

УДК 616.89-008.441.13-092:616.8-097
<https://doi.org/10.20538/1682-0363-2025-3-127-137>

Neurotransmitters, factors of neuroimmune inflammation and endocrine regulation in alcohol dependence

Vetlugina T.P., Epimakhova E.V., Prokopieva V.D., Shumilova S.N., Voevodin I.V.

*Mental Health Research Institute, Tomsk National Research Medical Center (NRMС), Russian Academy of Sciences
4 Aleutskaya St., 634014 Tomsk, Russian Federation*

ABSTRACT

Alcohol dependence remains a global medical and social issue, despite the advancements in studying its pathogenesis and the diversity of available treatment methods. This determines the relevance of further research aimed at revealing the complex neurobiological effects of ethanol on the human body. A fundamental knowledge of the mechanisms of formation and course of alcohol dependence is the theoretical basis for the development of new pathogenetically substantiated methods of prevention, diagnosis, and treatment of alcohol-related disorders, which will contribute to enhancing the social functioning of patients and reducing the economic burden of socially sensitive diseases.

The aim of the review was to analyze recent studies conducted by Russian and foreign authors on the role of neurotransmitters, neuroimmune inflammation factors, and endocrine regulation in the pathogenesis of alcohol dependence.

Keywords: alcohol dependence, alcoholism, neurotransmitters, neuroimmune inflammation, corticotropin-releasing factor, cortisol.

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The publication was prepared with the financial support of the grant of the Russian Science Foundation (Project No. 25-25-00188, <https://rscf.ru/en/project/25-25-00188/>)

For citation: Vetlugina T.P., Epimakhova E.V., Prokopieva V.D., Shumilova S.N., Voevodin I.V. Neurotransmitters, factors of neuroimmune inflammation and endocrine regulation in alcohol dependence. *Bulletin of Siberian Medicine*. 2025;24(3):127–137. <https://doi.org/10.20538/1682-0363-2025-3-127-137>.

Нейромедиаторы, факторы нейроиммунного воспаления и эндокринной регуляции при алкогольной зависимости

Ветлугина Т.П., Епимахова Е.В., Прокопьева В.Д., Шумилова С.Н., Воеводин И.В.

*Научно-исследовательский институт (НИИ) психического здоровья, Томский национальный
исследовательский медицинский центр (НИМЦ) Российской академии наук
Россия, 634014, г. Томск, ул. Алеутская, 4*

РЕЗЮМЕ

Алкогольная зависимость остается глобальной медико-социальной проблемой, несмотря на достигнутые успехи в изучении патогенеза заболевания и многообразие существующих методов лечения. Это определяет актуальность дальнейших исследований, направленных на раскрытие сложных нейробиологических эффектов этанола на организм человека. Фундаментальные знания механизмов формирования и течения

алкогольной зависимости являются теоретической базой для разработки новых патогенетически обоснованных методов профилактики, диагностики и лечения расстройств, связанных с алкоголем, что будет способствовать повышению социального функционирования пациентов, снижению экономических потерь от социально-значимых заболеваний.

Цель: анализ современных исследований российских и зарубежных авторов, касающихся изучения роли нейромедиаторов, факторов нейроиммунного воспаления и эндокринной регуляции в патогенезе алкогольной зависимости.

Ключевые слова: алкогольная зависимость, алкоголизм, нейромедиаторы, нейроиммунное воспаление, кортикотропин-рилизинг фактор, кортизол

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Статья подготовлена при финансовой поддержке гранта Российского научного фонда (проект № 25-25-00188, <https://rscf.ru/en/project/25-25-00188/>).

Для цитирования: Ветлугина Т.П., Епимахова Е.В., Прокопьева В.Д., Шумилова С.Н., Воеводин И.В. Нейромедиаторы, факторы нейроиммунного воспаления и эндокринной регуляции при алкогольной зависимости. *Бюллетень сибирской медицины*. 2025;24(3):127–137. <https://doi.org/10.20538/1682-0363-2025-3-127-137>.

INTRODUCTION

Alcohol dependence (alcoholism) as one of the primary addictive disorders remains a serious medical and social problem in Russia and worldwide due to a steady increase in the incidence of this pathology, the severity of its consequences, and limited treatment efficacy. Alcohol abuse leads to rising crime rates, violence, and orphanhood and causes a notably high level of disability and mortality among men aged 40–60, who at this age are the most productive in social and professional spheres. One of the approaches to solving the problem of reducing the growth rate of addiction is the development of new methods of diagnosis, individualized prediction, and effective therapies developed using fundamental knowledge about the disease pathogenesis.

The brain neurotransmitter systems, primarily the dopaminergic system, whose functional state is related to the activity of other systems, play a crucial role in the formation of addiction [1–3]. Alcohol and its metabolites, in particular acetaldehyde, activate peripheral immune cells and microglia leading to an increase in the production of pro-inflammatory cytokines and other mediators of neuroimmune inflammation, affecting the severity of the disease and cognitive and behavioral characteristics [4, 5]. Chronic alcohol consumption and repeated withdrawal cycles are stressors stimulating the hypothalamic-pituitary-adrenal axis (HPA axis) and glucocorticoid synthesis causing dysregulation of the brain reward system and perpetuating alcohol-seeking behavior [6, 7].

The aim of this review was to analyze recent studies conducted by both Russian and foreign authors regarding the role of neurotransmitters, neuroimmune inflammatory factors, and endocrine regulation in the pathogenesis of alcohol dependence.

We searched the electronic databases PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) and the scientific electronic library eLIBRARY (<https://www.elibrary.ru/>) for studies published during the last 15 years. The search was conducted using the following key words: alcohol dependence, alcoholism, neurobiology of alcoholism, neurotransmitters, inflammatory factors, cytokines, and hormones. The review includes 88 publications (clinical and experimental studies, meta-analyses, randomized controlled trials, and reviews) relevant to the problem under study.

NEUROMEDIATORS

Ethanol crosses the blood-brain barrier altering neurochemical processes in the brain and leading to the remodeling of synapses that regulate emotions, motivation, and overall human behavior. Currently, the primary neurophysiological mechanism underlying addiction to psychoactive substances (PAS) is considered to be the emotionally positive reactions that arise in response to the chemical effects of alcohol and other PAS on brain regions linked to the reward system [2, 8, 9].

Long-term studies conducted at the National Scientific Center for Narcology (Moscow, Russia) have established the leading role of dopamine (DA)

in the development of addiction to alcohol and other PAS. A vicious cycle underlying addiction formation has been described, characterized by alternating periods of increased and decreased DA levels during alcohol consumption, withdrawal syndrome, and remission. It has been shown that DA levels positively correlate with the severity of withdrawal symptoms. Elevated DA levels during the initial period of remission formation subsequently decrease and, as a rule, remain below normal, which may indicate that DA deficiency is the basis of persistent pathological craving for PAS [8].

