УДК: 616.89
DOI: https://doi.org/10.17816/nb624104

Существует ли анти-NMDA-рецепторный энцефалит? I. Проблемы диагностики

Е.В. Снедков[1], И.А. Волчек[2,3], И.В.Лемешев[1,4]

[1]Психиатрическая больница св. Николая Чудотворца, Санкт-Петербург, Россия
[2]Российский биотехнологический университет, Москва, Россия
[3]Научно-исследовательский центр иммунологии и аллергологии, Москва, Россия
[4]Северо-Западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия

Автор, ответственный за переписку: Илья Владимирович Лемешев, ilya.lemeshev@gmail.com

АННОТАЦИЯ

На основании комплексного анализа результатов клинических, нейрофизиологических, нейроиммунологических, нейробиологических и патологоанатомических исследований авторы обзора подвергают сомнению состоятельность концепции анти-NMDA-рецепторного энцефалита. Подчёркиваются важность изучения саногенетических механизмов в медицине и опасность поспешных интерпретаций нейробиологических данных в отрыве от клинических знаний

Ключевые слова: *анти-NMDA-рецепторный энцефалит, диагностика ANMDARE, циклоидный психоз, кататония при ANMDARE, саногенетические механизмы*.

Для цитирования:
Снедков Е.В., Волчек И.А., Лемешев И.В. Существует ли анти-NMDA-рецепторный энцефалит? I. Проблемы диагностики // Неврологический вестник. 2023. Т. LV. Вып. 4. С. 66–78. DOI: https://doi.org/10.17816/nb624104.

Рукопись получена: 30.11.2023 **Рукопись одобрена**: 13.12.2023 **Опубликована**: 10.01.2024

DOI: https://doi.org/10.17816/nb624104

Is anti-NMDA receptor encephalitis real? I. Diagnostic challenges

Evgeny V. Snedkov[1], Igor A. Volchek[2,3], Ilya V. Lemeshev[1,4]

[1]Psychiatric Hospital of St. Nicholas the Wonderworker, St. Petersburg, Russia
[2] Federal State Budgetary Educational Institution of Higher Education Russian Biotechnological University, Moscow, Russia
[3]Research Center for Immunology and Allergology, Moscow, Russia
[4]North-Western State Medical University named after I.I. Mechnikov, St. Petersburg, Russia

Corresponding author: Ilya V. Lemeshev, ilya.lemeshev@gmail.com

ABSTRACT

After conducting a thorough analysis of clinical, neurophysiological, neuroimmunological, neurobiological, and neuropathological research findings, the authors of the review question on the validity of the anti-NMDA receptor encephalitis concept. The review highlights the significance of studying sanogenetic mechanisms in medicine and warns against hasty interpretations of neurobiological data without clinical knowledge.

Keywords: *anti-NMDA receptor encephalitis, ANMDARE diagnosis, cycloid psychosis, catatonia in ANMDARE, sanogenetic mechanisms*.

For citation:
Snedkov EV, Volchek IA, Lemeshev IV. Is anti-NMDA receptor encephalitis real? I. Diagnostic challenges. *Neurology Bulletin*. 2023;LV(4):66–78. DOI: https://doi.org/10.17816/nb624104.

Received: 30.11.2023 **Accepted**: 13.12.2023 **Published**: 10.01.2024

Descriptions of "anti-NMDA[1] receptor encephalitis" (ANMDARE) are identical to the clinical presentation first outlined in 1849 by Luther Bell [1]. Bell did not assign a name to the disease. In the Wernicke–Kleist–Leonhard school, it was defined as a hyperkinetic attack of cycloid psychosis of mobility [2, 3]. In the International Classification of Diseases, 10th revision, cycloid psychoses are included in the categories F23.0 and F23.1.

Cycloid psychoses are characterized by an intermittent course; however, hyperkinetic attacks are accompanied by the risk of autochthonous development of a life-threatening febrile status due to diencephalic dysfunction.

According to existing research, unlike the genetic factors of bipolar affective disorder and nonsystemic schizophrenia (including periodic catatonia), which have a greater proportion, cycloid psychoses and systemic schizophrenia are associated with prenatal infections [4–6]. The proposed mechanism is the activation by the maternal immune system of the secretion of pro-inflammatory cytokines that can penetrate the blood–brain barrier, causing oxidative stress and protein expression changes in the developing structures of the diencephalon (in the first trimester of pregnancy) or the cerebral hemispheres (in the second trimester). This results in nonspecific histopathological changes in the brain by aberrations in neuronal growth/migration and receptor density, axonal projections, dendritic arborization, and congenital endocrine and immune imbalances [7–10]. Pro-inflammatory cytokines can cause long-term changes in glucocorticoid receptor gene expression with hyperreactive responses of the hypothalamic–pituitary–adrenal axis to stress loads [11].

The effects of maternal immune activation during pregnancy depend on the sex of the unborn child. Because estrogen positively and androgen negatively modulate corticotropin-releasing hormone synthesis, stress reactions are accompanied by sharper increases in glucocorticoid level in the blood plasma in women [12]. A direct relationship was found between the levels of pro-inflammatory cytokines (interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor α), immunoglobulin IgG or IgM classes in pregnant women, and the risk of psychosis in the postnatal life of their offspring [13, 14]. Immune marker levels were considerably higher in patients with acute transient psychotic disorders, including cycloid psychoses, than in controls [15].

Studies showed that herpes viruses (e.g., cytomegaloviruses), influenza viruses, adenoviruses, rhinoviruses, coronaviruses, rubella virus, bacterial urogenital infections, and toxoplasma are pathogens that may be etiologic factors of pathogenetic changes in the central nervous system of the embryo or fetus and manifest itself in the development of psychosis in adult life [4, 12, 16–18]. Because vaccination during pregnancy stimulates the maternal immune system and cytokine response, its consequences may be detrimental to the offspring [7].

The long-term psychiatric consequences of maternal infections are not limited to systemic schizophrenia and cycloid psychoses. A relationship was found between maternal infections and mental retardation, autism spectrum disorder, attention deficit hyperactivity disorder, Gilles de la Tourette's syndrome, and obsessive–compulsive disorder [7, 19, 20].

In cases where the mother's cytokine response to infection has a pathogenic effect on the development of the child's brain, its other components are extremely beneficial. Diaplacental transfer of maternal antibodies (immunoglobulins) ensures humoral immunity to infectious agents, which is crucial for survival, especially in early infancy [21]. Among them, antibodies to the GluN1 subunit of glutamate NMDA receptors (NMDAR1-AB) can be transmitted to the child [20, 22].

Classic neuronal (onconeural) autoantibodies are antibodies produced by the body in response to antigens of tumor cells, which attack the proteins of the nuclei and cytoplasm of neurons, causing their death, axonal degeneration, reactive gliosis, and microglia activation, i.e., a neuroinflammation pattern. Paraneoplastic autoimmune encephalitis and encephalomyelitis with pathomorphological changes in the brain develop in approximately 1% of cancer patients.

In the 21st century, the list of neuronal autoantibodies has expanded significantly owing to the discovery of immunoglobulins, which can also appear in the blood plasma and cerebrospinal fluid in

[1]NMDA—N-methyl-D-aspartic acid.

tumors; however, their effect is limited by the selective binding of synaptic receptor proteins on the surface of neurons. Almost 50 types of "autoantibodies to neuronal membrane receptors" have been identified, particularly antibodies to acetylcholine receptors, dopamine D_2 receptors, and GABA-A[2] and GABA-B receptors. NMDAR1-ABs were the most common [22–26].

The pathogenic role of autoantibodies on membrane receptors is unclear. No evidence has revealed that they cause inflammation or other damages to the mature brain [23, 26]. NMDAR1-AB are polypeptides like endorphins. The binding of both with synaptic proteins are identical, i.e., the corresponding receptors are temporarily immersed in membrane lysosomes, which ensures reversible desensitization. Their molecules do not penetrate the bodies of neurons [16, 22]. The production of endorphins is biologically beneficial, and its enhancement in response to stress minimizes the development of persistent post-stress disorders.

