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Recreational Drugs Addiction, Withdrawal and its Impact on the body: A Literature Review

Mustafa Abrar Zaman[1,2], Aseel Aljeshi[1,2], Kuragamage Dona Prabuddhi Thiloka Kuragama[1,2], Saif Bunni[1,2], Tonmoy Sarker[1,2], Aiza Kashif[1,2], Jyothsnaa Sathish[1,2], Hussien Abouzeid[1,2], Hamza Mohammad Omar Alouf[1,2], Jessarij Chinthamraks[1,2], Adhved Rajesh Krishnan[1,2], Shaan Patker[1,2], Simone Talreja[1,2], Datta Venkata Daivik Pentapati[1,2]

[1] St. George's University
[2] Northumbria University

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ABSTRACT

The use of drugs for recreational purposes has changed dramatically, involving a variety of substances such as opioids, hallucinogens, and cannabinoids. Although these substances are often initially used for recreational purposes, their psychoactive properties can contribute to the development of addiction, withdrawal syndromes, and significant physical and mental health complications. The mechanisms behind addiction, symptoms of withdrawal, and the pathophysiology of frequently abused recreational drugs are all examined in this literature review. Dysregulation of the endocannabinoid system is associated with cannabinoid addiction, which can result in physical dependence, mental health issues, and cognitive impairment. A public health emergency has been exacerbated by opioid abuse, and withdrawal is marked by intense psychological and autonomic symptoms. Lysergic acid diethylamide (LSD), and Phencyclidine (PCP) are examples of hallucinogens that change neurotransmission and can cause neurotoxicity, long-lasting perceptual abnormalities, and mental illnesses. Long-term recovery is still difficult to achieve, despite the promise of pharmacological treatments like opioid agonists and cannabinoid receptor modulators. To lessen the worldwide burden of recreational drug abuse, comprehensive treatment approaches that include pharmacotherapy, psychosocial interventions, and harm reduction techniques are essential.

Keywords: recreational drugs, withdrawal, addiction, opioids, psychedelics, hallucinogens, cannabinoids, endocannabinoid system, LSD, MDMA, PCP, Ketamine, DXM, dextromethorphan, club drugs, serotonin, glutamate, hyperalgesia, opioids receptor, opioid use disorder

1. Introduction

The idea of leisure time has changed throughout human history. Consuming alcohol recreationally has been the norm for years; however, intoxication recreationally has been extending to using psychedelics as well[1]. This implies the increased usage and normalization of using recreational drugs as an activity during leisure time. Recreational drugs are consumed under the impression that their usage is not addictive, regardless of their psychoactive nature, or whether they are synthetically or naturally made[2]. Drug addiction is the progression from recreational drug use to addiction which shifts from positive reinforcement, where drugs are taken for their pleasurable effects, to negative reinforcement, driven by the need to avoid discomfort. Initially, substances are used for their rewarding properties, but repeated use creates secondary reinforcements, where associated cues and contexts become triggers, perpetuating use and increasing the risk of addiction[3]. However, it is important to note that addiction is a chronic medical condition that can be cured, even with the complex involvement of genetics, brain circuits, environment, and a person's life experiences[4]. When someone abruptly discontinues the use of their addictive substance, they can experience physical and mental symptoms which are known as withdrawal[5]. Therefore, it is important to strategically wane people from their recreational use to limit withdrawal and address possible causes that lead to using drugs recreationally.

The misuse of recreational drugs is considered a challenging obstacle to world health, affecting around 30 to 35 million individuals across the globe[6]. Risk factors for drug abuse could be divided into three main categories: individual risk factors, family risk factors, and community risk factors. Individual risk factors include high impulsivity, adverse childhood experiences, previous history of exposure, increased access to the substance, and psychiatric conditions such as conduct disorder and major depressive disorder. Familial risk factors include prenatal maternal smoking, poor parental education, negligence, and the presence of substance-using family members. The main community risk factor was exposure to peers who were abusing drugs[7]. Common forms of cannabis use include hashish, which is formed from the resin glands of Cannabis sativa, and marijuana, which is made from the dried leaves and flowers of the plant. Synthetic cannabinoids, including Spice and K2, have become more well-known recently Although legalization of marijuana has advanced in a number of U.S. states, federal law still classifies cannabis as a Schedule I substance. Cannabis was the most frequently consumed illegal drug in the United States in 2013[8].

