



Complex diagnostics and prognostic aspects of neuro-endocrinological parameters in acute combined traumatic brain injuries

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Abstract

It is known that acute combined traumatic brain injury causes not only direct damage to brain structures, but also disrupts the functioning of distant organs, depending on the severity of the traumatic factor. Neuroendocrine disorders are often underdiagnosed in the clinic of acute combined traumatic brain injuries, which entails the development of complications in both the acute and chronic phases of the disease. The purpose of this work was to analyze the latest scientific evidence regarding neuro-endocrinological parameters in acute combined traumatic brain injuries to improve patient management protocols and improve overall survival rates. An analysis of scientific works from open databases over the past five years was carried out. It was found that the most common neuro-endocrinological conditions after traumatic brain injury are hypopituitarism, diabetes insipidus, hypothalamic dysfunction and cognitive impairment. Low blood pressure (both systemic and intracerebral), anemia and hypoxia can cause ischemic changes in the central endocrine glands. In the acute phase of acute combined traumatic brain injuries, signs of deficiency of somatotrophic, gonadotrophic and adrenocorticotrophic hormones predominate. Vasopressin deficiency in the acute phase is associated with an increased risk of developing cerebral edema, and oxytocin deficiency is associated with the development of neurodegenerative pathologies. Differential diagnosis of neuroendocrine disorders should be carried out on the basis of anamnestic data and indicators of the patient's biochemical and hormonal data. The data obtained emphasize the importance of timely diagnosis of neuroendocrine disorders along with neurological ones during the management of patients with traumatic brain injuries; they can be used

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Introduction

It is known that traumatic brain injury (TBI) in the clinic of internal medicine and neurology is defined as a disruption of the functioning of brain structures due to the negative (often mechanical) influence of the external environment of varying degrees of intensity [1]. According to statistics from T.A.Fatuki, every year almost three million people in the United States are hospitalized with traumatic brain injury, most often caused by falls from heights, impacts of various types on the skull, and road traffic accidents [2]. Retrospective studies show that less than 80% of hospitalized patients with TBI have a number of neurological, subjective symptoms from the organ of vision and vestibular apparatus, while the hormonal background of patients with clinical acute TBI in the initial stages is not taken into account [3]. Often, the inconsistency of the applied methods for diagnosing the state of functional activity of organs (functional and imaging) leads to underdiagnosis and insufficient understanding of the possible mechanisms of damage to the central nervous system (CNS), which determines the relevance of additional study of this problem.

Acute concomitant brain injuries affect more than ten million patients annually worldwide and more than one and a half million people annually in the United States [4]. The incidence of mild TBI, most often due to traffic accidents, is gradually increasing in low- and middle-income countries [4, 5]. According to published statistics from the Republic of Uzbekistan, acute TBI is diagnosed in every sixth person throughout life, while the total number of TBI cases per year exceeds forty million [6]. Moreover, 15% of patients with combined TBI have complications such as disability, and 10% have a fatal outcome [7]. Statistical data from K.E. Makhkamov and the scientific group of co-authors of the Republican Scientific Center for Emergency Medical Care in Uzbekistan [8] for 2021 indicate that on average they supervise more than five thousand patients with acute TBI per year and more than thirty thousand surgical interventions with this occasion on CNS. Why does it follow that adequate diagnosis of acute combined TBI is a pressing issue in the field of emergency medicine and neurology throughout the world.

Clinical symptoms, including a complex of neurological and endocrine signs, occur more often in the form of isolated neurological symptoms during the treatment of TBI [9] and require both general clinical and special imaging diagnostic methods. Combined syndromes that are identified in the post-traumatic period of TBI lead to a significant decrease in the quality of life of patients and deterioration in the dynamics of rehabilitation [10]. According to F.T. Makhmudov [11], in Uzbekistan, almost a quarter of patients with TBI require emergency psychiatric care in the acute phase of the disease. published in 2020, Thus, complex manifestations of TBI, including central endocrine and peripheral hormonal disorders, as opposed to solely neurological ones, worsen treatment results and symptomatic outcome for the patient.

