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# The Application and Research Progress of Non-Pharmacological Interventions in Rehabilitation of Drug Addiction Patients

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## Abstract

Drug addiction is a chronic brain disease characterized by compulsive drug use and high relapse rate, which is prevalent in China. Many studies have shown that drug replacement therapy is effective in controlling withdrawal symptoms, but the long-term withdrawal rate is only 15% - 30%, and it is difficult to repair the functional impairment and social dysfunction associated with addiction. Given the limitations of pharmacological treatments in terms of neurocognitive function restoration and social reintegration, this study reviewed the application of non-pharmacological interventions in the rehabilitation of drug addicts at home and abroad through literature review, sorted out the core intervention methods and mechanisms, and proposed clinical optimization strategies on this basis, aiming to provide reference for clinical decision-making of clinical medical staff.

## Keywords

Drug Addiction Patients, Non-Pharmacological Interventions, Rehabilitation

## 1. Background

In recent years, the global drug situation is not optimistic; drug addiction has become a global public health crisis and a major problem in the field of social governance. Research shows that from 1990 to 2023, the prevalence and disease burden of opioid use disorder increased threefold [1]. The scale of drug smuggling and trafficking continues to expand, the methods of drug production are increasingly diversified, and new psychoactive substances are spreading rapidly worldwide [2]. However, fewer than 10% of drug users in the world can obtain professional drug treatment [3]. The overall treatment gap is extremely large, and it is urgent to improve drug rehabilitation programs.

At present, pharmacological intervention is still the most common treatment mode in clinical detoxification rehabilitation, but there are obvious deficiencies in all kinds of detoxification drugs: Methadone is a substitution maintenance treatment drug mainly for opioid addicts. Its use is affected by factors such as daily dose, business hours of institutions, travel conditions of patients, etc. [4]. Moreover, the drug itself has dependence risk, and excessive use is easy to cause serious adverse reactions such as respiratory depression. Therefore, its maintenance treatment has a high dropout rate in the world, and drug compliance is often at a low level. Although traditional Chinese herbal compound preparations represented by Jitai tablets do not cause dependence, large-scale clinical trial data are still lacking, and the incidence of adverse events is relatively high. At the same time, drug addiction belongs to chronic recurrent brain diseases. In addition to pathological damage to the body, addicts are often accompanied by psychological disorders such as anxiety and depression. Clinically, they show complex physical and mental comorbidities, which greatly limits the selection range of therapeutic drugs [5]. Therefore, it is difficult to deal with the increasingly complex situation of drug by relying solely on pharmacological interventions, and it is urgent to strengthen the research on non-pharmacological interventions. In this context, the focus of research on rehabilitation measures for drug addicts has gradually shifted to the field of non-pharmacological interventions. Many studies have shown that non-pharmacological interventions such as psychobehavioral therapy, exercise therapy and physical-neuromodulation therapy effectively alleviate anxiety symptoms of drug addicts. Meanwhile, non-pharmacological interventions have no risk of secondary addiction, can coordinate multiple body systems, and alleviate pathological symptoms of patients' body and mind. Patients have good acceptance and compliance with it. To conclude, this work constitutes a narrative review, synthesizing the authors' examination of literature on the application and efficacy of non-pharmacological interventions for drug addiction. Its purpose is to provide a theoretical reference and practical foundation for clinicians and researchers, while also highlighting potential directions for future investigation.

It should be noted that the existing high-quality clinical evidence on non-pharmacological interventions is unevenly distributed across substance types, with the majority of the literature focusing on methamphetamine use disorder. Accordingly, the discussion and conclusions of this review are primarily grounded in data derived from this specific population.

## 2. Pathogenesis of Drug Addiction

Drug addiction is not a physiological dependence caused by a single factor, but a complex chronic encephalopathy in which pathological changes occur at multiple levels of neural structure, neurotransmitter regulation and psychological cognitive behavior. After drug addiction, compulsive drug-seeking and drug-taking behaviors will gradually form. After withdrawal, they are often accompanied by stubborn psychological craving and an extremely high relapse tendency.