Chronic ethanol consumption leads to long-term changes in the dopaminergic system, affecting neural networks associated with reward mechanisms and addictive behavior [9]. Experimental studies have demonstrated that both acute and chronic alcohol intoxication cause the most pronounced changes in the activity of the mesolimbic dopaminergic system in rats, confirming the involvement of this system in the neurobiology of alcohol effects [10, 11]. Alcohol activates dopaminergic neurons in the ventral tegmental area of the midbrain leading to an increased dopamine release in the cortico-limbic regions of the forebrain. Inhibition of D2 dopamine receptors by their antagonist, sulpiride, reduced voluntary alcohol intake in animals [12, 13].

It has been shown that long-term potentiation or suppression of cortical activity transmitted to the striatum, which expresses D1 dopamine receptors, controls alcohol-seeking behavior in experimental animals [14]. In animals with a progressively increasing preference for alcohol, a more pronounced reduction in the expression of D1 and D2 receptor mRNA in the striatum was observed compared to rats that maintained consistently low levels of alcohol consumption and those with consistently high preference scores [15].

Neuroimaging methods used in clinical research have expanded our understanding of the neurochemistry of alcoholism. Reviewing 30 years of functional magnetic resonance imaging (fMRI) use, D. Nutt et al. (2021) highlight the significant contribution of these studies to uncovering the mechanisms of reward and neuroadaptation resulting from chronic alcohol use, as well as the role of DA neurotransmission. At the same time, the authors note certain contradictions in the currently available data and emphasize the need for further longitudinal studies in this direction to identify biological markers for predicting addiction development and to develop

new therapeutic approaches for patients at all stages of the disease [2].

A longitudinal study of social drinkers (habitual drinking) was conducted using positron emission tomography (PET) to investigate the potential use of striatal D2 dopamine receptors as predictors of alcohol dependence development. When participants were re-evaluated 8–16 years after PET scanning, the authors found no evidence of a link between D2 receptor availability and the subsequent development of alcohol use disorder [16]. These results also underscore the need for continued research using neuroimaging methods.

Overall, the data obtained by various authors on the role of dopaminergic neurotransmission depend on research methods, the brain region studied, the duration of alcohol use, and the type of alcohol-seeking behavior examined. Nevertheless, DA and the brain regions where this neurotransmitter is actively synthesized and functions remain key in the formation of addiction syndrome and are primary targets in translational research [17, 18].

Other neurotransmitters also play an important role in the development of alcohol dependence, particularly gamma-aminobutyric acid (GABA), glutamate, and serotonin.

Chronic ethanol exposure disrupts the balance between inhibitory and excitatory neurotransmitters, with GABA being the primary inhibitory neurotransmitter in the brain. B.M. Roberts, E.F. Lopes, S.J. Cragg, analyzing publications on the modulation of dopamine release in the striatum through axonal mechanisms, provide evidence that GABA inhibits the activity of dopaminergic neurons, basal and induced DA synthesis, and suppresses DA release, thereby reducing overall DA neurotransmission. GABA can modulate DA output by affecting metabotropic GABA_A and GABA_B receptors [20].

A randomized double-blind placebo-controlled study evaluated the role of the GABA_B receptor in the neurobiology of alcohol-related behavior. In patients with alcohol dependence, administration of the selective GABA_B receptor agonist baclofen had a positive effect on some clinical characteristics of the disorder, and the maximum plasma concentration of baclofen negatively correlated with alcohol craving [20, 21]. These findings, along with preclinical studies, demonstrate that GABA_B receptor modulators, particularly baclofen, normalize impaired GABAergic transmission and have high translational potential for the treatment of alcohol use disorders [22].

Glutamate is the primary excitatory neurotransmitter. Glutamatergic signaling mediated by ionotropic (NMDA, AMPA) and metabotropic (G protein-coupled – mGluR) glutamate receptors is crucial. Ethanol-induced dysfunction of these receptors in various brain regions leads to significant alterations in glutamatergic neurotransmission [23]. Studies using PET imaging in individuals with alcohol dependence have provided evidence of the role of metabotropic glutamate receptor subtype 5 (mGluR5) in the clinical features of the disorder. Researchers observed increased mGluR5 binding in various brain regions with a particularly strong signal in the amygdala, which was associated with reduced alcohol craving [24].

Experimental data analysis has shown that a single (acute) administration of ethanol typically inhibits glutamatergic neurotransmission, while chronic ethanol use enhances it leading to a hyperexcitable state and anxiety characteristic of withdrawal syndrome. Prolonged ethanol exposure increases glutamatergic activity, accompanied by neuroplasticity changes in key brain regions, including the basolateral and central nuclei of the amygdala. These impairments may reduce behavioral flexibility, promote seeking behavior, and increase the likelihood of relapse [25, 26]. These findings support the hypothesis that some effects of chronic ethanol exposure are mediated by its impact on synaptic transmission of GABA and glutamate playing a significant role in maintaining dependence.

The potential use of various drugs (pregabalin and gabapentin) that modulate the GABA and glutamate systems is investigated for the treatment of patients with alcoholism. These studies have demonstrated that these neurotransmitter systems could be promising pharmacological targets for the pathogen-specific therapy of alcohol dependence [27, 28]. Such studies make it possible to obtain new data on the mechanisms of development of alcohol dependence and to identify biomarkers of treatment effectiveness.

Serotonin (5-hydroxytryptamine, 5-HT) is a neurotransmitter that regulates mood, sleep, appetite, learning, memory, and other physiological functions. Various types of serotonin receptors in the central nervous system (CNS) convert the chemical signal induced by serotonin into functional changes in the signal-receiving cell. D. Most, L. Ferguson, R.A. Harris (2014) analyzing studies of the molecular basis of alcoholism provide evidence of serotonin involvement in mediating both acute and chronic

effects of alcohol. Increased serotonergic transmission has been associated with lower alcohol consumption, while reduced transmission is linked to higher consumption both in experimental models and in individuals with alcohol dependence [30].

