studies using fMRI and positron emulsion tomography (PET) used stimuli organized into clusters. More modern fMRI technologies allow the use of event-related design, where individual samples are not grouped into clusters and can be submitted and analyzed one at a time. The cluster interlocked design provides good signal sensitivity and is indispensable in the study of cognitive processes that have their own temporal dynamics (for example, the process of maintaining attention for a certain period of time). However, an event-related design is preferable because it avoids the negative effects of grouping multiple samples into one block.

Proper organization of the study requires comparing the patterns of brain activation during the experimental task with those during the control task. The latter should be consistent with the experimental task in all respects, except for the parameters of interest to the researcher. It is extremely difficult to provide such conditions in MRI studies. For example, tasks that require deactivation are often used as control tasks (for example, visual fixation, which in itself is a special type of activity that produces a certain pattern of activation of brain structures). When examining patients with an altered pattern of brain activation who have difficulty completing test tasks, it is difficult to determine whether the changes in the pattern of brain activation are related to trauma or variation in the experimental task.

It is known that achieving the same result when performing the same task can normally be achieved by involving different brain functional systems, the components of which can be activated simultaneously, which makes it difficult to determine which brain regions belong to which functional system. The use of tasks for which the pattern of brain activation is normally well studied makes it possible to better interpret the results of patients with TBI. At the same time, the quality of tasks performed by patients should be comparable to that in the control group. Activation of the eponymous areas in normal conditions and in patients indicates that these areas are involved in the performance of this task and are probably necessary links for its completion. The areas that are activated in healthy people, but not in patients, are most likely not necessary for the task or belong to an alternative functional system. Brain regions that are activated only in patients are more likely to be untrained or suppressed in healthy people.

It is known that post-traumatic damage to the white matter is associated with the occurrence of cognitive impairments. Thus, in the study by R. Kumar et al., 38 patients with moderate TBI (Glasgow scale score 9-13 points) in the acute period, according to MRI data, there was a decrease in FA in the anterior and posterior femur of the inner capsule and in the knee of the corpus callosum. 6 months after the injury, along with the already identified disorders, a decrease in FA was found in the anterior part and knee of the corpus callosum, as well as in the anterior and posterior parts of the inner capsule in all patients with the corpus callosum with hemorrhagic type DAP. Such changes may indicate an ongoing process of demyelination and gliosis. The disorders identified in the long-term period after the injury (even if they were minor and local) positively correlated with visual attention disorders, the ability to switch and speed of psychomotor activity, as well as the performance of spatial tasks. The presence of hemorrhage in DAP and/or visible signs of DAP in the acute period after injury did not correlate with the severity of cognitive impairment 6 months after injury.

DT-MRI is one of the most sensitive methods for diagnosing white matter lesions, while repeated catamnestic studies are of great prognostic importance for determining the neurological outcome of an injury. S. Naganawa et al. [45] report on the use of DT-I in a repeated study of a 27-year-old woman with severe closed injury resulting from a car accident. A CT scan taken on the day of the accident showed the presence of small hematomas in the right temporal and parietal regions and a small hemorrhagic focus in the right lateral ventricle. The CT scan was performed 3 times: on the 4th day after the injury (SHG score- 6), when bilateral intraventricular hemorrhages, damage to the corpus callosum and a hematoma in the right parietal region were detected. A follow-up examination was performed 24 days after the injury, when the patient's status improved slightly (GG-11 points).

This study showed an increase (compared to the previous study) in the ventricles, a more extensive lesion of the corpus callosum, including the anterior regions, and fibers in the frontal lobes. The third study was conducted 2 months after the injury, when there were no significant changes in the patient's status (GG-11 points) and according to the DT-I studies.

A common consequence of DAP is cerebral atrophy, which begins approximately 3 weeks after moderate or severe TBI, and reaches a significant level after 8-12 months. The loss of brain matter volume continues up to 3 years after injury at a rate higher than during normal aging. The severity of post-traumatic atrophy is proportional to the severity of the injury and correlates with the GCG score at admission, the duration of coma, and post-traumatic amnesia. A similar pattern is observed with a mild injury.