### 2.1. Pathological Damage Mechanism of Neural Circuit

Drug addiction can simultaneously destroy the ventral tegmental area-nucleus accumbens reward circuit, prefrontal cortex-related executive control circuit, paraventricular nucleus of the thalamus-related circuit, etc. [6]. It causes abnormal reward system, decline of inhibition control function, distortion of motivation system and solidification of memory circuit [7] [8]. Liu *et al*. [9] 137 imaging studies uniformly verify that chronic methamphetamine addicts have atrophy of gray matter in nucleus accumbens, decrease of blood flow in dorsolateral prefrontal cortex and disorder of functional connectivity of whole brain. Therefore, the key reason why drug addiction is difficult to cure lies in pathological changes in neural circuits, in which the formation and extraction mechanism of addictive memories is the key neurobiological basis for driving substance use behavior or relapse of addictive symptoms [10]-[12]. At present, many studies have revealed the mechanism of pathological damage to neural circuits, but the specific mechanism of action and the dynamic changes in the process of drug addiction are not yet clear. In addition, the essence of drug addiction is the occurrence of organic pathological changes in the multi-brain region collaboration network, single body detoxification cannot reverse brain circuit damage, which is also the key reason for the high long-term relapse rate of drug detoxification alone [13].

### 2.2. Neurotransmitter and Molecular Plasticity Mechanism

Dopamine plays an important role in all stages of drug addiction [14] and can enhance drug-seeking behavior by continuously activating the mesolimbic reward circuit [15]. Saunders *et al*. [16] found that conditioned responses occur only under stimulation of the ventral tegmental area of the midbrain, proving that midbrain dopamine neurons are crucial. In addition, all kinds of addictive drugs will eventually directly or indirectly increase the concentration of dopamine in synaptic cleft [17]. After long-term stimulation, the body compensates for downregulation of dopamine D2 receptor quantity and sensitivity [18]. Volkow *et al*. [19] confirmed through positron emission tomography (PET) imaging that the concentration of D2 receptor in heroin addicts' brain decreased by 35%-50% compared with healthy people. The lower the receptor level, the more obvious the compulsive drug-seeking behavior of patients. Trifilieff *et al*. [20] further indicated that PET imaging consistently demonstrates blunted striatal dopamine release and diminished D2 receptor availability in addiction, which represent both a consequence of chronic drug use and a susceptibility factor for the development of addiction. Hypothalamus-pituitary-adrenal axis (HPA) is the main stress regulation endocrine pathway of the body. When patients are in a long-term drug abuse or compulsory detoxification state, they will face strong psychological and physiological double stress, thus activating HPA and making cortisol (COR) concentration continuously high [21]. Nikbakhtzadeh *et al.* [22] also indicated in their review that stress constitutes a significant risk factor for the development of addiction and relapse vulnerability, and that post-stress alterations in the HPA axis directly influence reward-related brain regions, including the ventral tegmental area and nucleus accumbens. Studies have shown that a sharp rise in COR is closely related to anxiety, depression, cognitive impairment and other stress symptoms, which are important drivers of drug craving [23]. In addition, abnormality of serotonin (5-HT) level is an important sign of withdrawal reaction and relapse impulse, "activation of HPA system-COR mediated-increase of 5-HT level" is an important pathway to induce drug craving and relapse, and reducing 5-HT secretion can block drug-induced relapse behavior [24]. Ciccocioppo [25] noted in his review that the 5-HT system serves a core function in impulse control, and that serotonergic deficits may result in impaired regulation of drug consumption, constituting a key determinant in the persistence of addictive behaviors. Glutamate participates in the encoding and consolidation of long-term memory through synaptic plasticity mediated by the activation of N-methyl-D-aspartate (NMDA) receptors [26] [27]. Addictive memory is abnormally persistent in the brain and constitutes an important neural basis for the long-term relapse risk after detoxification [28]. A transgenic mouse study [29] demonstrated that selective knockout of the NR1 subunit of NMDA receptors on dopamine D1 receptor-expressing neurons completely abolished the acquisition of conditioned place preference for cocaine-, morphine-, or ethanol-paired contexts, while leaving memory for sucrose reward and naloxone-induced aversion intact. This indicates that NMDA receptor-dependent neural plasticity is necessary for drug-associated contextual memory, but not for general reward learning.

### 2.3. Psychological and Behavioral Mechanisms of Addiction

On the basis of brain physiological damage, drug addicts will form abnormal cognitive patterns and behavioral habits, which belong to the external manifestation of addiction at psychological level. First, attention will unconsciously give priority to drug-related stimuli; secondly, cognitive level will underestimate the risk of illegal activities and health damage; finally, classical conditioned reflex will be established, and environmental incentives will directly trigger drug-seeking impulse. A large number of studies have shown that belief in self-abstinence is the key to preventing relapse, and self-awareness is the foundation of long-term stages [30]. Cognitive distortions and addictive behaviors are the process of addiction from organic diseases to external bad behavior patterns, and are also the main focus of psychological non-pharmacological interventions.

