



INTEGRATION OF NEUROIMAGING AND NEUROPSYCHOLOGICAL METHODS IN THE DIAGNOSIS OF MILD TO MODERATE CRANIOCEREBRAL TRAUMA

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ABSTRACT

The problem of diagnosing traumatic brain injury (TBI) of mild and moderate severity is becoming increasingly relevant in modern neurotraumatology. According to world statistics, mild and moderate TBI accounts for up to 80-85% of all cases of traumatic brain injury, which determines the high socio-economic significance of this problem. Of particular importance is the fact that the main group of victims are people of working age, which significantly affects the demographic and economic indicators of society.

Introduction. The modern concept of TBI diagnosis is undergoing significant changes due to the introduction of new neuroimaging technologies and the development of neuropsychological testing methods. However, the isolated use of individual diagnostic methods often does not allow us to obtain a complete picture of brain damage and its functional consequences. This is especially true in mild to moderate TBI, when structural changes may be minimal or absent altogether, in the presence of significant functional disorders.

The integration of neuroimaging and neuropsychological research methods is a promising direction in improving the diagnostic process. Modern neuroimaging techniques, including high-field magnetic resonance imaging, functional MRI, diffusion tensor imaging, and perfusion studies, make it possible to identify subtle structural and functional changes in the brain. In turn, neuropsychological testing provides a detailed assessment of cognitive functions, emotional status, and behavioral disorders.

Of particular importance is the problem of standardization of an integrated diagnostic approach and the development of algorithms for interpreting the data obtained. The development of artificial intelligence and machine learning technologies opens up new



opportunities for analyzing multiparametric data and creating predictive models of the course of the disease.

The relevance of integrating various diagnostic methods is also due to the need for early detection of patients at risk of developing post-traumatic complications and an unfavorable course of the recovery period. Timely and accurate diagnosis makes it possible to optimize therapeutic strategies and improve the outcomes of traumatic brain disease.

In recent years, a significant amount of data has been accumulated on the correlation between structural changes in the brain detected by neuroimaging methods and disorders of higher mental functions detected by neuropsychological testing. However, the systematization of these data and the development of practical recommendations for their clinical application remains an urgent task of modern neurotraumatology.

An integrated approach to the diagnosis of mild and moderate TBI, based on the integration of neuroimaging and neuropsychological methods, allows not only to improve the accuracy of diagnosis, but also to develop personalized rehabilitation programs that take into account the individual characteristics of each patient.

Quantitative structural MRI for TBI. Quantification of neuroimaging data is a promising method for investigating the relationship between brain and cognitive impairments in both acute and chronic stages of injury. There are few similar studies on significant patient samples, and so far they describe only the most general links between brain functioning and cognitive impairment. A quantitative assessment of violations in DAP allows for an accurate assessment of the violations that have occurred and is more applicable for research purposes than a qualitative assessment by a radiologist.

The first studies using quantification of neuroimaging data concerned an increase in ventricular volume, indicating white matter atrophy. The quantitative assessment was carried out by measuring the ventricles on CT or calculating the volume of cerebrospinal fluid. T1-sequences of MRI were also used to describe post-traumatic changes in white matter. Other studies have used segmentation of brain tissue into separate blocks. This method can be combined with the use of areas of interest. So, P. Berryhill et al. a decrease in the volume of gray matter and an increase in the amount of cerebrospinal fluid in the prefrontal areas were found in 14 children with severe TBI without local foci, compared with children with mild TBI. E. Wilde et al. Significant brain atrophy was shown, especially pronounced in the prefrontal and temporal regions in 16 children with severe and moderate trauma compared with the control group. Serra-Grabu-losa et al., using the same method, assessed the total brain volume, as well as the volume of the frontal regions and the hippocampus in adolescents with severe TBI (without extensive frontal foci) and showed a decrease in white matter volume, especially pronounced in the frontal lobes, a decrease in hippocampal volume and an increase in the volume of cerebrospinal fluid.