The use of the most sensitive diagnostic methods and the ability to examine the full range of severity of brain injuries allowed D. Rutgers et al. in a prospective study of 39 patients (24 with mild, 9 with moderate, and 6 with severe TBI) in the first 3 months after injury using T1, FLAIR, T2 weighted gradient echo and DT-I sequences, a reversible decrease in FA and an increase in the coefficient of diffusion (CD) in the corpus callosum knee in patients with mild TBI and a different pattern of disorders in patients with moderate and severe trauma (decreased FA and increased CD in the knee and decreased FA without a change in CD in the corpus callosum). A decrease in FA is usually associated with changes in the structure of the parenchyma, such as displacement and damage to fibers or edema. According to the data obtained, such disorders are more reversible in the anterior (knee) than in the posterior (cushion) parts of the corpus callosum. The data inconsistent with the results obtained may be due to differences in the organization of the studies themselves. So, in one of the studies in patients with mild trauma, examined on average 4 and 68 days after the injury, pathology from the knee of the corpus callosum was not observed, and a decrease in FA and an increase in CD were noted in the roller. In another study in patients with mild trauma, FA was reduced in the knee and cushion 24 hours after the injury. In patients with severe trauma examined 14 months after the injury, a decrease in FA was noted in the knee, body, and corpus callosum. In a study that studied patients with varying severity of injury, 7 days after the injury, changes were noted in the knee and the corpus callosum. There was also a decrease in CD, which indicated the presence of cytotoxic edema.

Cyclic fluctuations in cerebral circulation normally demonstrate synchronicity of functioning in the two hemispheres (in structures such as the motor and visual cortex, as well as the thalamus and hippocampus). The presence of such synchronicity indicates the preservation of interhemispheric connections provided by the structures of the corpus callosum. In the study by M. Quigley et al. Using fMRI, it was shown that agenesis of the corpus callosum leads to a decrease in interhemispheric connections (the number of ipsilateral connections prevailed over the contralateral ones) in the motor region and the area of representation of the auditory-speech analyzer.

The use of DT-I allowed A. Holodny et al. to more accurately verify the anatomical organization of the corticospinal tract (CST) in the area of its passage through the posterior femur of the inner capsule. To localize the motor zones, 8 healthy volunteers and 2 patients with tumors at the site of CST passage through the CST were asked to perform a series of taps (the so-called tapping test) alternately with the left and right hand/ foot. In 17 out of 20 cases, the CST fibers had a somatotopic organization when passing through the CST, while the fibers innervating the arms were located laterally and somewhat in front of the fibers innervating the legs. In the remaining three cases, the fibers innervating the arms and legs were displaced.

N.E. Zakharova et al., using MRI in T1, T2, T2-FLAIR and diffusion modes in the study of 22 patients with DAP due to severe TBI (SHG at the time of hospitalization 4-8 points) showed that in the first 2-17 days after injury, accompanied by the development of coma and varying degrees of disability subsequently, There are extensive changes in the structure of the pathways of the corpus callosum and CST. FA indicators were the most sensitive indicator of damage to the conductive pathways in DAP in the early stages after injury. A significant decrease in these indicators compared to the norm was detected both in the structures of the corpus callosum and CST at different levels in all the victims. For a more detailed analysis of the data obtained, three subgroups of patients were identified — without obvious signs of pyramidal insufficiency, with the presence of unilateral hemiparesis of varying degrees and the presence of tetraparesis.