## 3. Main Types of Non-Pharmacological Interventions and Their Effects

Non-pharmacological intervention refers to the systematic improvement of the physiological function, psychological state and social adaptability of drug addicts through psychological, behavioral, sports and physical means without the use of drugs. Non-pharmacological interventions applied to drug addiction rehabilitation can be roughly classified into four categories: psychobehavioral interventions, exercise interventions, physical-neuromodulation interventions, and other auxiliary interventions.

### 3.1. Psychobehavioral Intervention and Its Effect

Psychobehavioral intervention is a psychological treatment aimed at the cognitive, emotional and behavioral problems of addicts. It can reduce drug craving and prevent review by reshaping cognitive patterns and regulating intrinsic motivation, among other approaches. It mainly includes mindfulness intervention, cognitive behavioral therapy and motivation interview. Mindfulness-based relapse prevention (MBRP) can help drug addicts strengthen their belief in detoxification. Liu *et al.* [31] conducted a randomized controlled trial involving 58 young female methamphetamine dependents from Sichuan Province. The MBRP group (n = 29) received 4 weeks of MBRP training, while the control group (n = 29) received only routine treatment. The results showed that the MBRP group exhibited a significant reduction in the total score of the Obsessive Compulsive Drug Use Scale (OCDUS) from baseline (33.41 ± 8.17 vs. 29.83 ± 6.94, $P < 0.01$), and a significant increase in the total score of the Five-Factor Mindfulness Questionnaire (FFMQ) (117.45 ± 16.84 vs. 122.76 ± 15.36). These findings indicate that MBRP training can effectively enhance trait mindfulness and reduce psychological craving in methamphetamine-dependent individuals. Cognitive behavioral therapy helps addicts correctly deal with high-risk situations and negative emotions by changing their bad cognitive and behavioral patterns of drugs. Aslan *et al.* [32] conducted an 8-week nurse-led randomized controlled trial of cognitive-behavioral therapy involving 72 incarcerated males with methamphetamine use disorder in Türkiye. The intervention group received eight sessions covering cognitive restructuring, craving management, stress coping, and relapse prevention, while the control group received treatment as usual. The results showed that the intervention group exhibited a 38.5% reduction in craving intensity from baseline and a 26.7% improvement in overall stress coping strategies. All three coping domains showed significant improvements: social support seeking increased by 34.1%, problem-focused coping by 16.1%, and adaptive avoidance by 33.7%. In terms of effect sizes, stress coping demonstrated a large effect, while craving reduction showed a medium effect. The core purpose of motivational interviewing is to explore and resolve the ambivalence of individual behavior, and to promote behavior change by arousing the motivation for change in the addict's ambivalence. Polcin *et al.* [33] conducted a randomized clinical trial involving 217 methamphetamine-dependent individuals, in which participants were randomly assigned to either a 9-session intensive motivational interviewing group (IMI) or a single session of standard motivational interviewing combined with eight nutrition education sessions (SMI). The intervention was delivered weekly over 8 weeks, and all participants concurrently received standard outpatient group therapy three times per week. The results showed that both groups demonstrated significant improvements in the percentage of days abstinent from methamphetamine use (from baseline to follow-up) and in the drug composite scores of the Addiction Severity Index, with no significant differences between the two groups. However, the IMI group showed significantly greater improvements than the SMI group in the psychiatric composite scores of the ASI and in the number of days experiencing psychiatric problems over the past 30 days. These findings suggest that motivational interviewing can reduce drug use by enhancing intrinsic motivation for change among addicted individuals, but increasing intervention intensity may not confer additional benefits on drug use reduction itself, whereas greater intensity may be required for improving comorbid psychiatric symptoms.