Psilocybin-containing mushrooms are a common hallucinogenic substance found worldwide. Despite not causing any bodily harm, they are associated with several psychiatric complications. However, Recent studies have examined the use of psilocybin in treating obsessive disorders, despite the possibility of misuse, underscoring the need to comprehend its pharmacological characteristics[9]. Lysergic acid diethylamide (LSD), commonly known as acid, is a classic psychedelic that alters sensory perception. It can create visual distortions, vivid illusions, and a dreamlike state. While LSD may produce pleasant experiences "good trips", it can also lead to intensely distressing episodes, often referred to as "bad trips"[10]. 3,4-Methylenedioxymethamphetamine (MDMA), known as ecstasy, is a stimulant and is classified as a psychedelic that enhances wakefulness, euphoria, and sociability. Frequently used by adolescents, it is popular at dance parties and raves, earning the label "club drug"[10].

The opioid crisis is a public health emergency in the United States, causing widespread addiction, deaths, and severe social and economic consequences. In 2016 alone, opioids were linked to 42,000 overdose fatalities. Beyond the death toll, the crisis disrupts families and communities, leading to lost productivity, economic hardship, intergenerational trauma, and overwhelming demands on resources like emergency services, hospitals, and treatment centers[11]. In this review, the aim is to explore different recreational drug classes by examining the addiction and withdrawal symptoms, pathogenesis, and the possible and available treatment options.

2. Cannabinoids

2.1 ADDICTION AND WITHDRAWAL SYMPTOMS

Cannabinoids are biological substances derived from the plant Cannabis. This plant has several species, such as sativa, indica, and ruderalis[12]. Cannabis can be taken in different ways, and its usage in the field of medicine and for recreational purposes is vast. Symptoms of cannabinoid addiction include various physical, psychological, and behavioral problems. This is largely due to dysregulation of the endocannabinoid system, which plays an important role in addiction by mediating synaptic plasticity and reward signaling[13]. Cannabinoid addiction symptoms include drug-seeking behavior and cravings. This is mainly due to the action of cannabinoids that increase dopamine levels in the brain[14]. Tolerance is also another addiction symptom, where larger doses are needed to achieve the same effects[12]. Cognitive and psychotic symptoms that persist were also reported, specifically by synthetic cannabinoid users. An example of this is impaired memory, suggesting long-term mental health effects[15]. In addition, the use of cannabinoids has been linked with increased anxiety and depression, indicating emotional disturbances due to cannabinoid use[16].

Moreover, the withdrawal symptoms of cannabinoid use further highlight the challenges individuals face when attempting to discontinue prolonged use. Examples include anxiety, irritability, and mood swings[17]. Users may also have myalgias and decreased appetite[18]. Furthermore, sleep disturbances are common, including insomnia[19]. The withdrawal symptoms from synthetic cannabinoids tend to be more severe and have a faster duration of onset, compared to those associated with natural cannabinoids, highlighting the heightened risks associated with synthetic variants[19]. Together, the interplay of addiction and withdrawal symptoms underscores the challenging nature of cannabinoid dependency, emphasizing the need for comprehensive support during both phases of drug use and cessation.

2.2 PATHOGENESIS

Cannabinoids, when administered externally, give their cognitive symptoms by interacting with the body's endocannabinoid system[20]. The endocannabinoid system

is the body's natural mechanism that contains different receptors, such as CBR1 and CBR2, as well as numerous enzymes that carry out various processes. The receptors, CBR1 and CBR2, signal via the G protein-coupled system, causing different results, such as preventing bodily functions[20]. The receptors are found in different locations of the body; for example, CBR1 is found particularly in the brain, and CBR2 is found in the central and peripheral nervous system. However, Wu J's et al. tell us that more CBR1 receptors are found in the CNS compared to CBR2 and have a greater impact on brain activities like the reward pathway due to the effects of the glutamatergic, GABAergic, and dopaminergic systems.

Cannabinoids have psychoactive properties through tetrahydrocannabinol (THC) and non-psychoactive properties through cannabidiol (CBD)[21]. Both THC and CBD are components of cannabinoids and bind to CBR1, but only THC causes an activation of the receptor, creating sedating symptoms. Through these components, the endocannabinoid system causes different physiological and psychological responses.