MR morphometry is used to describe the structure of brain tissue (especially gray matter). This method does not presuppose preliminary hypotheses regarding the spatial location of foci and is quite sensitive to local pathology. However, the sensitivity of this method is low for areas with significant anatomical variation. The method has been used in several studies.: so, S. Gale et al. They found atrophy of gray matter in the frontal and



temporal regions, in the cingular cortex, subcortical regions and the cerebellum. Atrophy in a number of areas correlated with the performance of attention and scale tests. F. Tomaiuolo et al. The presence of atrophy of the corpus callosum, arch, anterior femoral inner capsule, superior frontal gyrus, parahippocampal gyrus of the optic cortex and chiasm was shown. The degree of atrophic changes did not depend on the severity of the injury, and did not correlate with mnestic functions, except for the correlation of direct narrative reproduction with atrophy of the middle parts of the corpus callosum.

In the study by B. Levine et al. 69 subjects with varying severity of TBI (23 of them with local foci) were examined one year after the injury using MRI and using the method of automatic tissue segmentation into gray and white matter and cerebrospinal fluid. Atrophy was noted in the prefrontal area, the cingulate gyrus, subcortical nuclei, posterior temporal, parietal and occipital regions. The degree of atrophy of white and gray matter was directly proportional to the severity of the injury. Disorders of mnestic processes and the speed of information processing are directly proportional to the degree of gray matter atrophy in patients with both local and diffuse lesions. The speed of information processing is more closely related to structural changes than other processes. Decision-making features, independent determination of task rules and their application and change depending on changing conditions correlated with atrophy of the ventral prefrontal areas.

Functional neuroimaging studies in TBI make it possible to study cerebral circulation and brain metabolism, which is especially important in the acute period. Most of these studies use single-photon emission computed tomography or PET. It is difficult to interpret the SPECT data due to the lack of control over comorbid conditions (for example, depression) that are associated with changes in cerebral circulation. PET, which is sensitive to poorly visualized metabolic changes using structural methods, allows us to obtain absolute estimates of glucose metabolism. Such studies are often carried out in the patient's passive state, cognitive testing (often using tests that do not always have a clear anatomical specificity) is carried out outside the scanning procedure, as a result of which the results obtained have rather heuristic significance.

Studies of the brain substrate of cognitive functions in normal conditions using functional neuroimaging methods have been actively conducted since the 1990s, forming a guideline for studying brain activation in pathology, in particular TBI. They allowed us to identify areas in which the metabolic rate turned out to be reduced, unchanged, or even elevated, thus reflecting impaired and preserved functions, as well as functions that have undergone compensatory restructuring. A similar functional reorganization can be noted in patients with local pathology, in whom, after the restoration of cognitive functioning, the metabolic rate in intact structures surrounding the lesion and structures contralateral to the lesion is increased.

Functional neuroimaging in moderate and severe trauma. Pre-existing tests or tasks specially designed for this study can be used as cognitive tasks in neuroimaging studies. Using fMRI, G. Prigatano et al. They showed more pronounced activation of the frontal lobes bilaterally when performing the tapping test with the right hand in healthy subjects compared with patients with severe TBI in the chronic period. Performing a



modified Stroop test during fMRI recording in patients with severe TBI in the chronic stage showed a decrease in activation in the anterior cingular cortex.

An example of using specially designed tests is the working memory test (n-back task), during which W. Perlstein et al. they showed deficits in associative processes, rather than the speed of processing and the ability to retain information in working memory, which manifested itself in a decrease in activation in the dorsolateral sections of the right prefrontal region and the left inferior frontal and parietal sections in patients with severe trauma compared with the control group with an increase in the load on working memory. B. Levine et al. [we used a test in which you need to press the button every time a letter appears on the screen, but when the color of the letter changes, you need to slow down the response. This study has an event-related design that allows us to analyze brain activation in different types of responses. So, with proper non-pressure, activation in the dorsolateral prefrontal cortex of the left hemisphere normally increases, which is associated with suppression of the response. At the same time, patients with severe TBI showed an increase in activation in the medial parts of the parietal region. In a situation of erroneous non-response in a group of healthy volunteers, there was an increase in activation in the dorsolateral prefrontal cortex of the right hemisphere, which corresponds to increased control over the response. At the same time, patients demonstrated increased activation in the prefrontal regions of the left hemisphere, the anterior cingular cortex, and the parietal region.