NMDAR1-AB belongs to the natural human autoimmune repertoire. Extensive screening studies in healthy people and patients with various mental and somatic diseases have revealed high seroprevalence (10%–15%). There is an exception that in patients with Parkinson's disease, NMDAR1-AB is detected almost half as often as among age-matched people without neuropsychiatric diseases. NMDAR1-AB seroprevalence increases with age; hence, 20% of people aged over 80 years are NMDAR1-AB carriers. NMDAR1-AB seroprevalence in migrants and refugees is higher than that in the general population [22, 24, 26–32]. Long-term follow-up of seropositive patients showed fluctuations in NMDAR1-AB levels. Various phenomena such as life stress, seasonal infections, and intestinal microbiota disorders lead to a temporary increase in their number [20, 28, 31]. Presented data indicate the neuroprotective function of NMDAR1-AB; these antibodies can serve as an indicator of its mobilization.

Neither the presence of NMDAR1-AB in the blood serum nor its titer predicts disease development [24]. Seropositive patients with acute psychosis differ from seronegative patients as regards the presence of a history of obstetric complications or neurotrauma and shorter duration of untreated psychosis. No differences were noted in their symptom profiles [33].

American neurologists who described ANMDARE in 2005–2007, owing to associations of acute polymorphic psychosis with the simultaneous detection of NMDAR1-AB in the cerebrospinal fluid and ovarian teratoma in patients, initially considered it "paraneoplastic" [34, 35]. However, further studies showed that ANMDARE is associated with ovarian teratoma in 20%–30% of cases [36, 37].

ANMDARE can be triggered by herpes [38]; influenza [39]; coronavirus infection (COVID-19) [40, 41]; vaccination against COVID-19 [40, 41]; vaccination against diphtheria, tetanus, pertussis, and poliomyelitis [42]; cryptococcal meningitis [43]; demyelinating process [44]; postpartum hormonal changes [45]; immunotherapy after organ transplantation [46]; emotional stress [47]; and any condition accompanied by a vigorous immune response [28, 31]. This is a strong argument in favor of the idiopathic nature of the disease.

Teratomas are congenital tumors. Maternal viral (usually adenoviral) infection during pregnancy is a key etiologic factor of ovarian teratoma [48]. In cases where an ovarian teratoma is observed in ANMDARE, it is referred to as two consequences of the same pathogenic exposure to pro-inflammatory cytokines that occurred during the patient's intrauterine life. The interpretation of an asymptomatic congenital tumor as a trigger for the sudden production of NMDAR1-AB and development of acute psychosis seems unusual. The resolution of psychosis after tumor resection can be explained by the disappearance of NMDAR1-AB from the blood during anesthesia [49], most likely due to the activation of stress-limiting brain systems (GABAergic, serotoninergic, and opioidergic) produced by it.

Approximately 80% of ANMDARE patients are women aged 18–45 years without premorbid characterological abnormalities [50, 51]. An attack may be preceded by a short period (5–7 days) of insomnia, headache, anorexia, nausea, vomiting, and fever. Suddenly, aimless psychomotor agitation occurs with hyperkinesis, impulsive behavior, oneiroid confusion, incoherent speech, sudden changes in affect and delusional ideas, transient illusions of vision and hearing, hyperthermia, and autonomic instability. Sometimes the hyperkinetic

[2]GABA— γ-aminobutyric acid.

phase develops after the polar opposite phase of torpor with freezing, catalepsy, akinetic mutism, and lack of reactions to what is happening.

Psychosis lasts from several days to a year, usually ending with complete recovery. However, in 8%–10% of cases, psychomotor agitation increases at lightning speed and is replaced by "silent hyperkinesia," and after a few days, death occurs [16, 34, 35, 51–54]. Approximately 50% of patients, including those previously operated for ovarian teratoma, subsequently have up to four relapses of ANMDARE, which also do not lead to defect formation. Intermissions last from 3 months to 13 years [37, 50, 53].

Several experts interpret any movement abnormalities, such as agitation, pathetic poses, immobility, and mutism, as "catatonic signs of ANMDARE" [36, 51, 55]. Meanwhile, motor disorders are limited to a quantitative increase or suppression of expressive and reactive movements (hyperkinesis or akinesia). Qualitative distortions of motor skills characteristic of catatonia (Wernicke's parakinesia, frontostriatal symptoms), such as stable muscle hypertonicity, step-by-step movements, automatic muscle resistance to passive stretching (not associated with the affect of fear), iterations, stereotypies, echopraxia, spastic contractions of individual muscle groups, dyskinesia, grimacing, and others [56], are not revealed in descriptions of ANMDARE not complicated by the use of antipsychotics. Clinicians see in these descriptions analogies with the presentations of Stauder's "fatal catatonia," Mitsuda's "atypical psychoses" [53, 55], and Wernicke–Kleist–Leonhard's cycloid psychosis of mobility [54, 57], fundamentally separated by these scientists from catatonia [2].

Approximately three-quarters of patients with later identified NMDAR1-AB are hospitalized in psychiatric hospitals with a diagnosis of acute polymorphic psychotic disorder and suspected psychoactive substance intoxication [16, 34] and/or schizophrenia [55]. Antipsychotics are prescribed to almost everyone [52, 58].

Because NMDAR1-AB deposits are mainly detected on the cytoplasmic membranes of hippocampal neurons [35], researchers investigated for symptoms of memory deficits in patients with ANMDARE [36, 52]. Wernicke's hypermetamorphosis of attention is typical for mobility psychosis/ANMDARE, in which patients are extremely distracted by random stimuli. Voluntary attention impairment is a common sign of brain stem lesions, particularly of the thalamic nuclei. Manifestations of Korsakoff syndrome, which is characteristic of organic hippocampal lesions, namely, fixation amnesia, amnestic disorientation, and confabulations of everyday content, during or at the end of an ANMDARE attack have not been described [37, 59]. Congrade amnesia during impaired consciousness is not a manifestation of Korsakoff syndrome.

NMDAR1-AB has been identified as an "ANMDARE diagnostic marker" [16]. However, NMDAR1-AB is detected with similar success in arterial hypertension, diabetes mellitus, systemic lupus erythematosus, Sjögren's syndrome, cerebellar ataxia, traumatic brain injury, stroke, epilepsy, rapidly progressing dementia, mania, schizophrenia onset, and other diverse diseases.

The presence of these "potent and hazardous autoimmune antibodies" is considered by some experts to be a reason for diagnosing ANMDARE and for immediate immunotherapy. They call ANMDARE, which occurs in the form of acute polymorphic psychomotor psychosis, "classical"; its other imaginary forms are called "atypical forms" [26, 55, 44].

Other authors argue against ANMDARE expansion diagnostics. Antibody tests can be false-positive, and not all mental/cognitive dysfunctions indicate organic encephalopathy. The diagnosis of ANMDARE is valid only if the paraclinical findings are consistent with its "well-characterized phenotype" [60].

Others still attach decisive importance to the "classical phenotype of autoimmune encephalitis," distinguishing between "seropositive" (≈40% of cases) and "seronegative" (≈60%) forms. The "pathogenic antibodies" that induce the development of characteristic symptoms in seronegative cases have not yet been identified. The diagnosis of seronegative autoimmune encephalitis is the same basis for immunotherapy, which theoretically can improve long-term outcomes [61].

Indeed, seropositive and seronegative ANMDARE do not differ in their clinical presentation, outcomes, incidence of concomitant teratomas, patterns of changes in the cerebrospinal fluid,

electroencephalography, and neuroimaging data [23]. There is one seemingly paradoxical exception to this rule: seronegative patients tolerate immunotherapy better than seropositive patients [62].

Leukocytosis is detected in the blood of patients with ANMDARE along with normal levels of C-reactive protein (a marker of inflammation) [63]. In the cerebrospinal fluid, moderate lymphocytic pleocytosis may occur, and the protein content is normal or slightly increased. These nonspecific abnormalities do not correlate with the severity of the condition and may persist during the recovery period [50, 52, 53]. They may serve as markers of adaptive humoral immunity activation [64]. The number of T-helper cells and pro-inflammatory cytokines in ANMDARE patients, regardless of immunotherapy, decrease, instead of their increase typical for encephalitis [22, 65].

On electroencephalogram, symmetrical high-amplitude bursts of delta waves ("extreme delta brush") are recorded in the frontoparietal regions. They do not correlate with tonic–clonic seizures, and no epileptiform discharges are observed [53, 66]. In the 1960s, this electroencephalographic pattern was described in Mitsuda's "atypical psychoses." Slow wave activity is directly proportional to the cortical expression of brain-derived neurotrophic factor and an increase in the number of cortical bonds [67].