In addition to the negative impact on the patient's quality of life and objective clinical indicators in the long-term period of the disease, neuroendocrine disorders are constituent elements in the pathogenesis of the development of early complications of TBI, according to C. Mahajan [12]. Among the critical neuroendocrine conditions in the clinic of brain injuries, hypopituitarism is distinguished [13], which often leads to a number of systemic complications. Hypopituitarism in patients with acute TBI has a dangerous effect on the peripheral organs of the endocrine system [14], which in turn complicates the management and control of post-traumatic conditions not only in the acute phase, but also in the long term of patient management. According to the data of Y.M.

Urmanova and D.I. Khamraev [15], published in 2020, among the neuroendocrine complications of patients with acute TBI in Uzbekistan, diabetes insipidus (DI) is often diagnosed, which requires constant monitoring in the long-term period of the disease, significantly affecting on the quality of patient rehabilitation.

Thus, the purpose of this study was to analyze the main nosological forms of neuroendocrine disorders and their pathophysiological mechanisms that occur in patients with acute combined brain injuries in order to improve comprehensive diagnostic and management protocols for patients with a focus on reducing the risks of complications at different stages of the disease.

Materials and methods

In order to analyze the latest data on approaches to complex diagnostics, symptomatic manifestations, features of pathogenesis and differential diagnosis of neuro-endocrine manifestations of acute combined TBI, a systematic analysis of scientific works in the field of emergency medical care, neurology, internal medicine, endocrinology, psychiatry and pathophysiology was carried out. To select data for the purpose of subsequent analysis, a number of scientific evidence-based publications were selected, which were published by relevant and reliable periodical medical publications with a high impact factor. The selection of processed articles and clinical recommendations was based on the principle of using advanced, relevant and evidence-based research data. The analysis included long-term observations of large cohorts of patients with TBI of varying severity, randomized clinical trials (with groups of patients who underwent experimental treatment regimens using hormonal therapy), statistical work (assessing the clinical status of patients with TBI with a predominance of a specific endocrine syndrome ; with the study of the prevalence of neuroendocrine symptoms of TBI in specific ethnic groups) and clinical cases (with complicated or non-standard clinical manifestations and the course of TBI from the endocrine, nervous or cognitive system). The work also included meta-analyses that covered large cohorts of patients over a period of 8 months to 5 years of observation of the development of the acute and late phases of TBI under the supervision of supervising physicians. The work included meta-analyses with an emphasis on the diagnosis and symptoms of neuroendocrine disorders during the course of TBI. Some of the analyzed scientific works are devoted to the use of new experimental models for studying the molecular mechanisms of TBI, which were carried out on experimental animals and are potentially effective methods for implementation in clinical practice.

Thus, the study included scientific works published in 2019-2023 in specialized and evidence-based medical publications of Uzbekistan, Europe and the United States, which presented new data on the pathogenesis, diagnosis and symptomatic manifestations of neuro-endocrine disorders in acute combined TBI. Academic search engines and resources such as Google Scholar, ResearchGate, PubMed, Medscape, Science Direct and EBSCO were used to search for papers. In most cases, material was used from open scientific databases of licensed publishing or search platforms for scientists. During the work, the researcher, that is, the author of the work, was identified - an authorized login, search and work (quoting, studying, gaining access to full-text material) on the platforms were used. Identified work with databases of scientific publications makes it possible to exclude duplication of results of the same scientists in different publications, related works (which duplicate the results obtained), irrelevant by date of publication or purpose of the study, as well as quickly check the citation and impact factor indicators of the work itself, and a medical publication. In addition to filtering the robot by publication date, a number of keywords were also used during the search. This helped to exclude articles and guidelines that related to infectious and hereditary pathologies of the brain, which were not the purpose of this work.