A characteristic feature of the first subgroup with the most favorable outcomes of DAP was a significant decrease in FA indicators in all the studied structures, however, without a clear asymmetry of indicators at similar levels of CST. At the same time, in the patients of the second subgroup with clear clinical signs of unilateral pyramidal symptoms, FA indicators at the level of the CVD and brain legs on the contralateral hemiparesis side were significantly lower than in the control. In addition, FA indices during CT significantly differed on the homolateral and contralateral hemiparesis sides, as well as at the level of the BVC and brain legs. The lowest FA values on both sides at all levels of CST and ICD at the bridge level were obtained in patients with tetraparesis and outcomes in deep disability or vegetative state. These data indicate that FA reliably reflects CST damage during TBI. The revealed significant correlation between the outcomes of DAP and FA indicators in the corpus callosum and during CST, obtained on the 2nd-17th day after injury, indicates a high prognostic significance of diffusion anisotropy. It can be assumed that primary damage to the pathways (in the structures of the CST and corpus callosum) in DAP leads to axonal degeneration, which causes a more significant decrease in anisotropy from the 2-3 th week after injury. Severe diffuse brain damage is a trigger for degenerative changes in the axons and myelin sheaths of the white matter of the brain, leading to their complete destruction and atrophy 2-3 months after injury.

The results of the study of healthy volunteers indicate that the average values of the measured diffusion coefficient (ICD) and FA did not significantly differ at the symmetrical levels of both corticospinal tracts. At the same time, the average FA values during CST were significantly lower at the level of the bridge than the legs of the brain and the posterior femur of the inner capsule. These results confirm the morphological data on a significantly increased density of CST fibers at the level of the CST and the legs of the brain than at the level of the bridge, where there are intersections with transverse fibers. Consequently, the indicators of diffusion anisotropy reliably reflect the degree of integration and unidirectionality of the conductive fibers of the white matter of the brain, which should be taken into account when studying various cerebral pathologies.

Prognosis of cognitive function recovery after TBI. Prognostically significant characteristics of injury include: the traumatic factor and the situation of injury, its type, severity, clinical form, primary-recurrence of injury, intrahemispheric localization, the side and level of predominant brain damage, the presence or absence of consequences and complications of TBI (for a detailed analysis of these factors, see). The individual characteristics of the patient and the peculiarities of treatment and rehabilitation also play an important role in restoring mental activity after TBI.

The probability of restoring mental functions varies with lesions in different parts of the right and left hemispheres, with the most severe disorders occurring in the frontal lobes. The data available in the literature indicate a greater severity of mental disorders in patients with damage to the right hemisphere compared with the left. When different hemispheres are affected, qualitatively different symptoms are noted. Thus, when the right frontal lobe is affected, there is a tendency to complacency-euphoria with unconsciousness, non-perception of the painful condition and, consequently, lack of an attitude towards rehabilitation. Disorders in the lesion of the left frontal lobe manifest themselves in the form of spontaneity (decreased motivation for activity, difficulty in forming voluntary activity, and recovery). The brain localization of the lesion is a reliable predictor of the possible sequence of restoration of various mental processes, the severity and structure of the defect likely in the long term.

It is possible to note a gradual deterioration in the quality and an increase in the recovery time of mental activity with damage to different levels of brain functioning: cortical-subcortical, subcortical and subcortical-diencephalic, oral-stem. These data allow us to conclude that the prognosis of recovery of mental activity in cortical-subcortical lesions is more favorable compared with deeper localization.

Mental activity can be almost completely restored in adults after a primary injury of mild or moderate severity. Repeated TBI can manifest itself as more severe mental disorders in the acute period and subsequent changes in various mental processes, as well as incomplete achievement of the previous level of the emotional and personal sphere.

The individual characteristics of the patient include the profile of the lateral organization of functions, age, and the state of physical and mental health in premorbidity. Studies show that the prognosis of recovery after injury (in particular, regression of asthenic syndrome in patients with mild and moderate trauma) The better, the more clearly the recovery of the patient's pre-injury lateral organization profile is observed. The profile features of the lateral organization of functions determine the features of impairment and recovery of functions after injury. So, left-handers may have disorders that differ from their counterparts in right-handers or do not occur at all. For example, the twilight state of consciousness in right-handers is more common when the left frontal-temporal region is affected, and in left-handers it can occur when the same parts of the right hemisphere are affected. The prognosis of recovery in patients with different profiles of lateral organization of mental functions is also different. Thus, some authors note a relatively favorable course and outcomes in moderate to severe trauma, and a rapid regression of aphasic disorders in left-handers compared with right-handers. There is also evidence that mental activity in patients with severe TBI with signs of left-handedness recovers longer than in right—handers, while individual injury outcomes in cortical-subcortical lesions do not differ significantly, and in deeper lesions, they are better in left-handers than in right-handers.