The administration of serotonergic agents (SSRIs and buspirone) resulted in reduced alcohol consumption across all models of alcoholism [30, 31]. Studies on serotonin levels in platelets of alcohol-dependent patients admitted for treatment demonstrated an increase in its concentration by day 12 of therapy, with this rise coinciding with a reduction in withdrawal symptom severity and improved clinical condition in the patients [32]. When examining individuals with alcohol and nicotine dependence who were divided into groups based on different phenotypes (age of alcohol use initiation, presence of withdrawal syndrome, alcohol-induced psychosis, aggression, etc.), thrombocytes of non-smoking patients exhibited an association between low 5-HT levels and the severity of alcohol dependence, whereas smokers showed a correlation with late-onset alcohol abuse. It has been suggested that platelet 5-HT could serve as a peripheral biomarker for different phenotypes of alcohol-related disorders [33]. The functions of serotonin and the role of the serotonergic system in addictive behavior are discussed in detail in a monograph [34].

In summary, literature analysis demonstrates that alcohol-induced modulation of the brain dopaminergic, GABAergic, glutamatergic, and serotonergic systems is a crucial molecular mechanism underlying the development of alcohol dependence and a potential target for treatment.

NEUROIMMUNE INFLAMMATORY FACTORS

Neuroimmune inflammation plays a significant role in the pathogenesis of alcohol dependence. Experimental studies have shown that acute and chronic ethanol consumption activates resident brain macrophages – microglia. Microglia activation leads to an increased secretion of cytokine mediators, such as high-mobility group protein B1 (HMGB1), which, through various subtypes of Toll-like receptors (TLR), triggers intracellular molecular cascades of reactions, resulting in increased expression of pro-inflammatory cytokines and the development of neuroinflammation. TLR4-dependent signaling plays a key role in this process [35, 36]. Neuroimmune inflammation adversely affects the function of neurons in brain

structures associated with behavior and emotions, contributing to the development and persistence of alcohol-related pathology.

Several recent reviews have analyzed the results of studies on the contribution of neuroimmune activation and neuroimmune inflammation to the formation of alcohol dependence [5, 37–39]. Repeated cycles of binge drinking/alcohol withdrawal cause persistent induction of HMGB1, mRNA, and TLR receptors in the brain, possibly underlying the loss of behavioral control, impulsivity, and anxiety, which promote reward-seeking behavior and increase the risk of developing alcohol use disorders [40, 41].

When alcohol is consumed, the gastrointestinal tract is exposed to the highest concentration of exogenous ethanol. Alcohol and its metabolite, acetaldehyde, disrupt the tight junctions between intestinal epithelial cells and increase intestinal permeability. Dysfunction of the intestinal barrier facilitates the release of bacterial components, such as the bacterial endotoxin lipopolysaccharide (LPS), other pathogen-associated molecular patterns (PAMPs), and intracellular proteins into the bloodstream. These molecules activate the immune system, primarily through TLR4 on immune cells, elevating levels of circulating cytokines that act as inducers of inflammation in the absence of pathogens, which is referred to as “sterile inflammation” [42–44]. Clinical studies have identified elevated levels of serum LPS, peptidoglycan, and other inflammatory markers, particularly IL-8 and IL-1 β , in actively drinking individuals. These levels correlated with the amount of alcohol consumed and with alcohol craving, decreasing after abstinence [45, 46].

Analysis of available data indicates alterations in the serum cytokine profile in patients with alcoholism, generally towards an increase in pro-inflammatory mediators, contributing to the formation of alcohol-related pathologies [47–49]. Associations have been identified between inflammation mediators and the severity of alcohol dependence, as well as with cognitive and behavioral characteristics [4, 50]. The results of a meta-analysis of cytokine studies in patients with alcohol use disorder revealed that the overwhelming majority of publications confirm the presence of an abnormal circulating pro-/anti-inflammatory cytokine profile in patients compared to controls, with variations depending on the disease stage. Elevated levels of pro-inflammatory cytokines (interleukins IL-6, TNF α , IL-8, and IL-12) are associated with the severity of dependence, alcohol

withdrawal syndrome, and alcohol craving [51]. Based on these findings, a number of cytokines/chemokines have been proposed as promising biomarkers of excessive alcohol consumption and prediction of the course of alcoholism [4, 50].

Peripheral cytokines, particularly IL-1 α , IL-1 β , IL-6, and TNF α , penetrate the blood-brain barrier through various mechanisms and enhance neuroinflammation and neuroadaptive changes in the CNS [52]. A series of reviews provide data from studies indicating that cytokines influence surrounding neurons by regulating neurotransmitter function and neurotransmission [37, 53–55].

ENDOCRINE REGULATING FACTORS

The effects of alcohol on the endocrine system have been thoroughly researched. Long-term alcohol consumption and repeated withdrawal cycles are believed to be stressors leading to endocrine dysregulation and neuroadaptive changes, the mechanisms of which are discussed in a number of reviews [6, 56–58]. The information presented in these reviews can be briefly summarized in the following statements: prolonged alcohol consumption and withdrawal are powerful stressors that stimulate the HPA axis and glucocorticoid synthesis; HPA axis activation leads to multiple neuroadaptive changes in the brain reward and stress systems which sustain increased motivation for alcohol consumption and largely determine pathological alcohol craving and relapse in dependent patients.

According to the literature, alcohol can directly activate the HPA by affecting corticotropin-releasing factor (CRF), disrupting the regulation of CRF signaling in hypothalamic and extrahypothalamic brain regions. Activation of the CRF system may contribute to alcohol-related behavioral changes, the development of negative emotional reactions, especially during withdrawal states, compulsive responses, and stress-induced resumption of psychoactive substances (PAS) [59, 60]. The actions of CRF are mediated by two subtypes of G-protein-coupled receptor (CRF1 and CRF2), with stress-related behavioral responses primarily mediated by CRF1 receptors [61].

Corticotropin-releasing factor (corticotropin-releasing hormone or corticoliberin), a neuropeptide expressed by neurons throughout the CNS, is a key regulator of the brain stress system and a key factor in the transition from remission to substance seeking to alleviate the negative emotional states of acute withdrawal and prolonged abstinence [62–64].

Experimental and clinical studies have attempted to promote corticotropin-releasing factor receptor 1 (CRF1) antagonists as potential therapeutic agents.

The CRF1 antagonist verucerfonte has been shown to suppress stress-induced alcohol seeking in rats [65]. A double-blind placebo-controlled study found no clinical effect of the CRF1 antagonist pexacerfonte in individuals with alcohol dependence and high anxiety [66]. M.M.Weera, N. W.Gilpin (2024) analyzed studies on the therapeutic potential of CRF1 antagonists and noted that clinical trials involving individuals with anxiety, depression, and alcohol use disorder have largely yielded negative results. At the same time, further research in this direction may lead to new therapeutic approaches for alleviating symptoms in patients with these conditions [68].