The binding of exogenous cannabinoids to their receptors disrupts the normal endocannabinoid levels in the body and instantly causes activation of the Gi protein system, decreasing cAMP levels[22]. Along with the activation of the G protein-coupled system, cannabinoids also activate via the β-arrestin pathway. β-arrestin regulates the G protein system, and studies show prolonged activation of β-arrestin increases the activity of CBR1[22]. This tells us there is a positive correlation between these pathways and receptor activation, thus leading to an increased sensitivity to THC, causing symptoms of psychoactivity and better pain relief.

2.3 TREATMENT

Cannabinoids are the most commonly used illicit narcotics around the world, hence treating cannabis use disorder (CUD) is imperative[23]. Abstinence, withdrawal symptoms, adverse effects, abuse severity, psychosocial improvement, and other aspects should be considered when developing effective treatment strategies. To do this, Bahji et al. performed the first network meta-analysis (NMA) which covered a variety of treatments in one study. The NMA concluded that overall, Nabilone (a cannabinoid agonist), Topiramate (an anticonvulsant), and FAAH inhibitors had the greatest reduction in cannabinoid consumption. However, due to the many neurotransmitter systems implicated in the pathophysiology of CUD as well as its withdrawal symptoms, different pharmacotherapies were found to work in specific areas of CUD[23]. For example, Dronabinol (cannabinoid agonist) improved retention in treatment in particular, whereas gabapentin (anticonvulsant) showed a reduction in cravings, according to Bahji et al. On the other hand, MA et al. centered their research on the usage of cannabis agonists (Dronabinol, Nabilone, and Nabiximols) to alleviate withdrawal symptoms. They discovered monotherapy with Dronabinol, like in Bahji et al.'s study, improved treatment retention while also reducing cravings in a dose-dependent manner. Furthermore, when administered alone, Nabilone corrected mood symptoms and disrupted sleep as well as regulated food intake. Although Dronabinol and Nabilone exhibited more efficacy at larger doses, they also had more adverse effects such as cognitive decline and reduced psychomotor task performance accordingly[24]. Nabiximols, on the contrary, demonstrated higher tolerability but produced variable outcomes for craving reduction, indicating that further study is needed before concluding its efficacy[24]. Additionally, when agonists were combined with medications such as Lofexidine and Zolpidem, the results were better in terms of sleep control, withdrawal symptoms, and cravings than when they were used alone. However, these findings did not appear to be consistent with outpatient therapy, highlighting the need for additional research[3]. Various drugs have been explored for the treatment of CUD, but there is no single pharmacotherapy regimen capable of addressing all areas of concern, such as reducing use, withdrawal symptoms, and severity. Some medications showed promise in one or two areas but had side effects that impacted other areas of interest. As a result, even though medications like cannabis agonists are used off-label to treat CUD, they are yet to be approved for mainstream treatment[25].

In general, because of inconsistent data on the efficacy of pharmaceuticals in treating CUD, psychosocial therapies are considered the first line of treatment, with motivational enhancement therapy (MET) and cognitive behavioral therapy (CBT) being the most effective[25]. Moreover, the findings of JP et al. and Bahji et al. indicate that abstinence-based contingency management (CM) in conjunction with MET and CBT yielded higher abstinence rates. These findings were demonstrated to be persistent in the short term (up to 14 weeks), with abstinence rates doubling and consumption decreasing by 25%. However, there is less evidence of efficacy in the long term following treatment[25]. Unfortunately, access to psychotherapies such as CBT and MET was frequently found to be limited around the world, possibly due to the stigma and costs associated with psychotherapy in some countries[23]. A possible approach to address this issue was to use technology to encourage psychosocial therapy online, which could save both time and money[25].

3. Opioids

3.1 OPIOID ADDICTION

Opioid addiction is a condition marked by compulsive use, impaired control over use, and continued use despite adverse effects. The reinforcing effects of opioids are transmitted via the interaction with the brain's mu-opioid receptors, which contribute to an intense release of dopamine in the reward system, hence the euphoric effects[26]. Chronic exposure to opioids induces neuroadaptive changes that reduce sensitivity to natural rewards, facilitating dependence[27]. Clinically, patients with opioid addiction often present with negative behavioral symptoms like neglecting important responsibilities, withdrawing socially, and engaging in risky behaviors to obtain opioids, as well as physiological signs including miosis, slowed breathing, and sedation[27,28]. The psychological component of dependency also presents itself with ongoing cravings and an inability to stop use despite physical, social, or legal harm. Treatment of opioid addiction is a complex process that involves a multimodal approach: pharmacological interventions, such as methadone or

buprenorphine, combined with psychosocial therapies to target the underlying neurobiological and behavioral aspects of the disorder[29].