### 3.2. Exercise Intervention and Its Effect

Exercise intervention is a non-invasive intervention method to relieve withdrawal physical discomfort, relieve drug craving, improve negative emotions, improve physical fitness and comprehensively promote physical and mental health of addicts through planned and standardized various types of somatic movement training. In drug addiction treatment, the commonly used exercise interventions mainly include aerobic exercise, psychosomatic exercise, high intensity intermittent training and resistance training. Aerobic exercise improves cardiorespiratory function and mental health mainly through sustained exercise of moderate intensity. Lyu *et al*. [34] studied the effect of acute aerobic exercise on craving and risk decision-making in methamphetamine use disorder (MUD) patients. 30 male MUD participants were recruited for randomized controlled experiment. The results showed that acute aerobic exercise can effectively reduce craving and enhance decision-making performance, especially in the field of impulsive and short-sighted decision-making. However, the present study is limited in its ability to establish correlations between a single experimental session and long-term benefits, as well as associations with gender. In another study, Tang *et al*. [35] randomly divided 100 MUD patients into 12-week control group, in which the experimental group received moderate-to-vigorous aerobic exercise (MVE) intervention and the control group received low-to-moderate-intensity exercise intervention. It was found that MVE helped to relieve negative emotions and reduce drug craving. Physical and mental exercise could also reduce drug craving and improve physical fitness of drug addicts. Zhang *et al*. [36] conducted a randomized controlled trial in which 48 men with methamphetamine use disorder were randomly divided into Tai Chi group and running group, and were intervened 3 times a week for 12 weeks. It was found that Tai Chi improved the patients' attention and reaction ability compared with running. High intensity interval training involves alternating short bursts of high intensity exercise with intermittent recovery periods, demonstrating significant efficacy in reducing drug craving in individuals with substance addiction. He *et al*. [37] conducted a randomized controlled experiment on 40 methamphetamine dependent men and found that long-term high intensity intermittent training increased the activation of ventrolateral prefrontal cortex in MUD men and reduced drug craving. Resistance training enhanced muscle strength and endurance by resisting resistance, often in the form of equipment exercise, elastic band, weight training, etc. Nygard *et al.* [38] conducted a randomized controlled trial of 40 subjects three times a week for 12 weeks and found that maximum strength training improved bone and muscle health.

### 3.3. Neurophysical Regulation Intervention and Its Effect

physical-neuromodulation intervention is a kind of non-invasive physical rehabilitation method, which can reduce drug craving, improve cognition and regulate emotion of drug addicts by acting on addiction related brain areas through external conduction. The two commonly used neurophysiological modulation interventions in the field of addiction treatment are repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation. A randomized controlled trial conducted by Wang *et al.* [39] divided 64 methamphetamine dependents into sham stimulation control group and high frequency repetitive transcranial magnetic stimulation (HF-rTMS) intervention group. The final study found that HF-rTMS could alleviate drug craving and improve cognitive decision-making ability of subjects. Wang *et al.* [40] further found that HF-rTMS combined with physical exercise can further optimize the subject's mood and reduce drug craving. Transcranial direct current stimulation regulates cortical excitability by applying weak direct current to the scalp, thus reducing drug craving and improving cognitive function in drug addicts. Borzooee *et al.* [41] found that transcranial direct current stimulation reduced craving and improved executive function in opioid addicts in a randomized controlled trial. Ahmed *et al.* [42] conducted a double-blind randomized controlled trial involving 40 male patients with opioid dependence in India. Craving and psychosocial functioning were assessed using the Obsessive-Compulsive Drug Use Scale and the Addiction Severity Index at baseline, immediately post-treatment, and at 2- and 4-week follow-ups. At baseline, no significant differences in OCDUS scores were observed between the two groups. Following treatment, the Active group showed significantly greater reductions in craving than the Sham group at Day 5 and Day 14, with the effects maintained at Day 28 [42]. This study further confirmed that five sessions of right dorsolateral prefrontal cortex transcranial direct current stimulation can produce rapid, significant, and sustained reductions in opioid craving.

### 3.4. Main Types of Other Non-Pharmaceutical Interventions

Besides psychobehavioral intervention, exercise intervention and physical-neuromodulation intervention, acupuncture and external treatment of traditional Chinese medicine, digital therapy and family intervention also play an important role in drug addiction rehabilitation. Clinical studies by Wu *et al.* [43] found that acupuncture has the advantages of treating withdrawal syndrome and has the potential to prevent relapse. Shen *et al*. [44] conducted a three-arm randomized controlled experiment on methamphetamine dependents from 12 communities in Sichuan Province, China, and found that gamified adaptive method bias correction can reduce participants' drug craving. Sarani Yaztappeh *et al*. [45] conducted a randomized clinical trial for high-risk adolescents, dividing 60 adolescents into selective defense group, family-based defense group and control group. The results showed that family intervention plays an important role in preventing substance abuse. Robbins *et al*. [46] showed that compared with conventional therapy, family therapy has advantages in reducing drug use and maintaining family member participation in treatment.