The main stress-releasing hormone is cortisol, a glucocorticoid steroid hormone secreted by the adrenal cortex in response to effect of adrenocorticotrophic hormone (ACTH). ACTH secretion, in turn, is stimulated by corticotropin-releasing factor. High levels of cortisol correlating with the severity of the clinical condition have been detected in biological fluids (serum, plasma, and CSF) of patients with alcohol withdrawal syndrome, alcohol delirium, and alcohol abusers [7, 68–70].

As part of a double-blind placebo-controlled clinical and laboratory study, the use of the glucocorticoid receptor (GR) antagonist mifepristone was tested as treatment of alcohol dependence. Patients receiving mifepristone compared with placebo showed a significant reduction in alcohol craving and alcohol consumption during one-week treatment phase and one-week post-therapy period [71]. In a randomized double-blind placebo-controlled study involving patients with alcohol dependence, the effect of a single oral administration of cortisol on craving was investigated [72]. It was found that cortisol administration significantly increased craving on the first day of testing in less severe cases but decreased it in patients with more severe forms. The authors conclude that the different effects of cortisol on craving, depending on disease severity, are still difficult to explain and emphasize the importance of developing new treatment approaches targeting alcohol-mediated neurobiological dysregulation.

G.F. Koob, N.D.Volkow (2016) conceptualize substance use disorder as a three-stage cycle: binge/intoxication; withdrawal/negative affect; and preoccupation/anticipation [9]. Neurotransmission

dysregulation occurs within three functional domains: incentive salience/pathological habits, negative emotional states, and executive function, which are mediated by key elements of neural circuits (basal ganglia, extended amygdala, and prefrontal cortex). Impaired executive function during the preoccupation/anticipation stage leads to alcohol craving and perpetuation of the addiction cycle. Each stage is characterized by specific alterations in neurotransmitter and neuromodulator systems, manifesting in the core components of neural circuits – the basal ganglia, extended amygdala, and prefrontal cortex. In summary, stage-specific changes include increased dopamine and glutamate neurotransmission; reduced function of the dopamine component in the reward system; recruitment of stress-related neurotransmitters; and dysregulation of peptidergicneuromodulatory systems (glutamate/GABA). The application of this three-stage model may facilitate the individualization of pharmacological treatments for alcohol dependence [73].

Literature reviews discuss the concept of positive and negative reinforcement as an important aspect of the neurobiology of psychoactive substances (PAS) use [74–77]. The positive reinforcing effects of alcohol, which induce pleasurable sensations, are primarily mediated by dopamine, opioid peptides, serotonin, and GABA. Negative reinforcement associated with negative emotional states involves increased recruitment of corticotropin-releasing factor and glutamatergic systems, along with reduced GABA transmission.

CONCLUSION

The analysis of the current state of the problem discussed in the review demonstrates that the main aim of research is to develop new strategies to improve the effectiveness of therapy for alcoholism and prevent early relapses of the disease. To do this, recently conducted and future studies should focus on further elucidation of the complex neurobiological effects of ethanol, identification of molecular pharmacological targets, and the search for measurable objective markers of disease stages.

Alcoholism is a chronic disease with alternating periods of relapse and remission. There are various approaches to defining remission and calculating its duration. In Russian addiction medicine, remission is typically calculated starting from 1 month of complete abstinence from alcohol and disappearance of intoxication symptoms [78]. Despite the diversity of alcoholism treatment methods, the issue of achieving

and maintaining therapeutic remission remains relevant. After completing a course of treatment, only 50% of patients maintained sobriety for up to three months, while 34% continued to consume alcohol despite treatment [79]. Furthermore, only 7.1% of individuals with alcohol abuse reported abstinence for two years [80].

A one-year follow-up of 877 patients after outpatient treatment revealed that about 65% of those surveyed experienced at least one transition from remission to relapse during the follow-up period. [81]. The state of remission in alcohol dependence is unstable and dynamic; it cannot be considered equivalent to mental health, as the clinical structure permanently includes alcohol craving of varying degrees of severity, which is the core syndrome of dependence, and its actualization (activation of craving) is considered to be one of the main causes of disease relapse [78, 82–85].

The problem of finding ways to prevent relapse, particularly the search for predictive markers of craving activation to improve the effectiveness of therapy and the stability of remission, is becoming increasingly important. In psychiatry and addiction medicine, alongside the importance of expensive neuroimaging and omics technologies, the potential of a rapidly expanding field of research focused on identifying peripheral biomarkers that provide affordable non-invasive methods of monitoring the course of the disease and the effectiveness of therapy has been highlighted. Researchers most often consider factors related to inflammation, oxidative stress, and endocrine mediators of the stress response as potential biomarkers [86–88].

It is important to emphasize the significant expediency of using as craving markers not individual parameters but a complex of peripheral biomarkers reflecting the interrelated processes of alcohol dependence pathogenesis – neurotransmission, neuroimmune inflammation, and endocrine regulation. Such an approach would enhance the value and reliability of clinical and biological research findings, which could be used for a personalized approach to treatment based on individual patient profiles.