3.2 OPIOID WITHDRAWAL

Opioid withdrawal represents the syndrome that occurs when chronic use is abruptly stopped, leading to a cascade of painful physical and psychological symptoms. The condition occurs as a result of unregulated, disturbed central and peripheral nervous system function due to the absence of opioid receptor stimulation[30]. Symptoms generally begin within 6-12 hours for short-acting opioids and 24-48 hours for long-acting formulations. Initial manifestations include restlessness, yawning, rhinorrhea, and diaphoresis[31]. In this process of withdrawal, there is intense gastrointestinal distress, muscle cramps, and sleep disturbances[28]. While rare, opioid withdrawal can be life-threatening; the severity of the withdrawal syndrome may potentiate relapse, especially among those without medical support[28]. Evidence-based practices for management include alpha-2 adrenergic agonists, such as clonidine, which are used to mitigate autonomic hyperactivity, and opioid agonists, such as methadone or buprenorphine, used to manage and taper symptomatically[32].

3.3 PATHOGENESIS OF OPIOIDS

The three opioid receptors include mu- receptor, kappa-receptor, and delta-receptor. These receptors can be found in the brain, spinal cord, and peripheral tissues. The mu-receptor primarily helps relieve pain by inhibiting the release of neurotransmitters, while the kappa and delta receptors can induce sedation and alter mood[33]. However, with chronic use of opioids, the patient can exhibit tolerance due to hyperalgesia, or when the body becomes more sensitive to pain in which the patient may continue to increase the dosage, elevating the risk of drug dependence[33,34]. Additionally, when used alongside other sedative medications, it can increase the risk of respiratory depression. Therefore, current studies are focusing on minimizing these adverse effects[34].

3.4 OPIOID MEDICAL REGULATION AND TREATMENT

According to INCB data, opioid use has increased 250% worldwide since 2000, from 5 million S-DDD in 2000 to 13 million S-DDD in 2014 before plateauing. Between 2015 and 2018, the percentage of people aged 15 to 64 who used opioids for non-medical purposes rose from 0.7% (35 million) to 1.2% (58 million). Eighty to ninety percent of the world's opioid use occurs in high-income areas such as North America, Western/Central Europe, and Oceania[35]. An estimated 109,500 opioid-related fatalities occurred worldwide in 2019[35]. However, mortality from prescribed opioids has consistently declined after availability decreases and legal limits. Furthermore, the use of illicit and synthetic opioids (such as heroin and fentanyl) has increased recently (by 60–80%), which could lead to an increase in mortality due to opiods[35].

Opioid use disorder (OUD) is a chronic, curable, and recurring illness with a low success rate if detoxification is the only treatment[30]. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines the severity of OUD based on several levels of problematic opioid misuse[30]. Therefore, prescribed medications are often used in the management of OUD. There are several medications that can be used as replacement therapy, as sudden withdrawal can lead to many symptoms as mentioned earlier. The World Health Organisation recommends the opioid receptor partial agonist buprenorphine, the opioid receptor antagonist naltrexone, and the opioid receptor full agonist methadone as treatment options for opioid use disorder, and the US Food and Drug Administration (FDA) has approved these three medications[36]. Out of the three mentioned, buprenorphine displays the highest levels of safety, treatment retention, and reduction in the use of illegal opioids, according to a number of studies and meta-analyses[36]. In addition to its activity on the mu-opioid receptor, buprenorphine may also have therapeutic effects on mood through antagonism of the kappa opioid receptor[36]. However, even with safer treatment plans for OUD, the main issue of compliance with the medication remains.