## 4. Conclusions

In conclusion, non-pharmacological interventions have become an indispensable core component of the substance use disorder treatment system. They have unique value in improving psychosocial function, improving treatment compliance and preventing relapse, and complement drug substitution therapy. Currently, non-pharmacological interventions applied to drug addiction rehabilitation can be roughly summarized into four categories: psychobehavioral intervention, exercise intervention, physical-neuromodulation intervention, and other auxiliary intervention methods. The intervention content has its own emphasis, forming a complementary rehabilitation concept with drug therapy. However, the field still faces shortcomings such as uneven research quality and short follow-up period. In the future, efforts should be made to promote multi-center large sample long-term follow-up research, unify operation norms and evaluation indicators, and develop digital rehabilitation programs to promote the transformation of addiction rehabilitation from symptom control to comprehensive functional rehabilitation.

Although this review primarily centers on methamphetamine use disorder, the involved neurobiological repair mechanisms (e. g., prefrontal cortex functional recovery and reward circuit modulation) possess generalizability across substance addictions. Nevertheless, direct extrapolation of these intervention effects to opioid or alcohol use disorders should be approached with caution, taking into account the distinct pharmacological profiles of each substance.

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## Author Contributions

Conceptualization, Yuanyuan Cheng; validation, Xiaotao Zhuang; investigation, Yarui Yue, Longxian Zhang; writing—original draft preparation, Yuanyuan Cheng, Longxian Zhang, Yarui Yue, and Han Lu; writing—review and editing, Guixiang Kuang; supervision, Han Lu; project administration, Han Lu; funding acquisition, Han Lu. All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References


[1] Kang, J., Kim, H.J., Kim, M.S., Il Shin, J., Aalruz, H., Abate, Y.H., *et al.* (2026) Global Burden of Amphetamine, Cannabis, Cocaine and Opioid Use in 204 Countries, 1990-2023: A Global Burden of Disease Study. *Nature Medicine*, **32**, 527-544. https://doi.org/10.1038/s41591-025-04137-0

[2] Lee, J., Yang, S., Kang, Y., Han, E., Feng, L., Li, J., *et al.* (2017) Prevalence of New Psychoactive Substances in Northeast Asia from 2007 to 2015. *Forensic Science International*, **272**, 1-9. https://doi.org/10.1016/j.forsciint.2016.10.010

[3] Balkhy, H. (2025) Strengthening Public Health Response to Substance Use in the Eastern Mediterranean Region. *Eastern Mediterranean Health Journal*, **31**, 357-358. https://doi.org/10.26719/2025.31.6.357

[4] Frank, D., Bennett, A.S., Cleland, C.M., Meyerson, B.E., Russell, D.M., Walters, S.M., *et al.* (2025) "I Still Can Feel the Sickness": Withdrawal Experiences of People on Methadone Maintenance Treatment. *Journal of Substance Use and Addiction Treatment*, **170**, Article 209616. https://doi.org/10.1016/j.josat.2024.209616

[5] Li, H. and Gao, X. (2026) Network Meta-Analysis of Non-Pharmacological Interventions for Psychiatric Symptoms among Individuals with Substance Use Disorders. *Journal of Addictive Diseases*, **2026**, 1-16. https://doi.org/10.1080/10550887.2026.2626423

[6] Koob, G.F. and Volkow, N.D. (2016) Neurobiology of Addiction: A Neurocircuitry Analysis. *The Lancet Psychiatry*, **3**, 760-773. https://doi.org/10.1016/s2215-0366(16)00104-8

[7] Feltenstein, M.W., See, R.E. and Fuchs, R.A. (2021) Neural Substrates and Circuits of Drug Addiction. *Cold Spring Harbor Perspectives in Medicine*, **11**, a039628. https://doi.org/10.1101/cshperspect.a039628

[8] Bogdan, R., Hatoum, A.S., Johnson, E.C. and Agrawal, A. (2023) The Genetically Informed Neurobiology of Addiction (GINA) Model. *Nature Reviews Neuroscience*, **24**, 40-57. https://doi.org/10.1038/s41583-022-00656-8

[9] Liu, G.X.H., Tayebi, M., Bristow, B., Wang, J., Lin, Y., Newburn, G., *et al.* (2025) How Does Methamphetamine Affect the Brain? A Systematic Review of Magnetic Resonance Imaging Studies. *Drug and Alcohol Dependence*, **276**, Article 112862. https://doi.org/10.1016/j.drugalcdep.2025.112862

