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Нужны ли новые диагнозы в психиатрии, или нам достаточно помнить о *bouffée délirante* Валантена Маньяна? (К статье Е.В. Снедкова и соавт. «Существует ли анти-NMDA-рецепторный энцефалит?»)

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АННОТАЦИЯ

Новые клинические наблюдения и новые научные данные приводят к выделению новых болезней. Примером подобного рода служит анти-NMDA-рецепторный энцефалит, преимущественно развивающийся у молодых женщин в связи с тератомой яичников и другими предположительными этиологическими факторами, проявляющийся многочисленными неврологическими и психиатрическими симптомами, придающими острому состоянию сходство с первичными психическими нарушениями, и сопровождающийся появлением антител к NMDA-рецепторам. Существование анти-NMDA-рецепторного энцефалита как отдельного нейropsychиатрического расстройства подвергается сомнению отдельными экспертами. В данной статье приводится анализ свежей публикации одной из групп противников нового диагноза.

Ключевые слова: *анти-NMDA-рецепторный энцефалит, мания Белла, фебрильная шизофрения, смертельная кататония.*

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Are the new diagnoses needed in psychiatry, or is it enough for us to remember valentin magnan's bouffée délirante? (To the article by E.V. Snedkov and co-authors 'Is anti-NMDA receptor encephalitis real?')

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ABSTRACT

New clinical observations and new scientific data lead to the identification of new diseases. Anti-NMDA receptor encephalitis, which mainly develops in young women due to ovarian teratoma and other suspected etiological factors, manifested by numerous neurological and psychiatric symptoms that give an acute condition resembling primary mental disorders, and accompanied by the appearance of antibodies to NMDA receptors, is one example of this kind. Some experts are questioning whether anti-NMDA receptor encephalitis should be considered a separate neuropsychiatric disorder. This article analyses a recent publication by one of the groups opposing the new diagnosis.

Keywords: *anti-NMDA receptor encephalitis, Bell's mania, febrile schizophrenia, lethal catatonia.*

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The evolution of psychiatry, along with other manifestations, includes changes in the classification of diseases and the emergence of new diagnostic forms. Novel diagnostic concepts are not always understood and approved by professionals. In the past, the concept of *dementia praecox* by Emil Kraepelin was opposed by prominent psychiatrists, including K Wernicke, A Meyer, K Bongeffer AE Hoche, E Kretschmer, K Kleist, K Leonhard, VP Serbsky, and SS Korsakov.

Kraepelin's theory of *dementia praecox*, which is now called schizophrenia, thanks to Eugen Bleuler, was further developed; however, the taxonomy of schizophrenia differed and still differs in individual diagnostic classifiers and remains the subject of professional discussions.

Furthermore, some long-existing psychiatric diagnoses are losing relevance, such as neurasthenia, which is absent in current classifications and has faded into obscurity.

Moreover, the fundamental difference between psychiatry and related neurology, as well as infectious and internal diseases, is the speculative nature of clinical concepts and the limited possibility of their objectification. The inconsistencies of psychiatric judgments that inevitably arise in this regard create a wider diversity in the taxonomy of mental disorders than in the classification of diseases in internal medicine.

The inconsistencies and certain subjectivism of ideas (immanent in the nature of psychiatry as a special field of medical knowledge) underlie the rejection by a noticeable part of the professional community of the psychiatric section of the new edition of the International Classification of Diseases, 11th revision (ICD-11; a diagnostic tool that, we believe, is far from ideal but more beneficial than ICD-10).

Despite the similar attitude of experts and practitioners toward new phenomena, traditional ideas in psychiatry change, and along with the revision of the taxonomy of already known mental disorders and their diagnostic criteria, new forms of mental and behavioral disorders are identified and new psychiatric diagnoses are revealed (coupled with disappearance of some old ones).

New diagnoses include disruptive mood dysregulation disorder (DMDD), which was first included in the Diagnostic and Statistical Manual

of Mental Disorders, 5th edition (DSM-5), and is characterized by recurrent irritability and angry outbursts in children and adolescents aged 6–18 years.

DMDD is not limited to other mental disorders in children and adolescents, such as oppositional defiant disorder, conduct disorder, or bipolar disorder, although it can form comorbid combinations with these conditions, and therefore, according to the DSM developers, it should be classified to a separate diagnostic unit.

This disorder reveals depressive conditions in this classifier (DSM-5 depressive and related disorders). This is probably to attract the attention of researchers and doctors to the new diagnosis and prompts the possibility of its use in clinical practice.

Another example of a new psychiatric diagnosis is a diagnostic category that has recently emerged in suicidology.

Schuck et al. stated that standard strategies, such as reporting suicidal thoughts and assessing past suicide attempts, are insufficiently effective in reducing suicide rates.