4. Hallucinogens

4.1 PATHOGENESIS OF HALLUCINOGENS

The unique mechanisms of action of hallucinogens like MDMA, Phencyclidine (PCP), ketamine, and Dextromethorphan (DXM) are distinct, contributing to their specific clinical profiles, adverse effects, and withdrawal syndromes, as discussed ahead. The neurotransmitter systems most affected by these agents are serotonin, glutamate, and dopamine, which give the agents their hallucinogenic, dissociative, and euphoric properties, respectively[37,38].

Lysergic acid diethylamide (LSD) is primarily an agonist at the serotonin 5-HT2A receptor. This agonistic process results in augmented cortical glutamate concentration disturbed sensory processing, and heightened activity. The intensity of this activity results in intense visual and auditory hallucinations[37]. Other common side effects are anxiety, paranoia, tachycardia, and hyperthermia, with rare cases of persistent psychosis or hallucinogen-persisting perception disorder (HPPD)[37]. Withdrawal symptoms include mood swings and fatigue, though the drug is considered non-addictive due to the lack of direct dopaminergic stimulation, psychological intensity, rapid tolerance development, and weak reinforcement signals making them non-addictive for most users[37].

A releasing agent and reuptake inhibitor of serotonin, dopamine, and norepinephrine, MDMA functions by resulting in profound euphoria and increased sensory perception such as enhanced light perception, heightened sensitivity to sound, and amplified tactile sensations. However, this overabundance of serotonin depletes stores, causing post-use depression. Neurotoxicity, secondary to oxidative stress, can lead to long-term cognitive deficits emotional dysregulation, sleep disturbances, and reduced attention span[39,40]. Short-term dangers include hyperthermia, hyponatremia, and cardiovascular complications. Withdrawal symptoms include depression, fatigue, and anhedonia[39,40].

The drug PCP modulates NMDA receptors in a non-competitive manner, obstructing glutamatergic neurotransmission and promoting dissociative and hallucinogenic modes along with a distorted perception of reality. It also prompts the release of dopamine, which

contributes to its euphoric effects[38,40]. Adverse effects include hypertension, rhabdomyolysis, and acute psychosis. Chronic use produces memory deficits and mood disturbances, with withdrawal symptoms consisting of depression and cognitive deficits[38,40].

Ketamine also inhibits NMDA receptors, disrupting glutamate flow and inducing dissociative states. Chronic use has been associated with neuronal apoptosis, particularly in prefrontal areas, and bladder toxicity in the form of ketamine-induced cystitis[41]. Acute adverse effects include hypertension, tachycardia, and respiratory depression. Withdrawal effects are usually mild but can include cravings and mood dysregulation[41].

Many antitussives have DXM as an ingredient in them and acts as a weak NMDA receptor antagonist and sigma-1 receptor agonist. At high doses, it produces dissociative and hallucinogenic effects. It also mildly inhibits serotonin reuptake, increasing the risk of serotonin syndrome when given with serotonergic drugs[42,43]. Side effects can include confusion, ataxia, and nausea. With chronic abuse, cognitive impairment occurs, and withdrawal symptoms are associated with dysphoria and fatigue[42,43]. These psychoactive compounds exert similar but distinct mechanisms of action, leading to unique clinical effects and adverse outcomes. Understanding their pathophysiology is essential for delineating the types of interventions required to address public health concerns related to their use and abuse[37,43].

4.2 WITHDRAWAL AND ADDICTION

4.2.1 Lysergic Acid Diethylamide (LSD)

The psychedelic LSD primarily acts on serotonin receptors (5-HT2A). Research indicates that LSD does not typically produce physical dependence or withdrawal symptoms, as it does not directly stimulate dopamine pathways associated with addiction. However, psychological dependence can occur in some users, particularly those who use it frequently for its mind-altering effects[44]. Long-term use has been associated with Hallucinogen Persisting Perception Disorder (HPPD), where users experience flashbacks or persistent visual disturbances long after cessation[45]. Additionally, LSD can exacerbate underlying psychiatric conditions, such as schizophrenia, in susceptible individuals[46].

4.2.2 4-Methylenedioxymethamphetamine (MDMA)

Often classified as an entactogen, MDMA has both stimulant and mild hallucinogenic properties. It primarily affects serotonin, dopamine, and norepinephrine systems. Chronic MDMA use can lead to serotonin depletion, resulting in withdrawal symptoms such as depression, fatigue, irritability, and cognitive impairments[47]. Unlike classic psychedelics, MDMA has a higher potential for abuse due to its euphoric effects. Studies have also highlighted neurotoxicity with prolonged use, particularly affecting serotonin neurons, which may contribute to long-term mood disorders[48].