[10] Liu, L., Wang, C., Wang, H., Miao, L., Xie, T., Tian, Y., *et al.* (2024) Identification of the circRNA-miRNA-mRNA Network for Treating Methamphetamine-Induced Relapse and Behavioral Sensitization with Cannabidiol. *CNS Neuroscience & Therapeutics*, **30**, e14737. https://doi.org/10.1111/cns.14737

[11] Keyes, P.C., Adams, E.L., Chen, Z., Bi, L., Nachtrab, G., Wang, V.J., *et al.* (2020) Orchestrating Opiate-Associated Memories in Thalamic Circuits. *Neuron*, **107**, 1113-1123.e4. https://doi.org/10.1016/j.neuron.2020.06.028

[12] Liu, H.M., Liao, M.L., Liu, G.X., Wang, L.J., Lian, D., *et al.* (2023) IPAC Integrates Rewarding and Environmental Memory during the Acquisition of Morphine CPP.

*Science Advances*, **9**, eadg5849. https://doi.org/10.1126/sciadv.adg5849

[13] Volkow, N.D. and Morales, M. (2015) The Brain on Drugs: From Reward to Addiction. *Cell*, **162**, 712-725. https://doi.org/10.1016/j.cell.2015.07.046

[14] Schultz, W. (2011) Potential Vulnerabilities of Neuronal Reward, Risk, and Decision Mechanisms to Addictive Drugs. *Neuron*, **69**, 603-617. https://doi.org/10.1016/j.neuron.2011.02.014

[15] Barbano, M.F., Qi, J., Chen, E., Mohammad, U., Espinoza, O., Candido, M., *et al*. (2024) VTA Glutamatergic Projections to the Nucleus Accumbens Suppress Psychostimulant-Seeking Behavior. *Neuropsychopharmacology*, **49**, 1905-1915. https://doi.org/10.1038/s41386-024-01905-3

[16] Saunders, B.T., Richard, J.M., Margolis, E.B. and Janak, P.H. (2018) Dopamine Neurons Create Pavlovian Conditioned Stimuli with Circuit-Defined Motivational Properties. *Nature Neuroscience*, **21**, 1072-1083. https://doi.org/10.1038/s41593-018-0191-4

[17] Volkow, N.D., Fowler, J.S. and Wang, G.J. (2002) Role of Dopamine in Drug Reinforcement and Addiction in Humans: Results from Imaging Studies. *Behavioural Pharmacology*, **13**, 355-366. https://doi.org/10.1097/00008877-200209000-00008

[18] Atar, A. (2026) Neurobiological Consequences of High-Fat High-Sugar Diets on the Mesocorticolimbic System: A Narrative Review. *Current Nutrition Reports*, **15**, Article No. 6. https://doi.org/10.1007/s13668-026-00729-5

[19] Volkow, N.D., Fowler, J.S., Wang, G.J., Baler, R. and Telang, F. (2009) Imaging Dopamine's Role in Drug Abuse and Addiction. *Neuropharmacology*, **56**, 3-8. https://doi.org/10.1016/j.neuropharm.2008.05.022

[20] Trifilieff, P., Ducrocq, F., van der Veldt, S. and Martinez, D. (2017) Blunted Dopamine Transmission in Addiction: Potential Mechanisms and Implications for Behavior. *Seminars in Nuclear Medicine*, **47**, 64-74. https://doi.org/10.1053/j.semnuclmed.2016.09.003

[21] Dveirin, H., Acuna, V., Tran, M.L., Antici, E.E. and Kuhlman, K.R. (2025) Salivary Cortisol and Affective Responses to Acute Psychosocial Stress among Adolescents. *Psychoneuroendocrinology*, **172**, Article 107265. https://doi.org/10.1016/j.psyneuen.2024.107265

[22] Nikbakhtzadeh, M., Ranjbar, H., Moradbeygi, K., Zahedi, E., Bayat, M., Soti, M., *et al*. (2023) Cross-Talk between the HPA Axis and Addiction-Related Regions in Stressful Situations. *Heliyon*, **9**, e15525. https://doi.org/10.1016/j.heliyon.2023.e15525

[23] Wemm, S.E. and Sinha, R. (2019) Drug-Induced Stress Responses and Addiction Risk and Relapse. *Neurobiology of Stress*, **10**, Article 100148. https://doi.org/10.1016/j.ynstr.2019.100148

