# NEUROBIOLOGICAL INDICATORS OF CLINICAL STATUS AND PROGNOSIS OF THERAPEUTIC RESPONSE IN PATIENTS WITH PAROXYSMAL SCHIZOPHRENIA

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***Abstract.*** *Modern ideas about the involvement of neuroinflammation and neuroplasticity processes in the pathogenesis of endogenous mental disorders determine and clarify various aspects of their pathogenesis, determine the need for multidisciplinary clinical and neurobiological studies of their brain mechanisms to objectively assess the acuity and severity of pathological processes in the brain in these diseases., as well as to individually predict the effectiveness of the treatment of these socially significant diseases personalized approach.*

***Keywords:*** *schizophrenia, neurobiological indicators, endogenous mental disorders, predicting the effectiveness of therapy.*

**Introduction.** The problem of diagnostic assessment of mental disorders, which is decisive in the choice of therapy, remains one of the most pressing issues in modern psychiatry and, in particular, is associated with differences in the interpretation of psychopathological conditions and the content of terms, which applies to the concept of negative diseases in schizophrenia. Terms such as" negative disorders"," defect"," deficiency states " are often used as synonyms [1-4]. Ideas about deficits and negative symptoms have varied over a wide range, from considering it in terms of non-specific symptoms in a variety of contexts to identifying deficiency disorders as a key sign of the endogenous schizophrenia process [5-8]. In domestic psychiatry, it was proposed to distinguish between two types of defects:"fershroben", which is accompanied by" pathological autistic activity", and" asthenic autism", which is a simple deficiency with phenomena [9], and to check for deficiency disorders, use a chronodynamic criterion that implies the stability of symptoms during schizophrenia remission. Meanwhile, S. N. in the opinion of Mosolova, the criteria for resilience and non-reversion of deficiency diseases, as well as the specificity of initial conditions, are not generally accepted today, and deficiency symptoms should be understood as relatively constant specific diseases that continue throughout the disease from premorbid to remission and resistance to therapy [10-14].

Emphasizing the importance of differentiating the negative signs and residual manifestations of the disease, residual disorders were examined in the form of schizophrenia reactions, phases and post-procedural development of residual effective psychopathological symptoms and relatively permanent cases in which the procedural changed individual had a life together [15-17].

Proposed a dichotomic approach to the classification of schizophrenia, distinguishing type 1, characterized by the presence of positive symptoms (hallucinations and delusions), a positive response to antipsychotic treatment against drugs, maintaining good cognitive function, and increased activity of D2 dopamine receptors; and Category 2, where negative symptomatology is noted (blurred effect, poor speech and loss of control), which is characterized by a weak reaction to antipsychotics, disorders and neuroanatomic pathologies. At the same time, the dichotomic approach is limited to diagnostic instability and low prognostic value, not consistent with the factor analysis of schizophrenia psychopathology, which consistently demonstrates more than two factors [18-22].

Currently, an agreement has been reached to include five components in the concept of negative symptoms: flattened effect, speech impoverishment (alogia), weakening of social ties (asociality), anhedonia and Abulia [23]. This restructuring takes into account the phenomenological correlation of negative symptoms with cognitive, depressive, and disorganization symptoms.

Negative symptoms occur in patients with schizophrenia spectrum disorders at the same frequency as hallucinations (60%) [24]. A high proportion of rapid progressive formation of negative changes among young individuals after the first attacks [25]. Negative symptoms are associated with a decrease in social activity and quality of life [26], regardless of the presence of depression or positive symptoms (especially those associated with a sense of motivation and pleasure), with a decrease in the positive emotional response to communication and a decrease in the ability to socially influence [27].

It is recommended to distinguish negative symptoms as primary and secondary [28]. Primary negative symptoms are manifestations of a schizophrenia process that exists for a long time or continuously. They can appear before the start of therapy, in the early psychotic period, and with the onset of stabilization after the manifestation of psychosis, they are preserved and become a component of remission. Primary negative symptoms are assessed by patients and their loved ones as changes in character rather than symptoms of the disease; they are mainly manifested by a decrease in motivation, initiative, decision-making, planning ability; find a weak response to resistance to treatment, torpidity or antipsychotic therapy [29].

Primary negative symptoms are characterized by a stable structure that lasts at least a year when it excludes diseases such as depression, anxiety, delusions and hallucinations or side effects of treatment [30]. At the same time, irreversible symptoms corresponding to the classic concepts of schizophrenia defect occur only in a small percentage of patients.

Secondary negative symptomatology is not part of the schizophrenia process, but is positioned as a treatment or a secondary effect of the disease; the residual can be the result of effective symptoms, depression, side effects of antipsychotics (extrapyramidal disorders), hospitalization and Social Communication Disorders. A decrease in the speed of emotional reactions, motor inhibition, slowing down of speech, a social barrier are characteristic. These symptoms are transitorial and can disappear when the factors that cause them are leveled, adequate therapy is carried out [31].