The study of patients with mild trauma. The study of patients with mild trauma differs from that for patients with moderate and severe trauma in a number of parameters. With mild trauma, qualitatively different pathological processes are available for research, since patients with moderate and severe TBI are studied in the chronic phase, after the disappearance of acute manifestations. Most studies of mild trauma take place in the acute or subacute period. With a mild injury, the pathology of the disorder is more homogeneous than with moderate or severe. The number of minor injuries is higher than that of more severe ones, which makes it possible to recruit extensive experimental groups; however, it should be borne in mind that patients with minor injuries are symptomatic only for a short period of time, during which time it is necessary to conduct a study.

Mild TBI includes concussions and mild bruises with short-term impairment of consciousness. And although in most cases there is a complete recovery, in 15% of cases the symptoms persist. J. Chen et al. Athletes with concussion were studied 1-14 months after injury using fMRI and tests for verbal and non-verbal working memory. It was shown that patients had reduced activation of the dorsolateral prefrontal cortex on the right, additional foci of activation were noted in the posterolateral and other cortical regions. The quality of the tasks was more variable than normal, not significantly different from it.

Concussion is one of the few disorders that can be investigated before and after its occurrence, when the condition before the injury is a control for the condition after the injury. Such studies, in particular, can be carried out by screening groups with an increased likelihood of concussion (for example, athletes) and their subsequent



examination after injury. Such a design allows you to control variables such as interindividual variability, group effects, and the effect of repeated scanning. K. Jantzen et al. Four football players were examined a week after a concussion, who underwent a screening study before the injury, and their results were compared with football players who were examined twice but did not have a concussion. Patients with concussion had more pronounced and extensive foci of activation when performing a serial activity task.

Thus, the choice of the research protocol is determined not only by the research or clinical task, but also by the nature of the brain injury (the mandatory presence of diffuse cerebral disorders along with local pathology, increased vulnerability of certain brain structures and, as a result, the presence of "nuclear" disorders, the gradual development of the pathological process), as well as the capabilities of the fMRI method (problems of adequate signal fixation the effect of additional factors on brain activation, the need to analyze the data obtained within the framework of the theory of the systemic organization of mental functions). Neuropsychological assessment of cognitive impairments in patients with TBI

Functional diagnostics of the defect structure. The neuropsychological approach to the diagnosis and correction of cognitive impairments in the Russian tradition is based on the theory of A.R. Luria on the systemic dynamic organization and localization of higher mental functions (HPF), which made it possible to develop a method for the syndrome analysis of disorders. According to this theory, mental functions are complex hierarchically organized functional systems. Their individual links are provided by the functioning of certain areas of the brain, each of which makes its own specific contribution to the holistic work of the functional system. Abnormal functioning of individual parts of the brain due to traumatic brain injury can lead to deficits in mental processes, affecting various levels and links of their provision.

Topical diagnostics was initially one of the main tasks of neuropsychological examination in the TBI clinic, but its role has faded into the background due to the widespread use of neuroimaging methods in the brain injury clinic. At the same time, the neuropsychological approach remains the most sensitive in the topical diagnosis of subtle, mild brain changes associated with a decrease in the functional state of various brain structures, as evidenced by the high correlation of the results of neuropsychological testing and functional diagnostic methods.