Results and discussion

As A.G. Kolias and co-authors indicate in their work [16], brain injuries include various criteria of structure, intensity, volume and magnitude of influence (or bruises) on the patient's brain with a traumatic effect on cells, tissues and structures of the brain. Today, endocrine disruption is no longer considered a rare or uncommon complication of acute TBI, as suggested by the hypothesis and findings of a 2023 paper by C. Mahajan et al [12]. The statistical prevalence of endocrine disorders in combined TBI varies in different scientific works depending on the time frame of trauma, the type of diagnostic methods used, as well as the variability of hormonal disorders and, on average, is detected in every fifth patient hospitalized with TBI [13]. Neuroendocrine conditions against the background of acute TBI include both direct mechanical, traumatic effects on the anatomical integrity of the central organs of endocrine regulation, and secondary factors mediated by increased cranial pressure, the development of swelling of brain tissue, neuro-inflammatory and neuro-degenerative processes in the CNS. Impaired hemostasis of endocrine regulation affects not only the central axis of hormonal regulation, but also affects the tissues of the internal environment of the body, which manifests itself in both the acute and long-term phases of TBI.

Hypopituitarism

The statistical distribution of cases of hypopituitarism diagnosed against the background of acute TBI changes over time of patient management and is estimated at approximately a quarter of all diagnosed TBI per year, as indicated by M. Kalas and co-authors in their 2023 work [17]. Scientific data from M. Bensalah in 2020 show that more than a third of patients have irreversible lesions of the adenohypophysis after suffering a TBI, the severity of which increases with repeated CNS injuries [16-17]. Their diagnosis requires an integrated approach, which includes both imaging methods (computed tomography (CT), magnetic resonance imaging (MRI)) and biochemical methods that determine the patient's hormonal status. According to the analyzed scientific works [11-16], hypoproduction of hormones of the adenohypophysis is more common in the clinic of combined TBI than an isolated deficiency of hormone secretion of the posterior lobe of the pituitary gland. According to M. Bensalah, the overall risk of disruption of the hormone-producing work of the central hypothalamic-adenopituitary axis after TBI in female victims is higher compared to male patients [18], which is proven by systematic determinations of changes in hormone levels at different stages of TBI. Late diagnosis of hypopituitarism in the acute phase of TBI is often associated with the manifestation of nonspecific symptoms from the musculoskeletal, nervous and cardiovascular systems. A threat to the quality of life and the rehabilitation process in patients can be underdiagnosis of hypopituitarism in the late phase of patient management or even failure to detect central endocrinological disorders. As W.You and co-authors indicate in their 2019 work, the severity of the traumatic factor, age, the presence and volume of subarachnoid hemorrhages (which are diagnosed using MRI), neurosomatic conduction disorders (diagnosed using functional tests and an encephalogram), the presence of fractures The skull base is associated with an increased risk of adenohypophysis dysfunction [19]. According to J. Martin-Grace, hypopituitarism due to TBI is often accompanied by insufficiency of the hormone-synthesizing function of the adrenal cortex [20], which is manifested by an imbalance of ions in the blood serum and disruption of the glomerular apparatus of the kidneys. It is important to diagnose these conditions at the hospital stage of managing patients with TBI, since in the long-term period these manifestations can be diagnosed as isolated conditions not associated with previous TBI.

The central endocrine axis "hypothalamus-adenopituitary-adrenal glands", as the controlling basis of the systemic homeostasis of the internal environment of the body, can be significantly

damaged during combined brain injuries, both directly and indirectly [20]. According to N. Sabet [21] and co-authors, on the one hand, a direct mechanical effect on the anatomical structures of the central endocrine axis is possible: parts of the hypothalamus, adenohypophysis, or due to a fracture of the bones of the base of the skull with subsequent hemorrhages, which are visualized on CT and MRI. From another point of view, the most topographically vulnerable area for traumatic and compression injuries during TBI in the central endocrine axis is the diaphragm sella, since long somatic vessels pass here, supplying blood to the distal and anterior parts of the pituitary gland and draining the capillary system of the pituitary stalk [20]. Clinically, this can manifest itself as ischemic necrosis of the pituitary lobes, accompanied by hypopituitarism [19]. Since the vessels passing through the sella turcica feed the anterolateral lobe of the pituitary gland, the cells of which produce somatotropin, follicle-stimulating hormone and luteinizing hormone, the primary signs of hypopituitarism will appear through hypoproduction of these hormones [21]. Primary hypopituitarism, which according to A. Loggini and co-authors most often [22] is manifested by hypoproduction of somatotrophic hormone, will be clinically accompanied by hypoproduction of adrenocorticotrophic hormone, gonadotropic hormones and thyroid-stimulating hormone, respectively affecting the homeostasis of the adrenal glands, gonads and thyrocytes of the thyroid gland.