High-amplitude delta activity in the anterior parts of the brain is a marker of special forms of consciousness caused by the disconnection of the functional connection between the thalamus and cortex. These include dreams, deep meditation, and psychedelic states induced by ayahuasca or subanesthetic doses of ketamine. Phenomenologically, they are combined in the following way:

a) Disconnection from the outside world

b) Spontaneous formation of visualized, scene-like, and affectively rich ideas perceived in subjective space, completely replacing reality

c) Cognitive–motor dissociation

Bursts of delta waves coincide with the peaks of dream experiences. It is believed that delta rhythms are involved in the homeostatic processes of brain activity, integration of mental functions, transitions from unconsciousness to consciousness, processes of anxiety and hyperactivity reduction, healing, and restoration. Decreased delta activity correlates with negative symptoms and cognitive deficits [68, 69]. Mayer–Gross considered "extreme delta brush" as a biomarker of the "oneiric form of experience," accompanied by the mobilization of the protective and restorative systems of the brain.

Magnetic resonance imaging of the brain was unremarkable in this regard. In one-third of ANMDARE patients, signal intensity from the medial temporal lobes temporarily increases without identifying areas of increased contrast accumulation and edema [35, 50, 52].

Functional neuroimaging data in ANMDARE indicate impaired integration of white matter fibers in the thalamocortical, frontoparietal, and sensorimotor neural networks. Frontotemporal hypermetabolism is combined with hypometabolism in the parietal and occipital cortex [70]. Meinert considered disruption of the connectivity of the associative fibers connecting the subcortical centers with the cortex to be the brain basis of "amentia," which is acute idiopathic psychosis; one of its forms that he identified coincides descriptively with ANMDARE. Frontotemporal hypermetabolism is a distinctive feature of the pathophysiology of cycloid psychoses [71].

Autopsies of patients who died from an ANMDARE attack did not reveal any signs of neuroinflammation [23, 27, 26, 30, 63]. The pathoanatomical presentation becomes more complicated if the death was preceded by immunotherapy. Autopsies showed nonspecific microglial activation, neuronal degeneration, extensive gliosis, and fiber demyelination. However, in these cases, no hemorrhages, neuronophagia nodules, complement protein deposits, and T-lymphocyte infiltrates were observed—nothing that would indicate inflammatory damage to the brain (encephalitis) [34, 35, 44, 64, 72].

Outstanding clinicians K Wernicke, K Kleist, K Stauder, and K Leonhard correlated the source of the development of psychoses, which coincided with their clinical description of ANMDARE, with disturbances in the functioning of brain stem structures. Golant called them "diencephalopathic psychosis with a periodic course." Shmaryan described the pathophysiological mechanism of diencephalopathic psychosis as a "sensitization syndrome of the stem system," which sharply and specifically changes the functional state of cortical processes under certain conditions.

Modern studies on the role of stem structures in the development of ANMDARE are few [73–76].

Ideas about the forms of diseases are always formed empirically, and only then does pathophysiology help understand their essence (Claude Bernard, 1865). The ANMDARE story clearly illustrates how movement in the opposite direction can extremely confuse cause-and-effect relationships, the relationship between pathogenesis and sanogenesis, understanding the nature of the disease, and the rationale for therapeutic interventions.

NMDAR1-AB does not cause inflammation or brain tissue damage. This fundamentally contradicts the theory of "autoimmune encephalitis," which defines the polymorphic presentation of acute transient psychomotor psychosis [23, 25, 26, 32, 35]. The production of NMDAR1-AB is critical in humoral autoimmunity. NMDAR1-AB has biologically relevant regulatory, immunomodulatory, and neuroprotective functions [30, 31, 35, 43, 64, 77].

Symptoms can represent either a loss of one or another functional ability or a protective or compensatory mechanism that prevents further disorganization of mental activity. The study of sanogenetic mechanisms is no less crucial than the study of the pathogenesis of diseases. To date, we have limited understanding on which manifestations of the disease are associated with its pathogenic basis, which should be suppressed, which reflect the process opposing it, and which needs to be promoted [78–80]. The introduction of powerful biomedical technologies into clinical practice requires particularly balanced interpretations of neurobiological findings and strict adherence to the principle of *primum non nocere.*

ДОПОЛНИТЕЛЬНО

Финансирование. Исследование не имело спонсорской поддержки.

Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Вклад авторов. *Снедков Е.В.* — концепция и дизайн исследования, сбор и обработка материалов, обзор литературы, написание текста; *Волчек И.А.* — концепция и дизайн исследования, сбор и обработка материалов, обзор литературы, написание текста; *Лемешев И.В.* — обзор литературы, написание текста, внесение окончательной правки.

Funding. This publication did not receive support from any external sources of funding.

Conflict of interests. The authors declares no conflicts of interests.

Contribution of the authors. *E.V. Snedkov* — GC, literature review, data analysis, writing the main part of the text; *I.A. Volchek* — GC, literature review, data analysis, writing the main part of the text; *I.V. Lemeshev* — writing the main part of the text, conducting a literature review, and making final edits.

СПИСОК ИСТОЧНИКОВ

1. Bell L. On a form of disease resembling some advanced stages of mania and fever, but so contradistinguished from any ordinary observed or described combination of symptoms as to render it probable that it may be overlooked and hitherto unrecorded malady // Am. J. Insanity. 1849. Vol. 6. N. 2. P. 97–127.

2. Леонгард К. Систематика эндогенных психозов и их дифференцированная этиология. Пер. с нем. под ред. А.С. Тиганова. М.: Практическая медицина; 2010. 456 с.

3. Kleist K. Die klinische Stellung der Motilitatspsychoden // Zeitschrift fur die gesamte Neurologie und Psychiatrie, Referate und Ergebnisse. 1911. Vol. 3. P. 914–917.

4. Franzek E., Beckmann H. Season-of-birth effect reveals the existence of etiologically different groups of schizophrenia // Biological Psychiatry. 1992. Vol. 32. N. 4. P. 375–378. DOI: 10.1016/0006-3223(92)90042-x.

5. Stöber G., Franzek E., Beckmann H. The role of maternal infectious diseases during pregnancy in the etiology of schizophrenia in offspring // European Psychiatry. 1992. Vol. 7. N. 4. P. 147–152. DOI: 10.1017/S0924933800005241.

6. Stöber G., Kocher I., Franzek E. et al. First-trimester maternal gestational infection and cycloid psychosis // Acta Psychiatrica Scandinavica. 1997. Vol. 96. N. 5. P. 319–324. DOI: 10.1111/j.1600-0447.1997.tb09923.x.

7. Al-Haddad B.J., Oler E., Armistead B. et al. The fetal origins of mental illness // American Journal of Obstetrics and Gynecology. 2019. Vol. 221. N. 6. P. 549–562. DOI: 10.1016/j.ajog.2019.06.013.

8. Massrali A., Adhya D., Srivastava D.P. et al. Virus-induced maternal immune activation as an environmental factor in the etiology of autism and schizophrenia // Frontiers in Neuroscience. 2022. Vol. 16. P. 834058. DOI: 10.3389/fnins.2022.834058.

9. Ratnayake U., Quinn T., Walker D.W. et al. Cytokines and the neurodevelopmental basis of mental illness // Frontiers in Neuroscience. 2013. Vol. 7. P. 180. DOI: 10.3389/fnins.2013.00180.

10. Vasistha N.A., Pardo-Navarro M., Gasthaus J. et al. Maternal inflammation has a profound effect on cortical interneuron development in a stage and subtype-specific manner // Molecular Psychiatry. 2020. Vol. 25. N. 10. P. 2313–2329. DOI: 10.1038/s41380-019-0539-5.