For example, secondary negative symptoms compared to positive symptomatology may respond to effective antipsychotic therapy. Primary negative symptoms included permanent changes in the form of irreversible breakdown of various areas of mental activity: affective-stimulating, cognitive, emotional-voluntary, personal; secondary — mobile, temporary diseases

such as thymopathy and disorders due to the influence of psychopharmacotherapy and social deprivation of patients [32].

To determine whether negative symptoms are primary, clinicians must rule out the 4 most common causes of secondary negative symptoms: (1) Depression, (2) psychotic symptoms, (3) side effects of pharmacotherapy (4) substance abuse [32].

Differential diagnosis of negative, cognitive, depressive and Parkinsonian symptoms is the main task of scientific and practical psychiatry. It should be borne in mind that during the remission phase, psychopathological manifestations such as autistic behavior, emotional smoothness, decreased initiative and others can serve as an expression of positive diseases, in particular depression, anxiety, akinesia, delirium [33].

ICD-11 shows that if symptoms are not associated with affective disorder, drug or drug use, negative symptoms such as emotional flattening, speech impoverishment, Abulia, social barrier, or anhedonia can be detected. According to our data, there is a correlation between S100B protein levels and postshisophrenic depression ($R=0,047$, $p<0,001$) [34], which is consistent with literature data on increased S100B protein concentrations in affective disorders of varying degrees [34]. At the same time, no correlation was found between S100B protein levels and severity of negative symptoms, which makes it possible to consider an increase in S100B protein levels as one of the parameters for differential diagnosis of negative symptoms and depression in schizophrenia [35].

Primary and secondary negative symptoms have common external signs (low speech, reduced facial expressions), which makes them difficult to distinguish in clinical practice. W. From Carpenter's point of view, the ability to revert is the primary discriminatory factor of primary and secondary negative diseases [36].

Negative symptoms are found in 87,5% of patients (according to sans results), including primary – 47% and secondary – 40%. The most common symptom turned out to be emotional blunt (in 72% of cases). Low levels of social activity and significant levels of depression have been reported in patients with negative symptoms [37-39].

According to our data, in 52% of patients, more than a year before the manifest attack, the main negative symptoms of different degrees were observed and prevailed in male patients with the first episode of schizophrenia [40].

Primary and secondary negative symptoms can be permanent and temporary, but it is not always possible to distinguish primary and temporary negative symptoms from secondary negative symptoms. Primary persistent negative symptoms in foreign literature are called deficiency symptoms and are considered as a component of deficiency disorders, on the basis of which the deficiency and non-deficiency subgroups of schizophrenia are distinguished, which differ in clinical appearance, neuroimaging, neuropsychological and neurological characteristics, risk factors and pharmacological response profiles [41-44]. It is important to distinguish primary / secondary ALB symptom, [45] the formation of deficited hizophrenia I included to identify a completely homogeneous subgroup of patient, but the presence of primary and persistent ALB symptoms since the di EA e, poor premorbide performance and a weak response to treatment [46]. Carpenter concept, deficiency disorders include the following symptoms: flattened effect, limiting the range of emotional reactions, poverty of speech, loss of interest, decreased goal setting, restriction of social interaction. Subsequent studies have confirmed the hypothesis that defective schizophrenia is a specific form of the disease [47].

The purpose of the study: is to determine the correlation of quantitative clinical, neuroimmunological and neurophysiological indicators from the point of view of an objective assessment of the severity of pathological processes in the brain and determine the possibility of an individual prognosis of a therapeutic response in the treatment of manic and hallucinatory-delusional conditions within paroxysmal schizophrenia.

**Materials and methods.** The study, carried out in compliance with the standards of modern biomedical ethics, included 80 patients of the SOPB clinic with paroxysmal schizophrenia (F20.01-02 on ICD-10) (all women, 20-50 years old, with an average age of 36,3±11.4 years). manic-delusional diseases (30 patients) and hallucinatory-delusional (50 patients). All patients received syndrome psychopharmacotherapy. In all patients, quantitative clinical, neurophysiological (EEG) and immunological indicators are listed twice – before the start of the course of therapy (on visit 1) and at the stage of formation of remission (on visit 2). The clinical status of patients was determined by the positive and negative symptom scale (PANSS), taking into account both the total amount of PANSS scale scores and the sum of scores on lower measures of positive, negative and general psychopathological symptoms.

Von EEG (10 channels: F7, F3, F4, F8, c3, c4, T3, T4, P3, P4, O1 and O2, 10-20 system-wise, compared to Ipsilateral ear references A1 and A2) was recorded in a state of calm wakefulness with eyes closed. EEG spectral analysis was conducted in narrow frequency sub-bands: Delta (2-4 Hz), Theta-1 (4-6 Hz), Theta-2 (6-8 Hz), Alpha-1 (8-9 Hz), Alpha-2 (9-11 Hz), Alpha-3 (11-13 Hz), beta-1 (13-20 Hz), and beta-2 (20-30 Hz).