The anatomical region below the diaphragm of the sella turcica, through which the shortened portal arteries and veins of the central endocrine axis pass, feeds the medial and anterior regions of the adenohypophysis and clinically has a lower risk of rupture due to mechanical impact and necrosis, according to statistical data [15, 20-24]. Thus, in the clinical picture, hypopituitarism will be less often accompanied by a deficiency of thyroid-stimulating and adrenocorticotrophic hormone, which feed these shortened portal arteries and veins.

In the development of hypopituitarism against the background of acute TBI, anamnestic data of previous cases of TBI in the patient also play an important role, especially against the background of increased pressure due to repeated trauma. Studies on athletes by A. Muravskiy and co-authors in 2019 show [25] that professional boxers who undergo regular head injuries have increased titers of circulating antipituitary and antihypothalamic antibodies. As a result of acute combined TBI in patients with chronic CNS injuries, the development of neuro-endocrine disorders can become the leading manifestation (after neurological) due to autoimmune reactions [24] against the background of elevated antibodies to central endocrinological organs. This cohort of patients should be more carefully diagnosed for underlying conditions of autoimmune reactions to CNS tissue.

The extent of hypopituitarism associated with acute TBI also depends on genetic predisposition. Genotypically determined background inflammatory, autoimmune and neurodegenerative processes increase the permeability of the blood-brain barrier [26] both from ependymocytes and macroglia, and from the endothelial lining of blood vessels and the basement membrane, as indicated by the data of D. Pavlovic et al. The altered permeability of the barrier allows antigens of the central organs of endocrine regulation (hypothalamus, pituitary gland, pineal gland) to circulate in the blood, which triggers the mechanisms for the production of corresponding antibodies to these organs [25-27]. Acute TBI leads to a sharp increase in antibody titer, which is ultimately accompanied by hypopituitarism, which was studied by E. Javidi and co-authors in their works [28]. Other studies highlight a specific ApoE gene [29], polymorphism and mutations in which can serve as clinical predictors of the type of course and severity of the consequences of TBI in a patient. Published data by P. Muza [30], according to which polymorphism of the ApoE 3/E3 type indicates the predominance of neurological complications of TBI compared to

endocrinological ones, that is, with a minimal likelihood of developing hypopituitarism. The publication by P. Muza also indicates that ApoE polymorphism is also characteristic of neurodegenerative pathologies of the CNS, but in the focus of TBI, especially repeated ones, significantly correlates with an increased risk of developing chronic traumatic encephalopathy. The authors of a number of genetic studies [31, 32] argue that the determination of messenger RNA in the blood plasma at the time of admission of a patient with acute TBI makes it possible to differentiate a cohort of patients with an increased risk of developing hypopituitarism and neuro-endocrine complications.

The problem of clinical diagnosis of hypopituitarism lies in the variability of clinical manifestations in both the acute and chronic phases, as well as the presence of nonspecific subjective manifestations. In the acute phase of TBI [13], impaired consciousness, refractory hypotension, decreased muscle reflexes and deficiency of adenohypophysis hormones may not be diagnosed from the point of view of the endocrinological syndrome, while hypoproduction of gonadotropic hormones may appear in the chronic phase. Often, hypopituitarism is diagnosed in the chronic phase [33], which, according to N. Glynn et al., is currently a serious problem in the management of patients with TBI, since hormonal imbalance affects a number of peripheral organs of the endocrine system, which significantly worsens the quality of life and rehabilitation outcomes. In this phase, symptoms of deficiency of somatotropin, gonadotropins, thyroid-stimulating (impaired basal metabolism, dyslipidemia) and adrenocorticotrophic hormone predominate [33, 34]. In addition to changes in the panel of adenopituitary hormones, it is important to note the insulin resistance that develops against the background of TBI, which is manifested by increased fasting glucose levels [31]. As a result, hypogonadism and hypothyroidism due to hypopituitarism can impair cognitive functions, including memory, socialization, and the development of depressive disorders.