REFERENCES

1. Anokhina I.P. Main Biological Mechanisms of Psychoactive Substance Addiction. *Journal of Addiction Problems*. 2013;6:40–59. (In Russ.). URL: <https://www.elibrary.ru/item.asp?id=21074215>
2. Nutt D., Hayes A., Fonville L., Zafar R., Palmer E.O.C., Paterson L. et al. Alcohol and the brain. *Nutrients*. 2021;13(11):3938. DOI: 10.3390/nu13113938.
3. Gimenez-Gomez P., Le T., Martin G.E. Modulation of neuronal excitability by binge alcohol drinking. *Front. Mol. Neurosci*. 2023;16:1098211. DOI: 10.3389/fnmol.2023.1098211.
4. Manzardo A.M., Poje A.B., Penick E.C., Butler M.G. Multiplex immunoassay of plasma cytokine levels in men with alcoholism and the relationship to psychiatric assessments. *Int. J. Mol. Sci*. 2016;17(4):472. DOI: 10.3390/ijms17040472.
5. Coleman L.G.Jr, Crews F.T. Innate immune signaling and alcohol use disorders. *Handb. Exp. Pharmacol*. 2018;248:369–396. DOI: 10.1007/164_2018_92.
6. Proskuryakova T.V., Shamakina I.M., Shokhonova V.A., Tarabarko I.E., Anokhina I.P. Activity of the Hypothalamic-Pituitary-Adrenal System under Conditions of Single and Chronic Exposure to Psychoactive Substances and during Their Withdrawal. *Narcology*. 2017;16(10):84–98. (In Russ.). URL: <https://elibrary.ru/item.asp?id=30622038>.
7. Blaine S.K., Nautiyal N., Hart R., Guarnaccia J.B., Sinha R. Craving, cortisol and behavioral alcohol motivation responses to stress and alcohol cue contexts and discrete cues in binge and non-binge drinkers. *Addict. Biol*. 2019;24(5):1096–1108. DOI: 10.1111/adb.12665.
8. Anokhina I.P. Main Biological Mechanisms of Psychoactive Substance Addiction. *Journal of Addiction Problems*. 2017;(2-3):15–41. (In Russ.). URL: <https://www.elibrary.ru/item.asp?id=30103919>
9. Koob G.F., Volkow N.D. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry*. 2016;3(8):760–773. DOI: 10.1016/S2215-0366(16)00104-8.
10. Mikhailova M.A., Gainetdinov R.R. Effect of Acute Ethanol Injection on the Mesolimbic Dopamine System on Freely-Moving Rats. *Russian Journal of Physiology*. 2019;105(7):853–860. (In Russ.). DOI: 10.1134/S0869813919070069.
11. Lelevich S.V., Gushcha V.K., Doroshenko E.M. Neurotransmitter Disturbances in Some Parts of the Rat Brain and Their Correction under Chronic and Intermittent Alcohol Intoxication. *Bulletin of Yanka Kupala Grodno State University. Issue 5. Economics. Sociology. Biology*. 2020;10(1):150–158. (In Russ.). URL: <https://elibrary.ru/item.asp?id=42367025>
12. Ding Z.M., Ingraham C.M., Rodd Z.A., McBride W.J. The reinforcing effects of ethanol within the posterior ventral tegmental area depend on dopamine neurotransmission to forebrain cortico-limbic systems. *Addict. Biol*. 2015;20:458–468. DOI: 10.1111/adb.12138.
13. Engleman E.A., Ingraham C.M., Rodd Z.A., Murphy J.M., McBride W. J., Ding Z.M. The reinforcing effects of ethanol within the prefrontal cortex and ethanol drinking: Involvement of local dopamine D2 receptor-mediated neurotransmission. *Drug and Alcohol Dependence*. 2020;214:108165. DOI: 10.1016/j.drugalcdep.2020.108165.
14. Ma T., Cheng Y., Roltsch Hellard E., Wang X., Lu J., Gao X., et al. Bidirectional and long-lasting control of alcohol-seeking behavior by corticostriatal LTP and LTD. *Nature Neuroscience*. 2018;21:373–383. DOI: 10.1038/s41593-018-0081-9.
15. Anokhin P.K., Razumkina E.V., Shamakina I.Yu. Comparative Analysis of mRNA Expression of Dopamine Receptors, Tyrosine Hydroxylase and Dopamine Transport Protein in the Mesolimbic System of Rats with Different Levels of Alco-