Currently, research groups aim at evaluating the acute mental state that precedes a suicide attempt, and hence, the concept of the abovementioned suicide crisis syndrome has been formulated. The main purpose of the new diagnosis is expanding the ability to identify suicidality and increase the efficiency of helping people on the verge of suicide.

The syndrome includes five components with proven diagnostic significance: entrapment¹, affective disorder, loss of cognitive control, increased arousal, and social withdrawal. It is expected that the use of a new diagnostic category for research and practical purposes will improve the quality of antisuicide care and reduce the number of suicides [1].

The emergence of a new psychiatric or neuropsychiatric diagnosis of anti-NMDA receptor encephalitis, which is a condition manifested by psychotic symptoms that can serve as a basis for the erroneous diagnosis of schizophrenia or other primary mental disorder but represents contraindications to the use of antipsychotics owing to ineffectiveness and high risk of treatment complications, is crucial.

¹Apparently, in this context, a psychological phenomenon is intended, including one arising in connection with a patient's social problems.

Dalmau et al. observed acute encephalitis with antibodies to NMDA receptors in a 34-year-old female patient, presented subsequent descriptions of a series of similar cases, and proposed the concept of anti-NMDA receptor encephalitis, highlighting the features of this condition: more common in women (women–men ratio, 8:2); the average age of patients is 21 years (range: 1–85 years), with 37% of cases occurring under the age of 18 years; antibodies to receptors are considered both a diagnostic marker and key link in the disease pathogenesis; the main triggers of the condition are tumors (mainly ovarian teratoma) and encephalitis caused by the herpes simplex virus; and multiple neuropsychiatric manifestations including psychotic symptoms, cognitive impairment, affective disorders, seizures, agitation, abnormal movements, and coma. The variety of psychopathological symptoms makes it difficult to distinguish the condition from a primary psychotic disorder.

In 80% of patients, improvement is achieved using immunotherapy and, if required, by tumor removal. Recovery is slow, predictive biomarkers for encephalitis has not yet been discovered, and methods to accelerate recovery have not yet been developed [2].

Although anti-NMDA receptor encephalitis exhibits all the indications of a separate disease based on the classical concepts of nosology (etiology, pathogenesis, patterns of course and outcome, and rational approaches to therapy), the right of a new diagnosis to exist is questioned by some experts, including Snedkov et al.

Snedkov et al. provided a negative answer to the question in the title.

Snedkov et al. showed a parallel association between anti-NMDA receptor encephalitis and Bell's mania and cycloid psychoses and Kleist–Leonhard nonsystematic schizophrenia (the authors call these forms nonsystemic, although in Russian translations from German and in English articles they cited, the term “nonsystemic” is used).

The authors' statement about the identity of anti-NMDA receptor encephalitis and Bell's mania is relatively controversial.

Accordance to its classical descriptions, Bell's mania, also called delirious mania, has similarities with catatonia and is often manifested by catatonic

symptoms, which is not a typical form of acute encephalitis discussed in the present study.

Mandatory criteria for Bell's mania diagnostics are manic manifestations combined with delirious symptoms, the presence of manic episodes or bipolar disorder in the patient's own or family history, and a therapeutic response to standard antimanic medications [3, 4].

Nothing similar, especially treatment response, is noted in anti-NMDA receptor encephalitis. In addition, the development of Bell's mania and anti-NMDA receptor encephalitis is associated with different etiological factors, mainly psychostimulants and neurological disorders in the former and tumors or some other causes in the latter.

Another difference between anti-NMDA receptor encephalitis and Bell's mania is that the former predominantly develops in young women (as mentioned by Professor Snedkov et al.), whereas the latter is not associated with gender differences, at least so definite ones.

Furthermore, electroconvulsive therapy and ketamine were found to be beneficial in the treatment of Bell's mania [5, 6], whereas in autoimmune encephalitis, such interventions are unlikely to improve the patient's condition; in any case, there is no evidence of their possible effectiveness in the disorder under discussion.

The concept of Bell's mania and anti-NMDA receptor encephalitis, as declared by Snedkov et al., is to some extent refuted by the authors themselves, so that the article provides data on the absence of catatonic symptoms in the latter, whereas for the former, catatonia, as mentioned above, is a frequent clinical manifestation.

The viewpoint of Snedkov et al. was partly confirmed by Restrepo-Martinez et al. who observed symptoms of delirious mania in 4 of 79 patients with anti-NMDA receptor encephalitis; however, in this case, the similarity of these two disorders is not shown, but only that the symptoms of one of them may be observed in the clinical presentation of the other, and the legitimacy of the existence of the latter diagnosis is not questioned [7].