11. Seckl J.R., Holmes M.C. Mechanisms of disease: Glucocorticoids, their placental metabolism and fetal programming of adult pathophysiology // Nature Clinical Practice Endocrinology &

Metabolism. 2007. Vol. 3. N. 6. P. 479–488. DOI: 10.1038/ncpendmet0515.
12. Lee Y.H., Cherkerzian S., Seidman L.J. et al. Maternal bacterial infection during pregnancy and offspring risk of psychotic disorders: Variation by severity of infection and offspring sex // American Journal of Psychiatry. 2020. Vol. 177. N. 1. P. 66–75. DOI: 10.1176/appi.ajp.2019.18101206.
13. Allswede D.M., Yolken R.H., Buka S.L. et al. Cytokine concentrations throughout pregnancy and risk for psychosis in adult offspring: A longitudinal case-control study // The Lancet Psychiatry. 2020. Vol. 7. N. 3. P. 254–261. DOI: 10.1016/S2215-0366(20)30006-7.
14. Cheslack-Postava K., Brown A.S. Prenatal infection and schizophrenia: A decade of further progress // Schizophrenia Research. 2022. Vol. 247. P. 7–15. DOI: 10.1016/j.schres.2021.05.014.
15. Malhotra S., Sahoo S., Balachander S. Acute and transient psychotic disorders: Newer understanding // Current Psychiatry Reports. 2019. Vol. 21. P. 1–11. DOI: 10.1007/s11920-019-1099-8.
16. Dalmau J., Armangué T., Planagumà J. et al. An update on anti-NMDA receptor encephalitis for neurologists and psychiatrists: Mechanisms and models // The Lancet Neurology. 2019. Vol. 18. N. 11. P. 1045–1057. DOI: 10.1016/S1474-4422(19)30244-3.
17. Davies C., Segre G., Estradé A. et al. Prenatal and perinatal risk and protective factors for psychosis: A systematic review and meta-analysis // The Lancet Psychiatry. 2020. Vol. 7. N. 5. P. 399–410. DOI: 10.1016/S2215-0366(20)30057-2.
18. Zimmer A., Youngblood A., Adnane A. et al. Prenatal exposure to viral infection and neuropsychiatric disorders in offspring: A review of the literature and recommendations for the COVID-19 pandemic // Brain, Behavior, and Immunity. 2021. Vol. 91. P. 756–770. DOI: 10.1016/j.bbi.2020.10.024.
19. Hansen N., Luedecke D., Malchow B. et al. Autoantibody-associated psychiatric syndromes in children: Link to adult psychiatry // Journal of Neural Transmission. 2021. Vol. 128. N. 6. P. 735–747. DOI: 10.1007/s00702-021-02354-8.
20. Pröbstel A.K., Zamvil S.S. Do maternal anti-N-methyl-D-aspartate receptor antibodies promote development of neuropsychiatric disease in children? // Annals of Neurology. 2019. Vol. 86. N. 5. P. 653. DOI: 10.1002/ana.25584.
21. Цахилова Р.Г., Кузнецов В.П., Хмельницкая А.В. и др. Влияние иммунного статуса матери на развитие плода и здоровье новорождённого (обзор литературы) // Проблемы репродукции. 2016. Т. 22. №6. С. 38–43. DOI: 10.17116/repro201622638-43.
22. Prüss H. Autoantibodies in neurological disease // Nature Reviews Immunology. 2021. Vol. 21. N. 12. P. 798–813. DOI: 10.1038/s41577-021-00543-w.
23. Ehrenreich H. Autoantibodies against N-methyl-D-aspartate receptor 1 in health and disease // Current Opinion in Neurology. 2018. Vol. 31. N. 3. P. 306. DOI: 10.1097/WCO.0000000000000546.
24. Gastaldi V.D., Wilke J.B., Weidinger C.A. et al. Factors predisposing to humoral autoimmunity against brain-antigens in health and disease: Analysis of 49 autoantibodies in over 7000 subjects // Brain, Behavior, and Immunity. 2023. Vol. 108. P. 135–147. DOI: 10.1016/j.bbi.2022.10.016.
25. Hansen N. NMDAR autoantibodies in psychiatric disease — an immunopsychiatric continuum and potential predisposition for disease pathogenesis // Journal of Translational Autoimmunity. 2022. Vol. 25. P. 100165. DOI: 10.1016/j.jtauto.2022.100165.
26. Wilke J.B., Hindermann M., Berghoff S.A. et al. Autoantibodies against NMDA receptor 1 modify rather than cause encephalitis // Molecular Psychiatry. 2021. Vol. 26. N. 12. P. 7746–7759. DOI: 10.1038/s41380-021-01238-3.
27. Dahm L., Ott C., Steiner J. et al. Seroprevalence of autoantibodies against brain antigens in health and disease // Annals of Neurology. 2014. Vol. 76. N. 1. P. 82–94. DOI: 10.1002/ana.24189.
28. Ehrenreich H. Autoantibodies against the N-methyl-D-aspartate receptor subunit NR1: Untangling apparent inconsistencies for clinical practice // Frontiers in Immunology. 2017. Vol. 8. P. 181. DOI: 10.3389/fimmu.2017.00181.
29. Hopfner F., Müller S.H., Steppat D. et al. No association between Parkinson disease and autoantibodies against NMDA-type glutamate receptors // Translational Neurodegeneration. 2019. Vol. 8. P. 1–7. DOI: 10.1186/s40035-019-0153-0.
30. Pan H., Oliveira B., Saher G. et al. Uncoupling the widespread occurrence of anti-NMDAR1 autoantibodies from neuropsychiatric disease in a novel autoimmune model // Molecular Psychiatry. 2019. Vol. 24. N. 10. P. 1489–1501. DOI: 10.1038/s41380-017-0011-3.
31. Pan H., Steixner-Kumar A.A., Seelbach A. et al. Multiple inducers and novel roles of autoantibodies against the obligatory NMDAR subunit NR1: A translational study from chronic life stress to brain injury // Molecular Psychiatry. 2021. Vol. 26. N. 6. P. 2471–2482. DOI: 10.1038/s41380-020-0672-1.
32. Pollak T.A., Kempton M.J., Iyegbe C. et al. Clinical, cognitive and neuroanatomical associations of serum NMDAR autoantibodies in people at clinical high risk for psychosis // Molecular Psychiatry. 2021. Vol. 26. N. 6. P. 2590–2604. DOI: 10.1038/s41380-020-00899-w.
33. Lennox B.R., Palmer-Cooper E.C., Pollak T. et al. Prevalence and clinical characteristics of serum neuronal cell surface antibodies in first-episode psychosis: a case-control study // The Lancet Psychiatry. 2017. Vol. 4. N. 1. P. 42–48. DOI: 10.1016/S2215-0366(16)30375-3.
34. Dalmau J., Tüzün E., Wu H. et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma // Annals of Neurology. 2007. Vol. 61. N. 1. P. 25–36. DOI: 10.1002/ana.21050.
35. Vitaliani R., Mason W., Ances B. et al. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma // Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 2005. Vol. 58. N. 4. P. 594–604. DOI: 10.1002/ana.20614.
36. Dalmau J., Lancaster E., Martinez-Hernandez E. et al. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis // The Lancet Neurology. 2011. Vol. 10. N. 1. P. 63–74. DOI: 10.1016/S1474-4422(10)70253-2.
37. Gabilondo I., Saiz A., Galán L. et al. Analysis of relapses in anti-NMDAR encephalitis // Neurology. 2011. Vol. 77. N. 10. P. 996–999. DOI: 10.1212/WNL.0b013e31822cfc6b.
38. Armangue T., Spatola M., Vlagea A. et al. Frequency, symptoms, risk factors, and outcomes of autoimmune encephalitis after