- hol Consumption. *Neurochemistry*. 2019;36(2):119–127. (In Russ.). DOI: 10.1134/S1027813319010035.
16. Jangard S., Jayaram-Lindström N., Isacson N.H., Matheson G.J., Plavén-Sigray P., Franck J., et al. Striatal dopamine D2 receptor availability as a predictor of subsequent alcohol use in social drinkers. *Addiction*. 2023;118(6):1053–1061. DOI: 10.1111/add.16144.
17. Anikhina I.P. New Insight into the Role of Dopamine in the Development of Alcoholism. *Journal of Addiction Problems*. 2021;201(6):17–27. (In Russ.). DOI: 10.47877/0234-0623_2021_06_17.
18. Kibitov A.O., Rybakova K.V., Brodyansky V.M., Berntsev V.A., Skurat E.P., Krupitsky E.M. Comparative Pharmacogenetic Study of Disulfiram or Cyanamide Efficacy for Alcohol
19. Dependence: the Key Role of Dopamine Neurotransmission Gene Polymorphisms. V.M. Bekhterev Review of Psychiatry and Medical Psychology. 2024;58(1):115–130. (In Russ.). DOI: 10.31363/2313-7053-2024-833.
20. Roberts B.M., Lopes E.F., Cragg S.J. Axonal modulation of striatal dopamine release by local γ -aminobutyric acid (GABA) signalling. *Cells*. 2021;10(3):709. DOI: 10.3390/cells10030709.
21. Farokhnia M., Sheskie M.B., Lee M.R., Le A.N., Singley E., Bouhlal S. et al. Neuroendocrine response to GABA-B receptor agonism in alcohol-dependent individuals: Results from a combined outpatient and human laboratory experiment. *Neuropharmacology*. 2018;137:230–239. DOI: 10.1016/j.neuropharm.2018.04.011.
22. Farokhnia M., Deschaine S.L., Sadighi A., Farinelli L.A., Lee M.R., Akhlaghi F. et al. A deeper insight into how GABA-B receptor agonism via baclofen may affect alcohol seeking and consumption: lessons learned from a human laboratory investigation. *Mol. Psychiatry*. 2021;26 (2):545–555. DOI: 10.1038/s41380-018-0287-y.
23. Augier E. Recent advances in the potential of positive allosteric modulators of the GABA_B receptor to treat alcohol use disorder. *Alcohol and Alcoholism*. 2021;56(2):139–148. DOI: 10.1093/alcalc/agab003.
24. Kibitov A.O., Kuznetsova M.N. Molecular Mechanisms of Alcohol Dependence: the Role of Brain Glutamate Receptors. *Journal of Addiction Problems*. 2019;5(176):58–98. (In Russ.). URL: <https://elibrary.ru/item.asp?id=32497447>
25. Akkus F., Mihov Y., Treyer V., Ametamey S.M., Johayem A., Senn S. et al. Metabotropic glutamate receptor 5 binding in male patients with alcohol use disorder. *Transl. Psychiatry*. 2018;8:1–8. DOI: 10.1038/s41398-017-0066-6.
26. Akhmadeev A.V., Kalimullina L.B. Disturbances of Glutamatergic Transmission in the Basolateral Nucleus of the Amygdala during the Development of Alcohol Dependence. *Russian Journal of Physiology*. 2016;102(4):385–397. (In Russ.). URL: <https://www.elibrary.ru/item.asp?id=25717819>
27. Roberto M., Kirson D., Khom S. The role of the central amygdala in alcohol dependence. *Cold Spring Harb. Perspect. Med*. 2021;11(2):a039339. DOI: 10.1101/cshperspect.a039339.
28. Kibitov A.O., Brodyansky V.M., Rybakova K.V., Krupitsky E.M. Modulation of GABA and Glutamate Systems as a Promising Pharmacological Target for Pathogenetic Therapy of Alcohol Dependence: Possibilities of Pharmacogenetic Analysis Based on a Double-Blind Placebo-Controlled Study. *Journal of Addiction Problems*. 2018;1(161):48–86. (In Russ.). URL: <https://elibrary.ru/item.asp?id=32497447>
29. Prisciandaro J.J., Hoffman M., Brown T.R., Voronin K., Book S., Bristol E. et al. Effects of Gabapentin on Dorsal Anterior Cingulate Cortex GABA and Glutamate Levels and Their Associations With Abstinence in Alcohol Use Disorder: A Randomized Clinical Trial. *Am. J. Psychiatry*. 2021;178(9):829–837. DOI: 10.1176/appi.ajp.2021.20121757.
30. Most D., Ferguson L., Harris R.A. Molecular basis of alcoholism. *Handb. Clin. Neurol*. 2014;125:89–111. DOI: 10.1016/B978-0-444-62619-6.00006-9.
31. Ciccocioppo R., Economidou D., Cippitelli A., Cucculelli M., Ubaldi M., Soverchia L. et al. Genetically selected Marchigian Sardinian alcohol-preferring (msP) rats: an animal model to study the neuro-biology of alcoholism. *Addict. Biol*. 2006;11(3-4):339–355. DOI: 10.1111/j.1369-1600.2006.00032.x.
32. Ko Y.E., Hwa L.S. Serotonin regulation of intermittent and continuous alcohol drinking in male and female C57BL/6J mice with systemic SB242084 and buspirone. *Alcohol. Alcohol*. 2023;58(3):280–288. DOI: 10.1093/alcalc/agad019.
33. Llinás S.G., Caballero A.J., Peñalver J.C., Valdés R. Platelet serotonin concentration and clinical status in alcohol withdrawal syndrome, preliminary results. *MEDICC Rev*. 2014;16(1):37–42. DOI: 10.37757/MR2014.V16.N1.8.
34. Nedic Erjavec G., Bektic Hodzic J., Repovecki S., Nikolac Perkovic M., Uzun S., Kozumplik O. et al. Alcohol-related phenotypes and platelet serotonin concentration. *Alcohol*. 2021;97:41–49. DOI: 10.1016/j.alcohol.2021.09.001.
35. Bokhan N.A., Ivanova S.A., Levchuk L.A. Serotonin System in the Modulation of Depressive and Addictive Behavior. Tomsk: National Research Tomsk State University Publishing House, 2013:102. (In Russ.). ISBN: 978-5-91701-090-8.
36. Airapetov M.I., Eresko S.O., Lebedev A.A., Bychkov E.R., Shabanov P.D. Alcoholization and Withdrawal of Ethanol Lead to Activation of the Neuroimmune Response in the Prefrontal Cortex of the Rat Brain. *Biomedical Chemistry*. 2019;65(5):380–384. (In Russ.). DOI: 10.18097/PBMC20196505380.
37. Pascual M., Calvo-Rodriguez M., Núñez L., Villalobos C., Ureña J., Guerri C. Toll-like receptors in neuroinflammation, neurodegeneration, and alcohol-induced brain damage. *IUBMB Life*. 2021;73(7):900–915. DOI: 10.1002/iub.2510.
38. Roberto M., Patel R.R., Bajo M. Ethanol and cytokines in the central nervous system. *Handb. Exp. Pharmacol*. 2018;248:397–431. DOI: 10.1007/164_2017_77.
39. Airapetov M., Eresko S., Lebedev A., Bychkov E., Shabanov P. The role of Toll-like receptors in neurobiology of alcoholism. *Biosci. Trends*. 2021;15(2):74–82. DOI: 10.5582/bst.2021.01041.
40. Niedzwiedz-Massey V.M., Douglas J.C., Rafferty T., Johnson J.W., Holloway K.N., Berquist M.D. et al. Effects of chronic and binge ethanol administration on mouse cerebellar and hippocampal neuroinflammation. *Am. J. Drug Alcohol. Abuse*. 2023;49(3):345–358. DOI: 10.1080/00952990.2022.2128361.
41. Crews F.T., Lawrimore C.J., Walter T.J., Coleman L.G.Jr. The role of neuroimmune signaling in alcoholism. *Neu-*