Premorbid emotional and personal characteristics largely determine the quality and completeness of recovery of mental activity in case of mild and moderate trauma. Predictably favorable are mental health, high activity in achieving clearly defined goals, a reasonably attentive attitude to one's health, and mastery of techniques for regulating it. On the contrary, premorbid mental and somatic ill health is an unfavorable factor in the prognosis of recovery of mental activity after TBI.

Severe mental disorders are more likely with radical neurosurgical interventions, but they can be avoided using minimally invasive techniques (for example, closed external drainage of chronic subdural hematomas).

A study of the dynamics of recovery in young patients (20-40 years old) with predominant damage to nonspecific structures of mild severity in the acute period (1-3, 7-10 and 14-16 days after injury) using neuropsychological examination was conducted by N.N. Privalova. The patients were divided into two groups: group 1 was characterized by a lower severity and rapid reversal of symptoms (minor cerebral disorders according to EEG data, scattered neurological symptoms, vestibular and non-gross hypertensive disorders), group 2 - more pronounced and persistent clinical symptoms (signs of involvement of limbico—diencephalic structures according to EEG data, hypertensive syndrome, vegetative vascular disorders, involvement of the upper stem structures). All the patients studied were characterized by a violation of the dynamic characteristics of the course of mental processes — impulsivity, instability of attention and control, impaired task performance, decreased selectivity of auditory-verbal memory and increased inhibition of traces. However, in patients of the 1st group, such dynamic disorders were not pronounced strongly and could be compensated even at the initial stage of the disease due to the activation of arbitrary regulation of mental activity. By the end of the 1st week after the injury, these patients showed regression of violations of the energy supply of the VPF, normalization of control over the implementation of various activity programs due to the preservation of regulatory functions provided by the cortical sections of the left hemisphere and their connections with the stem activating system. However, by the end of the acute period, these patients had increased violations of the selectivity of mnestic processes, and there was a reduced volume and inhibitability of traces of auditory-speech memory. Such violations may indicate the interest of predominantly right-hemisphere structures. In patients of the 2nd group, at the beginning of the acute period, pronounced violations of the energy supply of VPF were revealed: disorders of distribution, switching and concentration of attention, modal-nonspecific memory disorders (decreased volume, weakness of traces and their increased inhibition, impaired selectivity of mnestic processes and control over them). Regulatory violations manifested themselves in inertia and control violations, which led to a significant deterioration in the quality of work, especially in conditions of arbitrary acceleration. Such regulatory disorders indicate the involvement in the pathological process of the higher mediobasal divisions of the nonspecific system associated with the left-hemisphere prefrontal divisions, which limits the possibilities of compensation for dynamic disorders, since active inhibitory processes and selective activation processes are disrupted. By the end of the 1st week after the injury, there was no significant regression of cerebral, as well as mnestic and intellectual impairments. By the end of the acute period of the disease, there was some normalization of the functions of the energy block of the brain: disturbances in the dynamics of attention disappeared, and the time to complete stereotypical tasks decreased. At the same time, modal-nonspecific memory disorders and regulatory disorders persisted, which are mainly determined by the insufficiency of the functions of the anterior cortex of the left hemisphere of the brain.

Conclusions: Thus, the above studies indicate a sufficient sensitivity of the neuropsychological method in the study of the dynamics of cognitive impairment after TBI. The conducted studies make it possible to describe the different nature of cognitive impairments at different stages of recovery — the presence of predominantly cerebral symptoms at the initial stages of recovery and the formation of a more specific neuropsychological syndrome at later stages. Qualitative characterization of the dynamics of symptoms is necessary when planning rehabilitation measures.

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