herpes simplex encephalitis: A prospective observational study and retrospective analysis // The Lancet Neurology. 2018. Vol. 17. N. 9. P. 760–772. DOI: 10.1016/S1474-4422(18)30244-8.
39. Phillips O., Tubre T., Lorenco H. et al. Limbic encephalitis in a child with ovarian teratoma and influenza B. Case report and critical review of the history of autoimmune anti-N-methyl-D-aspartate receptor encephalitis // Journal of Neuroimmunology. 2021. Vol. 360. P. 577716. DOI: 10.1016/j.jneuroim.2021.577716.
40. Nabizadeh F., Balabandian M., Sodeifian F. et al. Autoimmune encephalitis associated with COVID-19: A systematic review // Multiple Sclerosis and Related Disorders. 2022. Vol. 62. P. 103795. DOI: 10.1016/j.msard.2022.103795.
41. Samim M.M., Dhar D., Goyal S. et al. AI-CoV Study: Autoimmune encephalitis associated with COVID-19 and its vaccines — A systematic review // Journal of Clinical Neurology (Seoul, Korea). 2022. Vol. 18. N. 6. P. 692. DOI: 10.3988/jcn.2022.18.6.692.
42. Martin S., Azzouz B., Morel A. et al. Anti-NMDA receptor encephalitis and vaccination: A disproportionality analysis // Frontiers in Pharmacology. 2022. Vol. 13. P. 940780. DOI: 10.3389/fphar.2022.940780.
43. Valdoleiros S.R., Calejo M., Marinho A. et al. First report of concomitant cryptococcal meningitis and anti-NMDAR encephalitis // Brain, Behavior & Immunity-Health. 2020. Vol. 2. P. 100036. DOI: 10.1016/j.bbih.2020.100036.
44. Zrzavy T., Endmayr V., Bauer J. et al. Neuropathological variability within a spectrum of NMDAR-encephalitis // Annals of Neurology. 2021. Vol. 90. N. 5. P. 725–737. DOI: 10.1002/ana.26223.
45. Doden T., Sekijima Y., Ikeda J. et al. Postpartum anti-N-methyl-D-aspartate receptor encephalitis: A case report and literature review // Internal Medicine. 2017. Vol. 56. N. 3. P. 357–362. DOI: 10.2169/internalmedicine.56.7442.
46. Konen F.F., Schwenkenbecher P., Jendretzky K.F. et al. Severe anti-N-methyl-D-aspartate receptor encephalitis under immunosuppression after liver transplantation // Frontiers in Neurology. 2019. Vol. 10. P. 987. DOI: 10.3389/fneur.2019.00987.
47. Obi C.A., Thompson E., Mordukhaev L. et al. Anti-N-methyl-D-aspartate receptor encephalitis triggered by emotional stress // Baylor University Medical Center Proceedings. Taylor & Francis, 2019. Vol. 32. N. 4. P. 605–606. DOI: 10.1080/08998280.2019.1647713.
48. Auriti C., De Rose D.U., Santisi A. et al. Pregnancy and viral infections: Mechanisms of fetal damage, diagnosis and prevention of neonatal adverse outcomes from cytomegalovirus to SARS-CoV-2 and Zika virus // Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease. 2021. Vol. 1867. N. 10. P. 166198. DOI: 10.1016/j.bbadis.2021.166198.
49. Teller J., Jung C., Wilke J.B. et al. Autoantibodies against NMDAR subunit NR1 disappear from blood upon anesthesia // Brain, Behavior & Immunity-Health. 2022. Vol. 24. P. 100494. DOI: 10.1016/j.bbih.2022.100494.
50. Kayser M.S., Titulaer M.J., Gresa-Arribas N. et al. Frequency and characteristics of isolated psychiatric episodes in anti-N-methyl-D-aspartate receptor encephalitis // JAMA Neurology. 2013. Vol. 70. N. 9. P. 1133–1139. DOI: 10.1001/jamaneurol.2013.3216.
51. Wu C.Y., Wu J.D., Chen C.C. The association of ovarian teratoma and Anti-N-Methyl-D-Aspartate receptor encephalitis: An updated integrative review // International Journal of Molecular Sciences. 2021. Vol. 22. N. 20. P. 10911. DOI: 10.3390/ijms222010911.
52. Васенина Е.Е., Левин О.Р., Ганькина О.А. и др. Аутоиммунный энцефалит с антителами к NMDA-рецепторам // Журнал неврологии и психиатрии. 2017. Т. 117. №2. С. 110–116. DOI: 10.17116/jnevro201711721110-116.
53. Шмуклер А.Б., Ивашкина А.А., Мурашко А.А. Случай анти-NMDA-рецепторного энцефалита с клинической картиной фебрильной кататонии // Бюллетень сибирской медицины. 2019. Т. 18. №4. С. 266–272. DOI: 10.20538/1682-0363-2019-4-266-272.
54. Giné Servén E., Boix Quintana E., Martínez Ramírez M. et al. Cycloid psychosis as a psychiatric expression of anti-NMDAR encephalitis. A systematic review of case reports accomplished with the authors' cooperation // Brain and Behavior. 2021. Vol. 11. N. 2. P. e01980. DOI: 10.1002/brb3.1980.
55. Komagamine T., Kanbayashi T., Suzuki K. et al. "Atypical psychoses" and anti-NMDA receptor encephalitis: A review of literature in the mid-twentieth century // Psychiatry and Clinical Neurosciences. 2022. Vol. 76. N. 2. P. 62. DOI: 10.1111/pcn.13317.
56. Foucher J.R., Bartsch A.J., Mainberger O. et al. Parakinesia: A Delphi consensus report // Schizophrenia Research. 2022. P. S0920-9964(22)00366-8. DOI: 10.1016/j.schres.2022.09.024.
57. Giné Servén E., Boix Quintana E., Guanyabens Buscà N. et al. Considerations of psychotic symptomatology in anti-NMDA encephalitis: Similarity to cycloid psychosis // Clinical Case Reports. 2019. Vol. 7. N. 12. P. 2456–2461. DOI: 10.1002/ccr3.2522.
58. Warren N., O'Gorman C., McKeon G. et al. Psychiatric management of anti-NMDAR encephalitis: A cohort analysis // Psychological Medicine. 2021. Vol. 51. N. 3. P. 435–440. DOI: 10.1017/S0033291719003283.
59. McKeon G.L., Robinson G.A., Ryan A.E. et al. Cognitive outcomes following anti-N-methyl-D-aspartate receptor encephalitis: A systematic review // Journal of Clinical and Experimental Neuropsychology. 2018. Vol. 40. N. 3. P. 234–252. DOI: 10.1080/13803395.2017.1329408.
60. Flanagan E.P., Geschwind M.D., Lopez-Chiriboga A.S. et al. Autoimmune encephalitis misdiagnosis in adults // JAMA Neurology. 2023. Vol. 80. N. 1. P. 30–39. DOI: 10.1001/jamaneurol.2022.4251.
61. Hébert J., Muccilli A., Wennberg R.A. et al. Autoimmune encephalitis and autoantibodies: A review of clinical implications // The Journal of Applied Laboratory Medicine. 2022. Vol. 7. N. 1. P. 81–98. DOI: 10.1093/jalm/jfab102.
62. Lee S., Kim H.D., Lee J.S. et al. Clinical features and treatment outcomes of seronegative pediatric autoimmune encephalitis // Journal of Clinical Neurology (Seoul, Korea). 2021. Vol. 17. N. 2. P. 300. DOI: 10.3988/jcn.2021.17.2.300.
63. Hayashi K., Hikiji W., Makino Y. et al. An autopsy case of suspected anti-N-methyl-D-aspartate receptor encephalitis // Journal of Forensic Science and Medicine. 2019. Vol. 5. N. 4. P. 213–216. DOI: 10.4103/jfsm.jfsm_59_18.
64. Tüzün E., Zhou L., Baehring J.M. et al. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis asso-