- neuropharmacology*. 2017;122:56–73. DOI:10.1016/j.neuropharm.2017.01.031.
42. Crews F.T., Coleman L.G. Jr., Macht V.A., Vetreno R.P. Alcohol, HMGB1, and innate immune signaling in the brain. *Alcohol. Res.* 2024;44(1):04. DOI: 10.35946/arc.v44.1.04.
 43. Blednov Y.A., Benavidez J.M., Geil C., Perra S., Morikawa H., Harris R.A. Activation of inflammatory signaling by lipopolysaccharide produces a prolonged increase of voluntary alcohol intake in mice. *Brain Behav. Immun.* 2011;25(Suppl. 1):S92–S105. DOI: 10.1016/j.bbi.2011.01.008.
 44. Kany S., Janicova A., Relja B. Innate immunity and alcohol. *J. Clin. Med.* 2019;8(11):1981. DOI: 10.3390/jcm8111981.
 45. Czerwińska-Błaszczak A., Pawlak E., Pawłowski T. The significance of toll-like receptors in the neuroimmunologic background of alcohol dependence. *Front. Psychiatry.* 2022;12:97123. DOI: 10.3389/fpsy.2021.797123.
 46. Leclercq S., De Saeger C., Delzenne N., de Timary P., Stärkel P. Role of inflammatory pathways, blood mononuclear cells, and gut-derived bacterial products in alcohol dependence. *Biol. Psychiatry.* 2014;76(9):725–733. DOI: 10.1016/j.biopsych.2014.02.003.
 47. Liangpunsakul S., Toh E., Ross R.A., Heathers L.E., Chandler K., Oshodi A. et al. Quantity of alcohol drinking positively correlates with serum levels of endotoxin and markers of monocyte activation. *Sci. Rep.* 2017;7(1):4462. DOI: 10.1038/s41598-017-04669-7.
 48. Panchenko L.F., Terebilina N.N., Pirozhkov S.V., Naumova T.A., Baronets V.Yu., Balashova A.A. et al. Serum Markers of Fibrosis and Endothelial Dysfunction in Patients with Alcoholism with Varying Degrees of Liver Fibrosis. *Pathological Physiology and Experimental Therapy.* 2015;59(3):18–27 (In Russ.). URL: <https://www.elibrary.ru/item.asp?id=26000984>
 49. Gao B., Ahmad M.F., Nagy L.E., Tsukamoto H. Inflammatory pathways in alcoholic steatohepatitis. *J. Hepatol.* 2019;70(2):249–259. DOI: 10.1016/j.jhep.2018.10.023.
 50. Girard M., Malauzat D., Nubukpo P. Serum inflammatory molecules and markers of neuronal damage in alcohol-dependent subjects after withdrawal. *World J. Biol. Psychiatry.* 2019;20(1):76–90. DOI: 10.1080/15622975.2017.1349338.
 51. Hillmer A.T., Nadim H., Devine L., Jatlow P., O'Malley S.S. Acute alcohol consumption alters the peripheral cytokines IL-8 and TNF- α . *Alcohol.* 2020;85:95–99. DOI: 10.1016/j.alcohol.2019.11.005.
 52. Adams C., Conigrave J.H., Lewohl J., Haber P., Morley K.C. Alcohol use disorder and circulating cytokines: A systematic review and meta-analysis. *Brain Behav. Immun.* 2020;89:501–512. DOI: 10.1016/j.bbi.2020.08.002.
 53. Pan W., Stone K.P., Hsueh H., Manda V.K., Zhang Y., Kastin A.J. Cytokine signaling modulates blood-brain barrier function. *Curr. Pharm. Des.* 2011;17(33):3729–3740. DOI: 10.2174/138161211798220918.
 54. Capuron L., Miller A.H. Immune system to brain signaling: Neuropsychopharmacological implications. *Pharmacol. Ther.* 2011;130(2):226–238. DOI: 10.1016/j.pharmthera.2011.01.014.
 55. Patel R.R., Khom S., Steinman M.Q., Varodayan F.P., Kiosses W.B., Hedges D.M. et al. IL-1 β expression is increased and regulates GABA transmission following chronic ethanol in mouse central amygdala. *Brain Behav. Immun.* 2019;75:208–219. DOI: 10.1016/j.bbi.2018.10.009.
 56. Varodayan F.P., Pahng A.R., Davis T.D., Gandhi P., Bajo M., Steinman M.Q. et al. Chronic ethanol induces a pro-inflammatory switch in interleukin-1 β regulation of GABAergic signaling in the medial prefrontal cortex of male mice. *Brain Behav. Immun.* 2023;110:125–139. DOI: 10.1016/j.bbi.2023.02.020.
 57. Becker H.C. Influence of stress associated with chronic alcohol exposure on drinking. *Neuropharmacology.* 2017;122:115–126. DOI: 10.1016/j.neuropharm.2017.04.028.
 58. Blaine S.K., Sinha R. Alcohol, stress, and glucocorticoids: From risk to dependence and relapse in alcohol use disorders. *Neuropharmacology.* 2017;122:136–147. DOI: 10.1016/j.neuropharm.2017.01.037.
 59. Wemm S.E., Sinha R. Drug-induced stress responses and addiction risk and relapse. *Neurobiol. Stress.* 2019;10:100148. DOI: 10.1016/j.ynstr.2019.100148.
 60. Schreiber A.L., Gilpin N.W. Corticotropin-releasing factor (CRF) neurocircuitry and neuropharmacology in alcohol drinking. *Handb. Exp. Pharmacol.* 2018;248:435–471. DOI: 10.1007/164_2017_86.
 61. Simpson S., Shankar K., Kimbrough A., George O. Role of corticotropin-releasing factor in alcohol and nicotine addiction. *Brain Res.* 2020;1740:146850. DOI: 10.1016/j.brainres.2020.146850.
 62. Domi E., Domi A., Adermark L., Heilig M., Augier E. Neurobiology of alcohol seeking behavior. *J. Neurochem.* 2021;157(5):1585–1614. DOI: 10.1111/jnc.15343.
 63. Koob G.F. The role of CRF and CRF-related peptides in the dark side of addiction. *Brain Res.* 2010;1314:3–14. DOI: 10.1016/j.brainres.2009.11.008.
 64. Haass-Koffler C.L., Bartlett S.E. Stress and addiction: contribution of the corticotropin releasing factor (CRF) system in neuroplasticity. *Front. Mol. Neurosci.* 2012;5:91. DOI: 10.3389/fnmol.2012.00091.
 65. Heilig M. Stress-related neuropeptide systems as targets for treatment of alcohol addiction: A clinical perspective. *J. Intern. Med.* 2023;293(5):559–573. DOI: 10.1111/joim.13636.
 66. Schwandt M.L., Cortes C.R., Kwako L.E., George D.T., Momenan R., Sinha R. et al. The CRF1 antagonist verucerfont in anxious alcohol-dependent women: translation of neuroendocrine, but not of anti-craving effects. *Neuropsychopharmacology.* 2016;41(12):2818–2829. DOI: 10.1038/npp.2016.61.
 67. Lee M.R., Rio D., Kwako L., George D.T., Heilig M., Momenan R. Corticotropin-Releasing Factor receptor 1 (CRF1) antagonism in patients with alcohol use disorder and high anxiety levels: effect on neural response during Trier Social Stress Test video feedback. *Neuropsychopharmacology.* 2023;48(5):816–820. DOI: 10.1038/s41386-022-01521-z.
 68. Weera M.M., Gilpin N.W. Central amygdala CRF1 cells control nociception and anxiety-like behavior. *Neuropsychopharmacology.* 2024;49(1):341–342. DOI: 10.1038/s41386-023-01693-2.
 69. Anokhina I.P., Veretinskaya A.G., Kuznetsova M.N., Vekshina N.L. Dopamine, Cortisol and Adrenocorticotrophic Hormone in the Blood and Cerebrospinal Fluid of Patients with Alcohol Withdrawal Syndrome and Delirium. *Journal of*