Diabetes insipidus

Another type of manifestation of neuroendocrinological disorders in acute TBI is represented by DI. This pathology develops against the background of central (neurological) or peripheral (nephrotic) acute conditions as a result of impaired functioning of the arginine-vasopressin system [35]. In patients with acute TBI, there are two possible pathophysiological paths for the development of DI: with central damage to the hypothalamus or with nephrotic insufficiency developing against the background of edematous syndrome, respectively. Dysregulation of vasopressin leads to disturbances in the water-electrolyte and osmotic balance in the circulating body fluids (blood, lymph, cerebrospinal fluid).

Topographically, this hormone is synthesized in the central parts of the endocrine system - the neurosecretory cells of the nuclei of the anterior group of the hypothalamus, and is released through the posterior part of the pituitary gland [36]. Research by A. Garrahy shows that the development of primary central DI is not always associated with direct trauma to the hypothalamic-pituitary structures [37], while the symptoms of polyuria and polydipsia syndrome indicate a violation of secretion or sensitivity to vasopressin. These manifestations may also be transient in nature, manifesting themselves in the acute phase of TBI. Primary central DI can also be caused by acute TBI of different localization, meningitis and encephalitis [36, 38]. Therefore, it is important to distinguish between DI due to predisposing conditions of infectious or inflammatory origin and acute central DI due to concomitant TBI.

The scientific work of A. Gempeler and co-authors in 2020 shows that DI in the observed cohort of patients (study duration - 6 years) with combined TBI develops on the second day after injury. Thus, the authors attribute this condition to early complications of TBI, which led to death in

almost 30% of cases observed by scientists [35]. The authors include increased intracranial pressure, cerebral edema, penetrating injuries of the skull and subarachnoid hemorrhages as factors predisposing to the development of DI in patients with acute concomitant TBI [36].

Morphologically, with combined brain injury, the pathogenesis of DI is triggered due to fronto-occipital dislocation of brain tissue, disruption of the integrity of the portal blood supply system of the hypothalamic axis, or trauma to the infundibular part of the hypothalamic-pituitary system [38]. As follows from the work of R. Tudor et al. in 2019 [39], DI against the background of TBI develops in every fourth patient with manifestation in the form of dysnatremia, so in the acute phase it is important to differentiate DI from primary adrenal insufficiency. Significant intracranial lesions in the form of hemorrhages and hematomas are accompanied by a sharp increase in intracranial pressure [38], which in turn can lead to transient disturbances in the functioning of the hypothalamic-pituitary axis. As M. Tomkins and co-authors point out in their 2022 work [40], the development of DN in TBI significantly improves clinical outcomes and rehabilitation processes due to the increased risk of early complications in the form of refractory hypernatremia, general tissue edema, seizures, decreased ventricular contractility, and encephalopathies. As DI progresses, sustained water loss leads to hypovolemic hypernatremia [40], which therapeutically requires maintenance of a stable circulating blood volume, often with the use of vasoconstrictor drugs.