These days, blood was selected and used laboratory technology "neuro-immuno-test" (Klushnik T. P. et al., 2014) measured the activity of plasma leukocyte elastase (Le) as an inflammatory marker, as well as levels of autoantibodies to the primary myelin protein (AAT-OBM). as a sign of destructive neuroplastic processes.

In the processing of mathematical data, the neurobiological indicators determined before the start of the course of therapy (in case of Visit 1) were compared with the clinical assessments of patients obtained before the start of the course of therapy (in case of Visit 1) and at the stage of formation of remission after the course of therapy (in case of Visit 2).

To do this, the correlation coefficients between all clinical and neurobiological indicators were first calculated. Then two groups of multiple regression equations were constructed describing the correlation of quantitative clinical, neuroimmunological and neurophysiological indicators.

In the first group of equations describing the neurobiological correlation of the severity of the initial (before the start of the course of therapy) condition of patients, clinical evaluations obtained in case 1 (on the PANSS scale) were used as dependent variables, and the values of neurobiological indicators of Case 1 were used as independent variables. reliable (at p level<0,05÷0,01) and most associated with the relevant clinical indicators of Visit 1. In the second group of equations describing mathematical models for predicting therapy effectiveness, clinical evaluations obtained in the remission formation phase (on the PANSS scale) were used as dependent variables, and the values of neurobiological indicators of Visit 1 were used as independent variables. reliable (at p level<0,05-0,01) and most associated with the relevant clinical indicators of Visit 2.

Research results and their discussion. Regression models, which include only 3-4 of the EEG spectral parameters obtained before the start of the therapy course (visit 1) and one of the

neuroimmunological indicators (Le or AAT-OBM), explain the change in starting (before the start of the therapy course) clinical indicators by 89% to 92% with a high confidence level. the amount and small size of the panss scale) in the group of patients with manic-delusional diseases and in the group of patients with hallucinatory-delusional diseases, the change in initial clinical indicators from 65% to 77%, that is, they adequately reflect the initial sharpness and severity of pathological processes in the brain.

Mathematical models of the prognosis, which include the same number of neurobiological indicators obtained before the start of the course of therapy, explain the change in the values of clinical indicators at the stage of formation of remission (visit 2) from 72% to 87%.) in the group of patients with manic-delusional disorders and in the group of patients with hallucinatory-delusional disorders, 65% to 77% of the values of clinical indicators in the 2nd visit.

This allows you to predict the individual quantitative values of the total sum of panss scale scores and the sum of small table scores of positive, negative and general psychopathological symptoms reflecting the state of patients after the syndrome therapy course at the stage of forming remission, according to the complex of neurophysiological and neuroimmunological indicators obtained before the start of the therapy course.

In patients with manic-delusional diseases, an individual prognosis of the effectiveness of the syndrome therapy course was more favorable (in the form of small values of the PANSS scale scores in case 2), the stronger the EEG symptoms were initially expressed-the activation of the temporal region of the right hemisphere and the maintenance of inhibition processes in the frontal region of the left hemisphere.

In patients with hallucinatory-delusional disorders, the therapeutic response was relatively worse (in the form of large values of PANSS scale scores in case 2), EEG symptoms are "hypofrontal", that is, a decrease in the functional state of the frontotemporal regions of the cortex (especially the left hemisphere).

In both groups of patients, the therapeutic response was relatively worse, the higher the number of autoantibodies to the total myelin protein in the blood plasma, which reflects the activation of destructive neuroplastic processes.

**Conclusions.** The findings highlight the role of the lack of neurophysiological inhibition processes (especially in the frontal and Central zones of the left hemisphere) in the pathogenesis of manic-predicative diseases and the role of "hypofrontal", that is, a decrease in the functional state of the frontotemporal regions of the cerebral cortex (especially the left hemisphere) supports the pathogenesis of hallucinatory-predicative diseases, as well as the involvement of neuroinflammation and destructive neuroplastic processes. processes in the pathogenesis of delusional states within paroxysmal schizophrenia.

The complexes of neurophysiological and neuroimmunological indicators obtained before the start of the course of therapy reflect not only the initial sharpness and severity of pathological processes in the brain, but also adaptive resources of the brain in terms of the possibility of responding to therapy.

This makes it possible to individually predict the effectiveness of standard syndrome course therapy for manic-delusional and hallucinatory-delusional disorders in the future, to timely adjust complex therapy to achieve satisfactory quality remission, and thus optimize the treatment of socially significant mental illness, such as paroxysmal schizophrenia.

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