Since the ultimate goal of therapeutic and rehabilitative measures in the brain injury clinic is the most complete restoration of the patient's physical and mental functioning, the main task of neuropsychological diagnostics is to analyze the structure of the defect of mental functions and the dynamics of its changes. To do this, it is necessary to identify the preserved and impaired links of mental functional systems, as well as to determine the hierarchy of disorders — the primary symptom directly related to the localization of brain damage and the secondary systemic consequences of this disorder. Such an analysis of the defect structure is necessary for the development of rehabilitation programs aimed at restoring damaged links of functional systems based on preserved ones.

Cognitive impairments in mild and moderate TBI are described based on the results of a study of various aspects of VPF: control functions, energy component of activity, mnemonic function, function of processing auditory and visual information. In general, according to a



number of studies, the most sensitive to trauma are control functions and dynamic indicators of cognitive activity, as well as mnemonic functions, which are the most popular objects of research.

A number of studies have evaluated the spectrum of cognitive impairments in TBI and studied the structural and functional organization of cognitive functions in this category of patients. The study of visual and diagnostic disorders in the TBI clinic makes it possible to study the brain organization of this group of functions, as well as to judge the localization and lateralization of the lesion. Violations of objective, simultaneous, and facial gnosis occur when the occipital brain is affected, and violations of the description of signs of shape, spatial position, and identification of nonverbalized images, largely based on the spatial-frequency description of the image, are associated with damage to the parietotemporal brain regions. A study of the processes of spatial-frequency analysis of facial images has shown that, normally, the right hemisphere is more focused on analyzing high—frequency components of the spectrum, and the left hemisphere is more focused on analyzing medium-frequency components, while low frequencies are not informative enough for analyzing visual images. Patients with damage to the parietal-temporal structures of the left hemisphere and intact right hemisphere analyze images of faces in the same way as healthy people, using higher-frequency parts of the spectrum. Patients with parietal-temporal lesions of the right hemisphere and intact left hemisphere recognize images of faces in a different way than healthy ones, using primarily medium frequencies, the presence of high frequencies in the spectrum only complicates the activity of the left hemisphere. The results obtained may indicate that the analysis of the spatial-frequency characteristics of an image occurs at the primary sensory pre-categorical level and does not depend on the semantic significance of stimuli, which confirms the assumption that there are interhemispheric differences not only at the cognitive, but also at an earlier stage of information processing.

In a study by R. Vangerploeg et al. Using neuropsychological diagnostic methods (for example, the California Auditory Memory Test), the structure of mnemonic disorders in patients with TBI of varying severity in the long-term period (from 3 months to a year or more) after injury was shown. In such patients, there are no noticeable impairments in the ability to encode the information received (the speed of memorization of words by patients did not differ from that of healthy people) and reproduce it (the productivity of recognizing words and reproducing them according to the proposed semantic categories did not differ from that in the norm). Consolidation of traces caused the greatest difficulties (especially with moderate and severe trauma) (patients very quickly forgot the words they had learned — the productivity of their reproduction noticeably decreased from the fifth test to playback after the interfering list of words). The results obtained are consistent with other studies in this field, which have established the presence of rapid forgetting of nonverbal stimuli in patients with TBI.

An important aspect of the study of mental functions in patients with TBI is the study of changes in their emotional response. Neuropsychological studies have made it possible to describe not only pronounced, but also relatively mild forms of disorders of the emotional and personal sphere, to develop adequate methods for its assessment, and to demonstrate the connection of emotional disorders with the localization of brain lesions. Emotional disorders



are mainly associated with damage to the frontal and temporal regions, when the influence of emotions on cognitive processes, perception and assessment of emotional states is disrupted. The anterior parts of the right hemisphere play a leading role in processing emotional information and evaluating negative emotional reactions. The role of the left hemisphere in processing emotional information is generally less significant, it plays a leading role in processing positive emotions, analyzes and summarizes emotional states.