ciated with ovarian teratoma // Acta Neuropathologica. 2009. Vol. 118. P. 737–743. DOI: 10.1007/s00401-009-0582-4.
65. Dao L.M., Machule M.L., Bacher P. et al. Decreased inflammatory cytokine production of antigen-specific CD4+ T cells in NMDA receptor encephalitis // Journal of Neurology. 2021. Vol. 268. P. 2123–2131. DOI: 10.1007/s00415-020-10371-y.
66. Gillinder L., Warren N., Hartel G. et al. EEG findings in NMDA encephalitis — a systematic review // Seizure. 2019. Vol. 65. P. 20–24. DOI: 10.1016/j.seizure.2018.12.015.
67. Faraguna U., Vyazovskiy V.V., Nelson A.B. et al. A causal role for brain-derived neurotrophic factor in the homeostatic regulation of sleep // Journal of Neuroscience. 2008. Vol. 28. N. 15. P. 4088–4095. DOI: 10.1523/JNEUROSCI.5510-07.2008.
68. Harmony T. The functional significance of delta oscillations in cognitive processing // Frontiers in Integrative Neuroscience. 2013. Vol. 7. P. 83. DOI: 10.3389/fninVol.2013.00083.
69. Steriade M., McCormick D.A., Sejnowski T.J. Thalamocortical oscillations in the sleeping and aroused brain // Science. 1993. Vol. 262. N. 5134. P. 679–685. DOI: 10.1126/science.8235588.
70. Nabizadeh F., Ramezannezhad E., Sardaripour A. et al. [18F] FDG brain PET and clinical symptoms in different autoantibodies of autoimmune encephalitis: A systematic review // Neurological Sciences. 2022. Vol. 43. N. 8. P. 4701–4718. DOI: 10.1007/s10072-022-06094-9.
71. Jabs B.E., Pfuhlmann B., Bartsch A.J. et al. Cycloid psychoses — from clinical concepts to biological foundations // Journal of Neural Transmission. 2002. Vol. 109. P. 907–919. DOI: 10.1007/s007020200074.
72. Martinez-Hernandez E., Horvath J., Shiloh-Malawsky Y. et al. Analysis of complement and plasma cells in the brain of patients with anti-NMDAR encephalitis // Neurology. 2011. Vol. 77. N. 6. P. 589–593. DOI: 10.1212/WNL.0b013e318228c136.
73. Dietl H.W., Pulst S.M., Engelhardt P. et al. Paraneoplastic brainstem encephalitis with acute dystonia and central hypoventilation // Journal of Neurology. 1982. Vol. 227. P. 229–238. DOI: 10.1007/BF00313390.
74. Lu T., Cai W., Qiu W. et al. Brainstem and vestibulocochlear nerve involvement in relapsing — remitting anti-NMDAR encephalitis // Neurological Sciences. 2016. Vol. 37. P. 149–151. DOI: 10.1007/s10072-015-2385-9.
75. Schäbitz W.R., Rogalewski A., Hagemeister C. et al. VZV brainstem encephalitis triggers NMDA receptor immunoreaction // Neurology. 2014. Vol. 83. N. 24. P. 2309–2311. DOI: 10.1212/WNL.0000000000001072.
76. Wang H.Y., Li T., Li X.L. et al. Anti-N-methyl-D-aspartate receptor encephalitis mimics neuroleptic malignant syndrome: Case report and literature review // Neuropsychiatric Disease and Treatmen. 2019. Vol. 2019. P. 773–778. DOI: 10.2147/NDVol.S195706.
77. Young D. The NMDA receptor antibody paradox: A possible approach to developing immunotherapies targeting the NMDA receptor // Frontiers in Neurology. 2020. Vol. 11. P. 635. DOI: 10.3389/fneur.2020.00635.
78. Бачерников Н.Е., Петленко В.П., Щербина Е.А. Философские вопросы психиатрии. Киев: Здоровья; 1985. 192 с.
79. Нуллер Ю.Л., Михаленко И.Н. Аффективные психозы. Ленинград: Медицина; 1988. 264 с.
80. Смирнов В.К. Психогигиена и психическое здоровье. В сб.: Психическое здоровье и пограничные состояния. Сб. науч. тр. / Под общ. ред. В.К. Смирнова. Горький: ГМИ; 1983. с. 38–58.

REFERENCES

1. Bell LV. On a form of disease resembling some advanced stages of mania and fever, but so contradistinguished from any ordinarily observed or described combination of symptoms, as to render it probable that it may be an overlooked and hitherto unrecorded malady. *Am J Insanity*. 1849;6(2):97–127.
2. Leongard K. *Sistematika endogennykh psikhozov i ikh differentsirovannaya etiologiya*. Per. s nem. pod red. A.S. Tiganova. M.: Prakticheskaya meditsina; 2010. 456 p. (In Russ)
3. Kleist K. Die klinische Stellung der Motilitätspsychosen. *Zeitschrift für die gesamte Neurologie und Psychiatrie*. 1911;3:914–917.
4. Franzek E, Beckmann H. Season-of-birth effect reveals the existence of etiologically different groups of schizophrenia. *Biol Psychiatry*. 1992;32(4):375–378. DOI: 10.1016/0006-3223(92)90042-x.
5. Stöber G, Franzek E, Beckmann H. The role of maternal infectious diseases during pregnancy in the etiology of schizophrenia in offspring. *European Psychiatry*. 1992;7(4):147–152. DOI: 10.1017/S0924933800005241.
6. Stöber G, Kocher I, Franzek E, Beckmann H. First-trimester maternal gestational infection and cycloid psychosis. *Acta Psychiatr Scand*. 1997;96(5):319–324. DOI: 10.1111/j.1600-0447.1997.tb09923.x.
7. Al-Haddad BJS, Oler E, Armistead B et al. The fetal origins of mental illness. *Am J Obstet Gynecol*. 2019;221(6):549–562. DOI: 10.1016/j.ajog.2019.06.013.
8. Massrali A, Adhya D, Srivastava DP et al. Virus-induced maternal immune activation as an environmental factor in the etiology of autism and schizophrenia. *Front Neurosci.* 2022;16:834058. DOI: 10.3389/fnins.2022.834058.
9. Ratnayake U, Quinn T, Walker DW, Dickinson H. Cytokines and the neurodevelopmental basis of mental illness. *Front Neurosci*. 2013;7:180. DOI: 10.3389/fnins.2013.00180.
10. Vasistha NA, Pardo-Navarro M, Gasthaus J et al. Maternal inflammation has a profound effect on cortical interneuron development in a stage and subtype-specific manner. *Mol Psychiatry.* 2020;25(10):2313–2329. DOI: 10.1038/s41380-019-0539-5.
11. Seckl JR, Holmes MC. Mechanisms of disease: Glucocorticoids, their placental metabolism and fetal 'programming' of adult pathophysiology. *Nat Clin Pract Endocrinol Metab*. 2007;3(6):479–488. DOI: 10.1038/ncpendmet0515.
12. Lee YH, Cherkerzian S, Seidman LJ et al. Maternal bacterial infection during pregnancy and offspring risk of psychotic disorders: Variation by severity of infection and offspring sex.