- Addiction Problems*. 2014;3:73–81. (In Russ.). URL: <https://www.elibrary.ru/item.asp?id=21670127>
70. Vetlugina T.P., Lobacheva O.A., Nikitina V.B., Prokopyeva V.D., Mandel A.I., Bokhan N.A. Hormones of the Stress-Realizing System in Alcohol Dependence: the Possibility of Predicting the Duration of Remission. *S.S. Korsakov Journal of Neurology and Psychiatry*. 2020;5(120):73–78. (In Russ.). DOI: 10.17116/jnevro202012005173.
 71. Vetlugina T.P., Prokopyeva V.D., Nikitina V.B., Lobacheva O.A., Yarygina E.G., Mandel A.I. et al. Search for Biological Factors Associated with the Stability of Therapeutic Remission in Alcohol Dependence. *Siberian Herald of Psychiatry and Addiction Psychiatry*. 2021;2(111):5–12. (In Russ.). DOI: 10.26617/1810-3111-2021-2(111)-5-12.
 72. Vendruscolo L.F., Estey D., Goodell V., Macshane L.G., Logrip M.L., Schlosburg J.E. et al. Glucocorticoid receptor antagonism decreases alcohol seeking in alcohol-dependent individuals. *J. Clin. Invest.* 2015;125(8):3193–3197. DOI: 10.1172/JCI79828.
 73. Soravia L.M., Moggi F., de Quervain D.J. Effects of cortisol administration on craving during in vivo exposure in patients with alcohol use disorder. *Transl. Psychiatry*. 2021;11(1):6. DOI: 10.1038/s41398-020-01180-y.
 74. Koob G.F. alcohol use disorder treatment: problems and solutions. *Annu. Rev. Pharmacol. Toxicol.* 2024;64:255–275. DOI: 10.1146/annurev-pharmtox-031323-115847.
 75. Roberto M., Spierling S.R., Kirson D., Zorrilla E.P. Corticotropin-Releasing Factor (CRF) and Addictive Behaviors. *Int. Rev. Neurobiol.* 2017;136:5–51. DOI: 10.1016/j.bs.irm.2017.06.004.
 76. Witkiewitz K., Litten R.Z., Leggio L. Advances in the science and treatment of alcohol use disorder. *Sci. Adv.* 2019;5(9): eaax4043. DOI: 10.1126/sciadv.aax4043.
 77. Anokhin P.K., Shagiakhmetov F.Sh., Kokhan V.S., Shamakina I.Yu. Dynorphin/Kappa-Opioid System of the Brain, Anti-Reward and Alcohol Abuse. *Journal of Addiction Problems*. 2020;5(188):47–63. (In Russ.). DOI: 10.47877/0234-0623_2020_5_47.
 78. Sinha R. Alcohol's Negative emotional side: the role of stress neurobiology in alcohol use disorder. *Alcohol. Res.* 2022;42(1):12. DOI: 10.35946/arcr.v42.1.12.
 79. Vinnikova M.A. Remissions in Addiction Syndrome: Possibilities of Formation, Stages of the Course, and Clinical Forms. *Journal of Addiction Problems*. 2017;4-5:83–102. (In Russ.).
 80. Meliksetyan A.S. Features of the Course of Remission in Patients with Chronic Alcoholism. *Narcology*. 2014;13(12):35–43. (In Russ.). URL: <https://elibrary.ru/item.asp?id=22627611>.
 81. Abidin E., Subramaniam M., Vaingankar J.A., Chong S.A. The role of sociodemographic factors in the risk of transition from alcohol use to disorders and remission in Singapore. *Alcohol. Alcohol.* 2014;49(1):103–108. DOI: 10.1093/alcalc/agt126.
 82. Maisto S.A., Hallgren K.A., Roos C.R., Witkiewitz K. Course of remission from and relapse to heavy drinking following outpatient treatment of alcohol use disorder. *Drug Alcohol. Depend.* 2018;187:319–326. DOI: 10.1016/j.drugalcdep.2018.03.011.
 83. Altshuler V.B. Clinical Manifestations and Patterns of the Course of Alcoholism. *Journal of Addiction Problems*. 2013;3:112–142 (In Russ.). URL: <https://elibrary.ru/item.asp?id=19101632>.
 84. Gofman A.G. Remission in Patients with Alcoholism. *Journal of Addiction Problems*. 2013;4:110–118. (In Russ.). URL: <https://elibrary.ru/item.asp?id=20159402>.
 85. Bernard L., Cyr L., Bonnet-Suard A., Cutarella C., Bréjard V. Drawing alcohol craving process: A systematic review of its association with thought suppression, inhibition and impulsivity. *Heliyon*. 2021;7(1):e05868. DOI: 10.1016/j.heliyon.2020.e05868.
 86. Martins J.S., Fogelman N., Wemm S., Hwang S., Sinha R. Alcohol craving and withdrawal at treatment entry prospectively predict alcohol use outcomes during outpatient treatment. *Drug Alcohol. Depend.* 2022;231:109253. DOI: 10.1016/j.drugalcdep.2021.109253.
 87. Uzbekov M.G., Gurovich I.Ya., Ivanova S.A. Potential Biomarkers of Mental Illnesses in the Aspect of a Systemic Approach. *Social and Clinical Psychiatry*. 2016;26(1):77–94. (In Russ.). URL: <https://www.elibrary.ru/item.asp?id=26539116>
 88. Milivojevic V., Sinha R. Central and peripheral biomarkers of stress response for addiction risk and relapse vulnerability. *Trends Mol. Med.* 2018;24(2):173–186. DOI: 10.1016/j.molmed.2017.12.010
 89. Coccini T., Ottonello M., Spigno P., Malovini A., Fiabane E., Roda E. et al. Biomarkers for alcohol abuse/withdrawal and their association with clinical scales and temptation to drink. A prospective pilot study during 4-week residential rehabilitation. *Alcohol*. 2021; 94: 43–56. DOI: 10.1016/j.alcohol.2021.04.004.

Author Information

Vetlugina Tamara P. – Dr. Sci. (Biology), Professor, Honored Scientist of the Russian Federation, Chief Researcher, Laboratory of Clinical Psychoneuroimmunology and Neurobiology, Mental Health Research Institute, Tomsk NRMC, Tomsk, vetluga21@mail.ru, <https://orcid.org/0000-0003-2068-0931>

Epimakhova Elena V. – Cand. Sci. (Biology), Researcher, Department of Addictive Disorders, Mental Health Research Institute, Tomsk NRMC, Tomsk, elenaepimakhova@mail.ru, <https://orcid.org/0000-0002-9304-4496>

Prokopieva Valentina D. – Dr. Sci. (Biology), Leading Researcher, Laboratory of Clinical Psychoneuroimmunology and Neurobiology, Mental Health Research Institute, Tomsk NRMC, Tomsk, valyaprok@mail.ru, <https://orcid.org/0000-0002-4811-984X>

Shumilova Sofia N. – Junior Researcher, Laboratory of Clinical Psychoneuroimmunology and Neurobiology, Mental Health Research Institute, Tomsk NRMC, Tomsk, sofashumilova97@gmail.com, <https://orcid.org/0000-0001-9248-4150>

Voevodin Ivan V. – Dr. Sci. (Medicine), Leading Researcher, Endogenous Disorder Department, Mental Health Research Institute, Tomsk NRMC, Tomsk, i_voevodin@list.ru, <https://orcid.org/0000-0002-3988-7660>

(✉) **Vetlugina Tamara P.**, vetluga21@mail.ru

Received on March 12, 2025;
approved after peer review on March 31, 2025;
accepted on April 17, 2025