The role of various departments of the nonspecific system (stem and limbic structures, mediobasal sections of the frontal and temporal lobes of the cortex) in emotional and personal disorders was studied in young patients (20-40 years old) with concussion in the acute period (1-3, 7-10 and 14-16 days after injury). The patients were divided into two groups: with predominant lesions of the caudal brainstem (involvement of the lower brainstem according to EEG data, vestibular disorders, multiple neurological symptoms, non-severe hypertensive phenomena) and the upper brainstem (signs of involvement of the upper brainstem structures on the EEG, hypertension syndrome, vegetative vascular disorders, oculomotor innervation disorders). The influence of the emotional factor on mnemonic and intellectual processes, cognitive and emotional self-assessment of patients' condition was studied. The identified emotional disorders are primarily manifested in the increased influence of the emotional factor on mnemonic and intellectual processes, inertia of affective processes, as well as impaired cognitive and emotional assessment of patients' condition.

In patients with impaired functions of the lower brain stem, the dynamics of the syndrome increases the dysfunction of the emotional zones of both hemispheres — the influence of the emotional factor on cognitive processes decreases. For patients with a predominant lesion of the upper brain structures, the dynamics of the syndrome is characterized by a general tendency to normalize emotional assessment with a slightly reduced cognitive one. Perception and evaluation of positive emotional expressions of moderate intensity become less differentiated (with a more adequate assessment of negative emotions). Presumably, the mechanism of the described disorders consists in patients with predominant dysfunction of the inferior cerebral structures in the suppression of the functions of the emotional zones of both hemispheres by the end of the acute period, and in patients with predominant upper cerebral disorders in the suppression of the emotional zones of the left hemisphere against the background of persistent irritation of the right hemisphere structures.

A combination of neuropsychological and neuroimaging approaches is particularly productive for studying the structure of a cognitive defect. In the study below, functional disorders in patients with moderate to severe TBI (1-1.5 years after injury) are noted at all stages of the processes of working memory (encoding, storing and reproducing information). The Sternberg letter recognition test did not cause significant difficulties in patients (with the exception of difficulties in distinguishing between target and non-target stimuli with an increased load on working memory). During the test, patients (unlike healthy subjects) showed an increase in activation at the stages of encoding (dorso and ventrolateral prefrontal cortex, additional motor area, paracentral lobe, insula and visual cortex) and information reproduction (dorso and ventrolateral prefrontal cortex). Normally, increased activation was noted only at the stage of trace retention (the fronto-parietal-thalamic system associated with



working memory, as well as the Broca's area associated with the repetition of stimuli in memory; activation of the occipital regions was not noted due to the relatively low load on working memory). Thus, at the stages of encoding and extracting traces in patients, brain regions associated with other components of working memory are involved, which can be considered as a compensatory mechanism for disruption of connections between prefrontal areas and subcortical and caudal regions forming a distributed functional system of working memory in conditions of diffuse axonal damage in TBI. It can be assumed that the involvement of additional neural resources in patients is associated with the presence of a task, and in the absence of such a task, there will be a decrease in brain activation.

Thus, the study of the structure of cognitive impairments demonstrates not a total loss of the studied function, but a violation of certain aspects of its course (links of the functional system), which is also revealed in the features of brain activation. The study of the functional structure of the defect (i.e. the identification of preserved and impaired links of the functional system at the brain and cognitive levels, as well as primary and secondary affected functions) is extremely important for planning correction specifically for impaired links (especially secondarily affected links) of the functional system.

The dynamics of cognitive functions in TBI. Despite the variety of primary brain changes, concomitant pathophysiological reactions, and intra- and extracranial complications that cause extreme variability in neuropsychological syndromes in TBI, it is possible to identify common features in the picture of cognitive impairments in this category of patients.