Hypothalamic syndrome

During the development of TBI, together with traumatic damage to neurons and neuroglia, hypoxic, apoptotic and dysmetabolic processes play an important role [2]. Acute combined TBI causes an imbalance of oxidative, metabolic and circulatory reactions, which aggravates existing background pathologies and often leads to terminal brain hypoxia [27], which manifests itself in the disruption of general clinical, biochemical and functional disorders of organs. Some scientists identify the term “hypothalamic syndrome” (HS) or “hypothalamic dysfunction” as a collective definition of neuroendocrine disorders caused by both internal hypoxic or traumatic and external factors influencing the neurosecretory neurocytes of the hypothalamus and the portal blood supply system. According to statistics from Z. Gan et al [41], the most common etiological cause of HS is TBI, ahead of CNS infectious diseases. In patients with acute combined TBI, the hydrodynamic influence of cerebrospinal fluid on the structures of the CNS increases, including on the hormone-producing cells of the anterior and medial groups of the hypothalamic nucleus, which anatomically project to the bottom of the third ventricle, as indicated in the work of Z. Gan and co-authors in 2019 [41]. Neurosecretory cells of the hypothalamus secrete vasopressin and oxytocin, damage to which worsens the neuroprotective and anti-inflammatory responses of nervous tissue in TBI [39, 42]. Experimental modeling of TBI in rats conducted by W. Chen and co-authors in 2023 showed that when exogenous oxytocin is administered during damage to the hypothalamic nuclei, a decrease in neuro-behavioral and seizure symptoms is observed, as well as a decrease in the permeability of the blood-brain barrier [42]. Compensation of oxytocin deficiency in TBI in the experiment showed statistically significant correlations with lower risks of developing neurodegenerative conditions, compared with a group of animals that did not receive oxytocin [43]. Data from M. Panaro and co-authors were published in 2020, according to which oxytocin is involved in the regulation of central inflammatory responses and neuroinflammation after hypoxic conditions of the brain [44], pro-inflammatory reactions of microglia in CNS tissues, and the activity of synaptic transmission between multipolar neurocytes, which determines its importance in role of a clinical marker of the course of HS in patients with TBI.

Secondary brain damage in acute TBI occurs against the background of significant swelling of the CNS tissue, which leads to unfavorable outcomes in the long-term period of the disease.

Aquaporins, highly selective transmembrane channels of neurocyte cells, take part in the pathogenesis of the development of post-traumatic edema of brain tissue. The work of K. Rauen et al. in 2020 [45] shows the important role of brain cell aquaporins in the development of edema in TBI by activating specific V1-a receptors in the experiment. The data obtained by K. Rauen are confirmed by the results of E. Zeynalov and co-authors in 2020: activation of the membrane receptor V1-a is responsible for vasoconstriction; V1-b receptor for the regulation of cognitive and behavioral reactions; V2 receptor for the activity of endocytic processes in the nephrogenic epithelium of the kidneys [46]. According to E. Zeynalov et al., in the majority of patients with acute TBI, cerebral edema develops against the background of hyperproduction of vasopressin (with activation of V1-b receptors) and hyponatremia as a result of the syndrome of inadequate secretion of antidiuretic hormone of the pituitary gland [46], which emphasizes the need for systematic monitoring of the ionogram and hormonal panel during TBI treatment. A three-year retrospective analysis of more than 500 patients with acute TBI who received vasopressin therapy showed a statistically significant reduction in the number of deaths in patients in the experimental group [47]. N. Dhillon and co-authors of this study [47] recommend the use of therapy that includes vasopressin drugs in patients with an increased risk of developing secondary complications during the treatment of TBI under the control of clinical indicators, that is, in a hospital setting.

Differential diagnosis of the above-mentioned neuroendocrinological syndromes such as deficiency of the hormone-secreting function of the hypothalamus and pituitary gland is given in Table 1. As follows from the data of scientific works [20, 32-35, 43], determination of the levels of hormones and ions has a decisive role in making the diagnosis of neuro-endocrine disorders, so as subjective symptoms are variable and nonspecific (Table 1).

Table 1. Differential diagnosis of neuroendocrine disorders in patients with acute combined traumatic brain injuries

No	Clinical signs	Hypothalamic syndrome	Diabetes insipidus	Hypopituitarism
1	<i>Headache</i>	Present in anamnesis	No in anamnesis	Absent
2	<i>Blood pressure in blood vessels</i>	Within the age norm/increased with vegetative-vascular course	Elevated at the time of the disease	Decreased at the time of the disease
3	<i>Glucose tolerance test</i>	Impaired glucose tolerance	Impaired glucose tolerance	Impaired glucose tolerance
4	<i>Blood C-peptide</i>	Promoted	Within the age norm	Promoted
5	<i>Serum cortisol</i>	Promoted	Within the age norm	Demoted

6	Plasma aldosterone	Promoted	Within the age norm	Demoted
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Source: compiled by the author