Am J Psychiatry. 2020;177(1):66–75. DOI: 10.1176/appi.ajp.2019.18101206.
13. Allswede DM, Yolken RH, Buka SL et al. Cytokine concentrations throughout pregnancy and risk for psychosis in adult offspring: A longitudinal case-control study. *The Lancet Psychiatry*. 2020; 7(3):254–261. DOI: 10.1016/S2215-0366(20)30006-7.
14. Cheslack-Postava K, Brown AS. Prenatal infection and schizophrenia: A decade of further progress. *Schizophr Res*. 2022;247:7–15. DOI: 10.1016/j.schres.2021.05.014.
15. Malhotra S, Sahoo S, Balachander S. Acute and transient psychotic disorders: Newer understanding. *Curr Psychiatry Rep*. 2019;21(11):113. DOI: 10.1007/s11920-019-1099-8.
16. Dalmau J, Armangué T, Planagumà J et al. An update on anti-NMDA receptor encephalitis for neurologists and psychiatrists: mechanisms and models. *Lancet Neurol*. 2019;18(11):1045–1057. DOI: 10.1016/S1474-4422(19)30244-3.
17. Davies C, Segre G, Estradé A et al. Prenatal and perinatal risk and protective factors for psychosis: A systematic review and meta-analysis. *Lancet Psychiatry*. 2020;7(5):399–410. DOI: 10.1016/S2215-0366(20)30057-2.
18. Zimmer A, Youngblood A, Adnane A et al. Prenatal exposure to viral infection and neuropsychiatric disorders in offspring: A review of the literature and recommendations for the COVID-19 pandemic. *Brain Behav Immun*. 2021;91:756–770. DOI: 10.1016/j.bbi.2020.10.024.
19. Hansen N, Luedecke D, Malchow B et al. Autoantibody-associated psychiatric syndromes in children: Link to adult psychiatry. *J Neural Transm*. 2021;128:735–747. DOI: 10.1007/s00702-021-02354-8.
20. Pröbstel AK, Zamvil SS. Do maternal anti-N-methyl-D-aspartate receptor antibodies promote development of neuropsychiatric disease in children? *Ann Neurol*. 2019;86(5):653–655. DOI: 10.1002/ana.25584.
21. Tcakhilova SG, Kuznetsov VP, Khmelnitskaya AV et al. The influence of the immune status of the mother on fetal development and the health of the newborn (a review). *Russian Journal of Human Reproduction*. 2016;22(6):38–43. (In Russ). DOI: 10.17116/repro201622638-43.
22. Prüss H. Autoantibodies in neurological disease. *Nat Rev Immunol*. 2021;21:798–813. DOI: 10.1038/s41577-021-00543-w.
23. Ehrenreich H. Autoantibodies against N-methyl-D-aspartate receptor 1 in health and disease. *Curr Opin Neurol*. 2018;31(3):306–312. DOI: 10.1097/WCO.0000000000000546.
24. Gastaldi VD, Wilke JB, Weidinger CA et al. Factors predisposing to humoral autoimmunity against brain-antigens in health and disease: Analysis of 49 autoantibodies in over 7000 subjects. *Brain Behav Immun*. 2022;108:135–147. DOI: 10.1016/j.bbi.2022.10.016.
25. Hansen N. NMDAR autoantibodies in psychiatric disease — an immunopsychiatric continuum and potential predisposition for disease pathogenesis. *J Transl Autoimmun*. 2022;5:100165. DOI: 10.1016/j.jtauto.2022.100165.
26. Wilke JBH, Hindermann M, Berghoff SA et al. Autoantibodies against NMDA receptor 1 modify rather than cause encephalitis. *Mol Psychiatry*. 2021;26:7746–7759. DOI: 10.1038/s41380-021-01238-3.
27. Dahm L, Ott C, Steiner J et al. Seroprevalence of autoantibodies against brain antigens in health and disease. *Ann Neurol*. 2014;76(1):82–94. DOI: 10.1002/ana.24189.
28. Ehrenreich H. Autoantibodies against the N-methyl-D-aspartate receptor subunit NR1: Untangling apparent inconsistencies for clinical practice. *Front Immunol*. 2017;8:181. DOI: 10.3389/fimmu.2017.00181.
29. Hopfner F, Müller SH, Steppat D et al. No association between Parkinson disease and autoantibodies against NMDA-type glutamate receptors. *Transl Neurodegener*. 2019;8:11. DOI: 10.1186/s40035-019-0153-0.
30. Pan H, Oliveira B, Saher G et al. Uncoupling the widespread occurrence of anti-NMDAR1 autoantibodies from neuropsychiatric disease in a novel autoimmune model. *Mol Psychiatry*. 2019;24(10):1489–1501. DOI: 10.1038/s41380-017-0011-3.
31. Pan H, Steixner-Kumar AA, Seelbach A et al. Multiple inducers and novel roles of autoantibodies against the obligatory NMDAR subunit NR1: A translational study from chronic life stress to brain injury. *Mol Psychiatry*. 2021;26(6):2471–2482. DOI: 10.1038/s41380-020-0672-1.
32. Pollak TA, Kempton MJ, Iyegbe C et al. Clinical, cognitive and neuroanatomical associations of serum NMDAR autoantibodies in people at clinical high risk for psychosis. *Mol Psychiatry.* 2021;26(6):2590–2604. DOI: 10.1038/s41380-020-00899-w.
33. Lennox BR, Palmer-Cooper EC, Pollak T et al. Prevalence and clinical characteristics of serum neuronal cell surface antibodies in first-episode psychosis: A case-control study. *Lancet Psychiatry*. 2017;4(1):42–48. DOI: 10.1016/S2215-0366(16)30375-3.
34. Dalmau J, Tüzün E, Wu H et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Annals of Neurology*. 2007;61(1):25–36. DOI: 10.1002/ana.21050.
35. Vitaliani R, Mason W, Ances B et al. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. *Annals of Neurology*. 2005;58(4):594–604. DOI: 10.1002/ana.20614.
36. Dalmau J, Lancaster E, Martinez-Hernandez E et al. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol.* 2011;10(1):63–74. DOI: 10.1016/S1474-4422(10)70253-2.
37. Gabilondo I, Saiz A, Galán L et al. Analysis of relapses in anti-NMDAR encephalitis. *Neurology*. 2011;77(10):996–999. DOI: 10.1212/WNL.0b013e31822cfc6b.
38. Armangue T, Spatola M, Vlagea A et al. Frequency, symptoms, risk factors, and outcomes of autoimmune encephalitis after herpes simplex encephalitis: A prospective observational study and retrospective analysis. *Lancet Neurol.* 2018;17(9):760–772. DOI: 10.1016/S1474-4422(18)30244-8.
39. Phillips O, Tubre T, Lorenco H et al. Limbic encephalitis in a child with ovarian teratoma and influenza B. Case report and critical review of the history of autoimmune anti-N-methyl-D-aspartate receptor encephalitis. *J Neuroimmunol.* 2021;360:577716. DOI: 10.1016/j.jneuroim.2021.577716.
40. Nabizadeh F, Balabandian M, Sodeifian F et al. Autoimmune encephalitis associated with COVID-19: A systematic review. *Mult Scler Relat Disord.* 2022;62:103795. DOI: 10.1016/j.msard.2022.103795.
41. Samim MM, Dhar D, Goyal S et al. AI-CoV study: autoimmune encephalitis associated with COVID-19 and its vaccines — a systematic review. *J Clin Neurol.* 2022;18(6):692–710. DOI: 10.3988/jcn.2022.18.6.692.