In the acute period of trauma, general cerebral symptoms usually come to the fore, such as nonspecific disturbances in the dynamics of mental processes — slowing down the pace of activity, increased exhaustion, and insufficient motivation. The presence of such violations of the background components of mental activity often makes it difficult to identify defects caused by a focal traumatic disorder, which manifest themselves gradually as the compensatory brain mechanisms become active. With a predominant lesion of the caudal cerebral divisions, there are various (depending on the location of the primary lesion) gnostic and mnesic disorders, as well as speech disorders. The predominant involvement of one of the hemispheres in the pathological process determines the nature of the observed disorders associated with a predominant violation of the verbal or non-verbal components of activity. When the anterior cerebral divisions are affected, there are violations of the function of arbitrariness.

Neuropsychological symptoms in TBI can be roughly divided into three groups. The first group includes a non-specific decrease in mental activity in general in the form of spontaneity, inactivity, pathological exhaustion, inertia, lethargy or impulsivity, decreased productivity of mental activity. The second group is represented by disorders of consciousness by the type of orientation disorders (in place, time and one's own personality), disorders of the emotional, personal and motivational spheres. The third group includes specific cognitive disorders such as disorders of praxis, gnosis, speech, visual-spatial functions, memory, and thinking.

In the TBI clinic, the structure of neuropsychological defects changes over time and depends on the recovery period after injury. In the acute period, a nonspecific decrease in mental activity usually comes to the fore, due to stem and subcortical disorders, combined with disorders of consciousness such as disorientation and amnesic confusion. The most



relevant during this period are neurotropic drugs that provide non-specific activation that increases the energy level of mental processes.

The intermediate recovery period is characterized by a decrease in the proportion of violations of the background components of mental activity and a more pronounced manifestation of cognitive impairments associated with a certain localization of brain damage. The structure of the neuropsychological syndrome is determined by the severity of the injury and the location of the main lesion. Emotional and personal changes can also be clearly manifested during this period. Drugs that have a more selective effect on higher mental functions become the most effective in this period. In the long-term period of injury, disorders are mainly caused by reduced neuropsychological syndromes with a specific structure and requiring selective correction. This determines the choice of neurotropic agents with the most selective action.

The severity and specificity of neuropsychological syndromes depend on the age and individual characteristics of patients, however, the form and predominant localization of disorders have a decisive influence on the formation of the symptom complex and its dynamics.

Severe diffuse brain lesions lead to the most severe and persistent defects in higher mental functions of the VPF. Such patients have been in serious condition for a long time due to loss of consciousness and impaired vital functions, which delays the timing of neuropsychological examination from the moment of injury. In some cases, limited contact and the severity of violations do not allow for a detailed examination. In such patients, nonspecific disorders of mental activity, emotional, personal and motivational changes are most grossly and vividly manifested. The defects of individual VPFS remain rather blurred for a long time, which makes it difficult to diagnose them differentially. Such disorders can be corrected to some extent, but in most cases these patients remain disabled.

With subcortical or cortical-subcortical localization of the focus in patients with severe TBI, when brain injury is accompanied by edema or intracranial hematoma, focal neuropsychological symptoms are more pronounced. Disorders may be more persistent and pronounced even in the long-term period after injury.

Focal lesions of moderate severity are less traumatic in relation to mental activity. Patients with predominantly cortical localization of the lesion in a relatively short time after injury achieve the degree of recovery of consciousness and vital functions that allows for a neuropsychological examination. Their orientation, background and neurodynamic parameters of mental processes are quickly restored. Emotional and personal disorders are rarely pronounced and persistent. The identified defects, as a rule, selectively affect individual links of the VPF. These symptoms are generally reversible and in most cases significantly regress. Catamnestic observation 1, 2 years or more after injury shows that HPV defects in such patients can be easily reversed and almost completely compensated: only the erased traces of previously existing focal disorders remain on the background of mild asthenic symptoms.

Conclusions: Thus: in patients with mild TBI, as a rule, significant preservation of VPF is revealed. However, almost all patients show marked deficits in one or another area of mental activity, while the most complexly organized functions of memory and processing of visual-



spatial information are the most vulnerable. These patients often have a decrease in the neurodynamics of mental activity.

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