Bell's mania is generally considered in a rather heterogeneous group of neuropsychiatric conditions, including febrile schizophrenia, deadly catatonia, neuroleptic malignant syndrome, and idiopathic

hyperthermia. The heterogeneity of this group of conditions, according to the authors of these notes, rather allows the inclusion of anti-NMDA receptor encephalitis in it than creates grounds for denying encephalitis to be considered as an independent neuropsychiatric disease.

We respect outstanding scientists such as Meinert and Bernard; however, we cannot help but notice that the relevant arguments in scientific discussions in the 21st century are rather the scientific facts obtained from high-quality scientific research than the expert judgments of the great scientists in the past, regardless of their scientific merits.

In support of their opinion, Snedkov et al. cited data on the relationship between maternal infectious diseases and mental disorders in children, including autism spectrum disorder. Notably, the respected authors put emphasis on autism spectrum disorder, apparently rejecting the condition as a psychiatric diagnosis to the same extent as anti-NMDA receptor encephalitis.

The article by respected authors contains considerable data from neurochemical, neuroimmune, neuromorphological, and other laboratory and instrumental studies and clinical descriptions of various mental disorders without explicit indications of how the information provided relates to the controversial (according to the present study) legitimacy of the anti-NMDA receptor encephalitis diagnosis.

Analyzing various sources, respected authors emphasized the multiple causes of anti-NMDA receptor encephalitis, ironically placing the abbreviation of this term in brackets to emphasize the insufficient consistency of this diagnostic phenomenon. This argument slightly provides credibility to the main thesis of the article, namely, the polyetiological nature of schizophrenia, which has been indicated by numerous studies conducted in the first half of the 20th century, which do not provide sufficient grounds for denying its existence.

Snedkov et al. reported unremarkable magnetic resonance imaging findings in acute encephalitis. Further, it can be mentioned that panic disorder, major depression, bipolar disorder, most cases of schizophrenia, and several other mental disorders are not accompanied by specific morphological manifestations detected using neuroimaging methods; however, the existence of these diseases does not seem to be opposed by other studies.

Snedkov et al. justified doubts on the existence of the diagnosis of anti-NMDA receptor encephalitis by the fact that antibodies to NMDA receptors are found in various diseases, but this argument can hardly be considered decisive. Such nonspecificity is a common occurrence in medicine. For example, an increase in the level of C-reactive protein is noted in systemic collagenosis, acute pneumonia, infective endocarditis, and some forms of schizophrenia. However, we believe that this is not a sufficient basis for denying the existence of these conditions as individual diseases.

Amyloid plaques are observed not only in Alzheimer's disease, and spherical cytoplasmic eosinophilic inclusions are revealed not only in dementia with Lewy bodies, but this does not prevent the two mentioned neurodegenerative diseases from being classified as independent nosological forms.

The authors highlighted the expression "powerful and hazardous autoimmune antibodies" (emphasizing their own skeptical attitude toward their pathogenetic significance). Nonetheless, other studies probably do not consider that some nonspecific factors manifest themselves differently depending on individual characteristics of susceptibility. For example, the Epstein-Barr virus, which does not cause disease development in most people, can play a dramatic role in the lives of individuals with particular sensitivity to its pathogenic influence, acting as an etiopathogenetic factor in the development of infectious mononucleosis, Burkitt lymphoma, nasopharyngeal cancer, multiple sclerosis, Parkinson's disease, and many other, including deadly, diseases.

In an annotation to their article, Snedkov et al. emphasized the danger of hasty interpretations of neurobiological data isolated from clinical knowledge. It should be noted that in traditional Russian psychiatry, the phrase "clinical knowledge" often sounds remarkable, but it is not always endowed with simple and easily comprehended content.

In addition, the authors of numerous and most serious publications on anti-NMDA receptor encephalitis, including researchers who first registered this acute neuropsychiatric disorder and presented descriptions of it, primarily Dalmau et al. [2], cannot be suspected of insufficient professional competence.

As mentioned previously, the critical difference between psychiatry and any other branch of clinical medicine has been assessed with extensive

possibilities for arbitrary interpretation, which enabled Snedkov et al. deny the existence of anti-NMDA receptor encephalitis and possibly some other mental disorders and certain diseases not related to psychiatry.

The main aspect for patients in a psychiatric and any other clinic is not the subject of psychopathological discussions, but the entries in the medical prescription sheets made by the bearers of one point of view or another. The ultimate benefit of patients and society is effective and safe treatment for mental disorders.

In conclusion, we believe that in future possible publications, our respected opponents in academic discussions will recommend rational approaches to

the treatment of mental (more precisely neuropsychiatric) disorders that, in their opinion, do not exist.

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