42. Martin S, Azzouz B, Morel A, Trenque T. Anti-NMDA receptor encephalitis and vaccination: A disproportionality analysis. *Front Pharmacol.* 2022;13:940780. DOI: 10.3389/fphar.2022.940780.
43. Valdoleiros SR, Calejo M, Marinho A et al. First report of concomitant cryptococcal meningitis and anti-NMDAR encephalitis. *Brain Behav Immun Health.* 2020;2:100036. DOI: 10.1016/j.bbih.2020.100036.
44. Zrzavy T, Endmayr V, Bauer J et al. Neuropathological variability within a spectrum of NMDAR-encephalitis. *Ann Neurol.* 2021;90(5):725–737. DOI: 10.1002/ana.26223.
45. Doden T, Sekijima Y, Ikeda J et al. Postpartum Anti-N-methyl-D-aspartate receptor encephalitis: A case report and literature review. *Intern Med.* 2017;56(3):357–362. DOI: 10.2169/internalmedicine.56.7442.
46. Konen FF, Schwenkenbecher P, Jendretzky KF et al. Severe anti-N-methyl-D-aspartate receptor encephalitis under immunosuppression after liver transplantation. *Front Neurol.* 2019;10:987. DOI: 10.3389/fneur.2019.00987.
47. Obi CA, Thompson E, Mordukhaev L et al. Anti-N-methyl-D-aspartate receptor encephalitis triggered by emotional stress. *Proc (Bayl Univ Med Cent)*. 2019;32(4):605–606. DOI: 10.1080/08998280.2019.1647713.
48. Auriti C, De Rose DU, Santisi A et al. Pregnancy and viral infections: Mechanisms of fetal damage, diagnosis and prevention of neonatal adverse outcomes from cytomegalovirus to SARS-CoV-2 and Zika virus. *Biochim Biophys Acta Mol Basis Dis.* 2021;1867(10):166198. DOI: 10.1016/j.bbadis.2021.166198.
49. Teller J, Jung C, Wilke JBH et al. Autoantibodies against NMDAR subunit NR1 disappear from blood upon anesthesia. *Brain Behav Immun Health.* 2022;24:100494. DOI: 10.1016/j.bbih.2022.100494.
50. Kayser MS, Titulaer MJ, Gresa-Arribas N, Dalmau J. Frequency and characteristics of isolated psychiatric episodes in anti-N-methyl-D-aspartate receptor encephalitis. *JAMA Neurol.* 2013;70(9):1133–1139. DOI: 10.1001/jamaneurol.2013.3216.
51. Wu CY, Wu JD, Chen CC. The association of ovarian teratoma and anti-N-methyl-D-aspartate receptor encephalitis: An updated integrative review. *Int J Mol Sci.* 2021;22(20):10911. DOI: 10.3390/ijms222010911.
52. Vasenina EE, Levin OS, Gankina OA et al. Autoimmune anti-NMDA-R encephalitis. *Zhurnal Nevrologii i Psikhiatrii*. 2017;117(2):110-116. (In Russ). DOI: 10.17116/jnevro201711721110-116.
53. Shmukler AB, Ivashkina AA, Murashko AA. A case of anti-NMDA-receptor encephalitis presenting as febrile catatonia. *Bulletin of Siberian Medicine*. 2019;18(4):266–272. DOI: 10.20538/1682-0363-2019-4-266-272.
54. Giné Servén E, Boix Quintana E, Martínez Ramírez M et al. Cycloid psychosis as a psychiatric expression of anti-NMDAR encephalitis. A systematic review of case reports accomplished with the authors' cooperation. *Brain Behav.* 2021;11(2):e01980. DOI: 10.1002/brb3.1980.
55. Komagamine T, Kanbayashi T, Suzuki K et al. "Atypical psychoses" and anti-NMDA receptor encephalitis: A review of literature in the mid-twentieth century. *Psychiatry Clin Neurosci.* 2022;76(2):62–63. DOI: 10.1111/pcn.13317.
56. Foucher JR, Bartsch AJ, Mainberger O et al. Parakinesia: A Delphi consensus report. *Schizophr Res.* 2022:S0920-9964(22)00366-8. DOI: 10.1016/j.schres.2022.09.024.
57. Giné Servén E, Boix Quintana E, Guanyabens Buscà N et al. Considerations of psychotic symptomatology in anti-NMDA encephalitis: Similarity to cycloid psychosis. *Clin Case Rep.* 2019;7(12):2456–2461. DOI: 10.1002/ccr3.2522.
58. Warren N, O'Gorman C, McKeon G et al. Psychiatric management of anti-NMDAR encephalitis: A cohort analysis. *Psychol Med.* 2021;51(3):435–440. DOI: 10.1017/S0033291719003283.
59. McKeon GL, Robinson GA, Ryan AE et al. Cognitive outcomes following anti-N-methyl-D-aspartate receptor encephalitis: A systematic review. *J Clin Exp Neuropsychol.* 2018;40(3):234–252. DOI: 10.1080/13803395.2017.1329408.
60. Flanagan EP, Geschwind MD, Lopez-Chiriboga AS et al. Autoimmune encephalitis misdiagnosis in adults. *JAMA Neurol.* 2023;80(1):30–39. DOI: 10.1001/jamaneurol.2022.4251.
61. Hébert J, Muccilli A, Wennberg RA. Autoimmune encephalitis and autoantibodies: A review of clinical implications. *J Appl Lab Med.* 2022;7(1):81–98. DOI: 10.1093/jalm/jfab102.
62. Lee S, Kim HD, Lee JS et al. Clinical features and treatment outcomes of seronegative pediatric autoimmune encephalitis. *J Clin Neurol.* 2021;17(2):300–306. DOI: 10.3988/jcn.2021.17.2.300.
63. Hayashi K, Hikiji W, Makino Y, Suzuki H. An autopsy case of suspected anti-N-methyl-D-aspartate receptor encephalitis. *J Forensic Sci Med.* 2019;5:213–216. DOI: 10.4103/jfsm.jfsm_59_18.
64. Tüzün E, Zhou L, Baehring JM et al. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis associated with ovarian teratoma. *Acta Neuropathol.* 2009;118(6):737–743. DOI: 10.1007/s00401-009-0582-4.
65. Dao LM, Machule ML, Bacher P et al. Decreased inflammatory cytokine production of antigen-specific $CD4^+$ T cells in NMDA receptor encephalitis. *J Neurol.* 2021;268(6):2123–2131. DOI: 10.1007/s00415-020-10371-y.
66. Gillinder L, Warren N, Hartel G et al. EEG findings in NMDA encephalitis — A systematic review. *Seizure.* 2019;65:20–24. DOI: 10.1016/j.seizure.2018.12.015.
67. Faraguna U, Vyazovskiy VV, Nelson AB et al. A causal role for brain-derived neurotrophic factor in the homeostatic regulation of sleep. *J Neurosci.* 2008;28(15):4088–40895. DOI: 10.1523/JNEUROSCI.5510-07.2008.
68. Harmony T. The functional significance of delta oscillations in cognitive processing. *Front Integr Neurosci.* 2013;7:83. DOI: 10.3389/fnint.2013.00083.
69. Steriade M, McCormick DA, Sejnowski TJ. Thalamocortical oscillations in the sleeping and aroused brain. *Science*. 1993;262(5134):679–685. DOI: 10.1126/science.8235588.
70. Nabizadeh F, Ramezannezhad E, Sardaripour A et al. [18F] FDG brain PET and clinical symptoms in different autoantibodies of autoimmune encephalitis: A systematic review. *Neurol Sci.* 2022;43(8):4701–4718. DOI: 10.1007/s10072-022-06094-9.
71. Jabs BE, Pfuhlmann B, Bartsch AJ, Cetkovich-Bakmas MG, Stöber G. Cycloid psychoses — from clinical concepts to biological foundations. *J Neural Transm (Vienna).* 2002;109:907–919. DOI: 10.1007/s007020200074.
72. Martinez-Hernandez E, Horvath J, Shiloh-Malawsky Y et al. Analysis of complement and plasma cells in the brain of patients with anti-NMDAR encephalitis. *Neurology*. 2011;77(6):589–593. DOI: 10.1212/WNL.0b013e318228c136.

73. Dietl HW, Pulst SM, Engelhardt P, Mehraein P. Paraneoplastic brainstem encephalitis with acute dystonia and central hypoventilation. *J Neurol.* 1982;227(4):229–238. DOI: 10.1007/BF00313390.
74. Lu T, Cai W, Qiu W et al. Brainstem and vestibulocochlear nerve involvement in relapsing-remitting anti-NMDAR encephalitis. *Neurol Sci.* 2016;37(1):149–151. DOI: 10.1007/s10072-015-2385-9.
75. Schäbitz WR, Rogalewski A, Hagemeister C, Bien CG. VZV brainstem encephalitis triggers NMDA receptor immunoreaction. *Neurology*. 2014;83(24):2309–2311. DOI: 10.1212/WNL.0000000000001072.
76. Wang HY, Li T, Li XL et al. Anti-N-methyl-D-aspartate receptor encephalitis mimics neuroleptic malignant syndrome: Case report and literature review. *Neuropsychiatr Dis Treat.* 2019;15:773–778. DOI: 10.2147/NDT.S195706.
77. Young D. The NMDA receptor antibody paradox: A possible approach to developing immunotherapies targeting the NMDA receptor. *Front Neurol.* 2020;11:635. DOI: 10.3389/fneur.2020.00635.
78. Bacherikov NE, Petlenko VP, Shcherbina EA. *Filosofskie voprosy psikhiatrii*. Kiev: Zdorovya; 1985. 192 c. (In Russ).
79. Nuller YuL, Mikhalenko IN. *Affektivnye psikhozy*. Leningrad: Meditsina; 1988. 264 p. (In Russ.)
80. Smirnov VK. Psikhogigiena i psikhicheskoe zdorov'e. In: *Psikhicheskoe zdorov'e i pogranichnye sostoyaniya*. Sb. nauch. tr. Pod obshch. red. V.K. Smirnova. Gor'kii: GMI; 1983:38–58. (In Russ)

ОБ АВТОРАХ

Снедков Евгений Владимирович, докт. мед. наук, проф., врач-психиатр;
ORCID: http://orcid.org/0000-0002-1438-1890;
eLibrary SPIN: 4353-6428;
e-mail: esnedkov@mail.ru

Волчек Игорь Анатольевич, докт. мед. наук, проф. кафедры кожных и венерических болезней с курсом косметологии Медицинского института непрерывного образования «РОСБИОТЕХ»; главный научный сотрудник научно-исследовательского центра иммунологии и аллергологии;
ORCID: http://orcid.org/0009-0000-1451-6145;
eLibrary SPIN:6743-2105;
e-mail: igor.volchek@gmail.com

Лемешев Илья Владимирович, заведующий дневным стационаром, врач-психиатр, Психиатрическая больница св. Николая Чудотворца; ассистент кафедры психиатрии и наркологии, СЗГМУ им. И.И Мечникова;
ORCID: http://orcid.org/0009-0002-0491-6545;
eLibrary SPIN: 7635-4548;
e-mail ilya.lemeshev@gmail.com

AUTHOR'S INFO

Evgenii V. Snedkov, M.D., D. Sci. (Med.), Prof., Psychiatrist;
ORCID: http://orcid.org/0000-0002-1438-1890;
eLibrary SPIN:: 4353-6428;
e-mail: esnedkov@mail.ru

Igor A. Volchek, M.D., D. Sci. (Med.), Prof. of the Department of Skin and Venereal Diseases with a Cosmetology Course of the Medical Institute of Continuing Education of the Federal State Budgetary Educational Institution of Higher Education "Russian Biotechnological University (ROSBIOTECH)"; Chief Researcher of the Research Center for Immunology and Allergology;
ORCID: http://orcid.org/0009-0000-1451-6145;
eLibrary SPIN:6743-2105; e-mail: igor.volchek@gmail.com

Ilia V. Lemeshev, M.D., Head of the Day Hospital Department, Psychiatrist, Psychiatric Hospital of St. Nicolas the Wonderworker, Assistant Professor at the Department of Psychiatry and Narcology; I.I. Mechnikov North-Western State Medical University;
ORCID: http://orcid.org/0009-0002-0491-6545;
eLibrary SPIN: 7635-4548; e-mail ilya.lemeshev@gmail.com