Cognitive and behavioral disorders

In patients with acute combined TBI, neuroendocrine disorders are associated not only with physiological changes in hormone-synthesizing cells, but also with cognitive, emotional and behavioral disorders due to trauma and deficiency of somatotropin, thyroid-stimulating and adrenocorticotrophic hormones [48]. Scientists A. Sander in long-term observation showed that psycho-emotional changes in patients with TBI affect both the process of rehabilitation of the victim and social reintegration with restoration of ability to work in the long term of patient management [49]. Among the most common consequences of the psycho-emotional sphere due to the influence of traumatic factors on brain tissue and central (regulating) endocrine organs, N. Turner and co-authors identify long-term social maladjustment, depressive disorders, and, less often, intellectual and psychological dysfunction [50]. In the chronic period of TBI, cognitive impairment can develop due to post-traumatic stress disorder against the background of central hormonal imbalance [26]. Thus, the management of a patient with TBI requires an integrated approach with the involvement of psychiatric specialists for the differential diagnosis of psychological and psychiatric conditions and the selection of the most adequate treatment tactics in each specific case.

Despite the fact that psychiatric and cognitive symptoms in patients with TBI are often considered in conjunction with post-concussion syndrome, studies have been published that indicate an increased risk of developing neuropsychiatric disorders in patients with acute TBI and hypofunction of the central endocrine glands, compared with patients with normal hormonal function. secreting function of the hypothalamus and pituitary gland [26, 27, 51]. Neuropsychiatric disorders in such patients are manifested by deficits in attention and memory with mild degrees of trauma; impairment of speech and visuospatial constructive skills in severe acute injuries [50, 51]. K. Silveira's 2020 study of patients with acute TBI showed [46] that among survivors of TBI in the late phase of the disease, symptoms of depression were diagnosed in more than 45% of correspondents, and 40% reported suicidal thoughts. A similar study by de L. Munter et al in 2020 [52] confirms that psychological distress is common in patients with TBI during the first year of the disease. Prognostic factors for the development of psycho-cognitive disorders in patients with TBI include the state of the patient's psycho-emotional sphere before injury, psychological complaints at the time of and after injury, reduced psychological flexibility and adaptability, and moral instability [52]. Timely diagnosis of psychological problems after TBI can improve the patient's quality of life, socialization activities and improve cognitive processes.

Conclusions

The most common clinical manifestation of neuroendocrine pathologies in combined acute traumatic brain injury are hormone deficiency and neuropsychiatric symptoms. The clinical consequences of acute brain injuries are heterogeneous and include both physical and cognitive impairments of a transient or chronic type, depending on the presence of a history of brain injuries, the duration and intensity of the traumatic factor. Among the pathogenetic factors influencing the involvement of hormonal disorders in the clinic of traumatic brain injuries are secondary hypopituitarism, hypothalamic syndrome and diabetes insipidus. Post-traumatic decrease in the

synthetic activity of hormone-producing cells of the pituitary gland in the form of somatotropin deficiency is often observed in both the acute and post-traumatic phases of patient management. Inhibition of the synthetic activity of chromotolfin cells of the adenohypophysis during brain injuries develops as a result of ischemic damage to structures in the area of the sella turcica, reactions of immunocompetent cells, hemorrhages and disruption of the portal blood supply system of the hypothalamic-pituitary axis. The most common disorders of the hypothalamic-pituitary axis in patients with acute brain injury in the acute and chronic stages are manifested by a deficiency of somatotropin, gonadotropin and adrenocorticotrophic hormone; deficiency of thyroid-stimulating hormone, which affects the imbalance of basic metabolic metabolism and dyslipidemia. Damage to neuroendocrine regulation can lead to death, dysnatremia, terminal systemic hypotension and disability. In the chronic period of brain injury, psychological disorders in the form of depressive syndromes, suicidal thoughts and social disintegration can develop as a result of post-traumatic stress disorder against the background of central hormonal imbalance. Further research on this issue in order to study the mechanisms of endocrinological damage in brain injuries and the structures of the central nervous system provide experimental modeling of brain damage of various etiologies. The data obtained make it possible to improve the early detection and diagnosis of secondary neuroendocrine disorders due to traumatic brain injury, as well as to increase the effectiveness of complex treatment and the quality of life of patients in the future.

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