[24] Craige, C.P. and Unterwald, E.M. (2013) Serotonin (2C) Receptor Regulation of Cocaine-Induced Conditioned Place Preference and Locomotor Sensitization. *Behavioural Brain Research*, **238**, 206-210. https://doi.org/10.1016/j.bbr.2012.10.034

[25] Ciccocioppo, R. (1999) The Role of Serotonin in Craving: From Basic Research to Human Studies. *Alcohol and Alcoholism*, **34**, 244-253. https://doi.org/10.1093/alcalc/34.2.244

[26] Kim, H., Choi, S., Lee, E., Koh, W. and Lee, C.J. (2024) Tonic NMDA Receptor Currents in the Brain: Regulation and Cognitive Functions. *Biological Psychiatry*, **96**, 164-175. https://doi.org/10.1016/j.biopsych.2024.03.009

[27] Zhang, K., Wen, M., Nan, X., Zhao, S., Li, H., Ai, Y., *et al*. (2025) NMDA Receptors

in Neurodegenerative Diseases: Mechanisms and Emerging Therapeutic Strategies. *Frontiers in Aging Neuroscience*, **17**, Article 1604378. https://doi.org/10.3389/fnagi.2025.1604378

[28] Cutler, M., Thati, A. and Grella, S.L. (2025) Drug-Related Engrams and Their Role in the Persistence and Recurrence of Drug-Related Behaviors. *Hippocampus*, **35**, e70040. https://doi.org/10.1002/hipo.70040

[29] Sikora, M., Tokarski, K., Bobula, B., Zajdel, J., Jastrzębska, K., Cieślak, P.E., *et al.* (2016) NMDA Receptors on Dopaminoceptive Neurons Are Essential for Drug-Induced Conditioned Place Preference. *Eneuro*, **3**, ENEURO.0084-15.2016. https://doi.org/10.1523/eneuro.0084-15.2016

[30] Setiawan, A., Sahar, J., Santoso, B., Mansyur, M. and Syamsir, S.B. (2024) Coping Mechanisms Utilized by Individuals with Drug Addiction in Overcoming Challenges during the Recovery Process: A Qualitative Meta-Synthesis. *Journal of Preventive Medicine and Public Health*, **57**, 197-211. https://doi.org/10.3961/jpmph.24.042

[31] Liu, X., Zhang, Y., Cheng, H., Dong, H., You, Y., Wu, Y., *et al.* (2024) Mindfulness-Based Relapse Prevention Targeting Psychological Craving and Trait Mindfulness in Young Chinese Women with Methamphetamine Dependence: A Randomized Controlled Trial. *Frontiers in Psychiatry*, **15**, Article 1339517. https://doi.org/10.3389/fpsyt.2024.1339517

[32] Aslan, R., Gezgin Yazıcı, H. and Gökçen, O. (2025) Effectiveness of Nurse-Led Cognitive Behavioral Therapy on Craving and Stress Coping among Incarcerated Young Men with Stimulant Use Disorder (Methamphetamine): A Randomized Controlled Trial. *Issues in Mental Health Nursing*, **46**, 918-927. https://doi.org/10.1080/01612840.2025.2538714

[33] Polcin, D.L., Bond, J., Korcha, R., Nayak, M.B., Galloway, G.P. and Evans, K. (2014) Randomized Trial of Intensive Motivational Interviewing for Methamphetamine Dependence. *Journal of Addictive Diseases*, **33**, 253-265. https://doi.org/10.1080/10550887.2014.950029

[34] Lyu, Z.H., Li, M.Y., Zhu, T., Yang, Y.F. and Wang, D.S. (2025) Benefits of Acute Aerobic Exercise to Ameliorate Craving and Risky Decision-Making in Individuals with Methamphetamine Use Disorder. *Drug and Alcohol Dependence*, **274**, Article 112735. https://doi.org/10.1016/j.drugalcdep.2025.112735

[35] Tang, Z., Zhu, Z., Ma, X., Lin, Y., Xu, J., Zhou, Q., *et al.* (2026) Psychological Effects of 12 Weeks of Moderate-to-Vigorous Exercise on Men with Methamphetamine Use Disorder: A Randomized Controlled Trial. *Substance Use & Addiction Journal*, **47**, 28-37. https://doi.org/10.1177/29767342251352608

[36] Zhang, L., Zeng, H., Sun, Y., Xue, H., Gao, L. and Zhu, W. (2024) Effect of Tai Chi Compared to Running on Drug Cravings, Attention Bias, and Physical Fitness in Men with Methamphetamine Use Disorder. *Healthcare*, **12**, Article 1653. https://doi.org/10.3390/healthcare12161653

[37] He, M., Wang, L., Xu, D., Liu, Y., Zhu, X., Zhu, D., *et al.* (2024) Long-Term High-Intensity Interval Training Intervention Improves Emotional Conflict Control in Association with Right Ventrolateral Prefrontal Activation in Males with Methamphetamine Use Disorder: A Randomized Controlled Trial. *Scandinavian Journal of Medicine & Science in Sports*, **34**, e70006. https://doi.org/10.1111/sms.70006

[38] Nygard, M., Mosti, M.P., Brose, L., Flemmen, G., Stunes, A.K., Sørskår-Venæs, A., *et al.* (2018) Maximal Strength Training Improves Musculoskeletal Health in Amphetamine Users in Clinical Treatment. *Osteoporosis International*, **29**, 2289-2298. https://doi.org/10.1007/s00198-018-4623-5

[39] Wang, W., Zhu, Y., Wang, L., Mu, L., Zhu, L., Ding, D., *et al.* (2022) High-Frequency Repetitive Transcranial Magnetic Stimulation of the Left Dorsolateral Prefrontal Cortex Reduces Drug Craving and Improves Decision-Making Ability in Methamphetamine Use Disorder. *Psychiatry Research*, **317**, Article 114904. https://doi.org/10.1016/j.psychres.2022.114904

[40] Wang, K., Li, Y., Yang, Y., Zhang, T. and Luo, J. (2026) Effects of High-Frequency rTMS Combined with Physical Exercise on Mood Disorders in Patients with Methamphetamine Use Disorder: A Randomized Clinical Trial. *Depression and Anxiety*, **2026**, Article 6470779. https://doi.org/10.1155/da/6470779

[41] Borzooee, B., Aghayan, S., Hassani-Abharian, P. and Emamian, M.H. (2024) Effect of Transcranial Direct Current Stimulation on Craving, Cognitive Functions, and Serum Brain-Derived Neurotrophic Factor Level in Individuals on Maintenance Treatment for Opioid Use Disorder, a Randomized Sham-Controlled Trial. *The Journal of ECT*, **40**, e38-e48. https://doi.org/10.1097/yct.0000000000001046

[42] Ahmed, I., Qutishat, M., Ikhlaq, R., Goyal, N. and AL-Huseini, S. (2025) Prefrontal Cortex Modulation Using Transcranial Direct Current Stimulation in Opioid Craving: A Sham-Control Double-Blind Study. *General Hospital Psychiatry*, **96**, 78-84. https://doi.org/10.1016/j.genhosppsych.2025.06.008

[43] Wu, J.M., Wei, D.Y., Luo, Y.F. and Xiang, X.Y. (2003) Clinic Research on Heroin De-Addiction Effects of Acupuncture and Its Potentiality of Preventing Relapse. *Journal of Chinese Integrative Medicine*, **1**, 268-272. https://doi.org/10.3736/jcim20030412

[44] Shen, D., Jiao, J., Zhang, L., Liu, Y., Liu, X., Li, Y., *et al.* (2025) Gamified Adaptive Approach Bias Modification in Individuals with Methamphetamine Use History from Communities in Sichuan: Pilot Randomized Controlled Trial. *JMIR Serious Games*, **13**, e56978. https://doi.org/10.2196/56978

[45] Sarani Yaztappeh, J., Bakhtiyari, M., Bakhshani, N.M., Mousavi, S.E., Masjedi-Arani, A. and Saberi Esfeedvajani, M. (2024) Effect of Selective and Family-Based Prevention on Addiction Susceptibility, Affiliation with Deviant Peers, Risk-Taking, and Risk and Protective Factors of Substance Use in High-Risk Adolescents: A Randomized Clinical Trial. *Journal of Education and Health Promotion*, **13**, 1-12. https://doi.org/10.4103/jehp.jehp_270_24

[46] Robbins, M.S., Feaster, D.J., Horigian, V.E., Rohrbaugh, M., Shoham, V., Bachrach, K., *et al.* (2011) Brief Strategic Family Therapy versus Treatment as Usual: Results of a Multisite Randomized Trial for Substance Using Adolescents. *Journal of Consulting and Clinical Psychology*, **79**, 713-727. https://doi.org/10.1037/a0025477