4.2.3 Phencyclidine (PCP)

The drug PCP is a dissociative anesthetic that acts as an NMDA receptor antagonist. It is known for its high potential for abuse and severe psychological dependence. Withdrawal symptoms include cravings, anxiety, depression, and cognitive disturbances like memory loss, difficulty concentrating, and mood disorders[49]. Chronic use can lead to persistent psychosis, characterized by hallucinations, paranoia, and disordered thinking, even after discontinuation[47]. The withdrawal symptoms of PCP is less studied compared to other substances, but its potent effects on glutamate and dopamine systems suggest a significant risk for addiction and long-term psychiatric complications.

4.2.4 Ketamine

Ketamine, another NMDA receptor antagonist, is used medically as an anesthetic and has gained attention for its antidepressant effects at sub-anesthetic doses. However, recreational use can lead to psychological dependence and withdrawal symptoms such as cravings, anxiety, and depression[47]. Chronic use is associated with bladder and urinary tract damage, as well as cognitive impairments to learning and memory. Ketamine's dissociative effects can also lead to persistent perceptual disturbances in some users[47].

4.2.5 Dextromethorphan (DXM)

A common ingredient in cough suppressants is DXM which acts as an NMDA receptor antagonist and serotonin reuptake inhibitor at high doses. Recreational use can lead to psychological dependence and withdrawal symptoms such as dissociative sedation, distorted visual perceptions, loss of motor coordination. Chronic use has been linked to cognitive deficits and serotonin syndrome in extreme cases. Abusing DXM is particularly concerning among adolescents due to its over-the-counter availability[50].

4.3 TREATMENT OF PSYCHEDELIC ADDICTION

There is a lack of research in treating psychedelic addiction, so a majority of the recommended treatment has been supportive or symptom management[51]. For example, the treatment of PCP intoxication essentially involves trying to reduce symptoms like agitation, hyperthermia, and seizures[51]. Hence, a close observation of patient symptoms and vital signs is required in order to achieve adequate treatment goals, furthermore, if a patient experiences delirium as a major symptom, one might proceed with endotracheal intubation[51].

The American Academy of Child and Adolescent Psychiatry has set in place suitable guidelines encompassing treatment goals[51]. For instance, people who have taken PCP recently orally can undergo GI decontamination using around 1kg worth of charcoal, which needs to be given every 4 hours[51]. Charcoal will help to absorb the PCP and it further increases the rate of nonrenal clearance[51]. Furthermore, because PCP is a weak base, previously, the process of acidifying the patient's urine was generally indicated however side effects like rhabdomyolysis and acidosis posed a big risk, hence this treatment is not indicated currently[51].

Furthermore, patients who are undergoing symptoms of PCP intoxication have been known to be extremely violent with staff and have occasionally been confined to restraints[51]. The anxiety and anger symptoms encompassed within the intoxication can be treated with Benzodiazepines which will also concurrently help reduce the frequency of vivid dreams experienced by the patient[51]. As for LSD intoxication treatment, initially, it is

recommended to limit environmental stimuli, however, if that does not seem to work efficiently then Benzodiazepines like Lorazepam or Diazepam is known to be extremely effective specifically in patients who have dysphoric reactions[52]. Additionally, medications like haloperidol can have counteractive actions and are hence not a treatment of choice for a patient with LSD intoxication[52]. Furthermore, research has been done on the use of antihypertensive drugs in the treatment of LSD intoxication and it shows that drugs like Clonidine can decrease the extent of flashbacks and hallucinogen persisting perception disorder (HPPD) and avoid the increased sympathetic system overactivity when a patient is undergoing LSD addiction[52]. Although there is not enough about the management of psychedelic addiction, many supportive treatments can help manage the negative side effects of their addiction.

5. Conclusion

The availability and normalization of psychoactive substances have made recreational drug use a major global health concern. The three drug classes—opioids, psychedelics, and cannabinoids—each exhibit unique addiction pathways, withdrawal symptoms, and modes of action. The endocannabinoid system is upset by cannabinoids, which causes long-term emotional and cognitive problems. Despite their potential for therapeutic use, psychedelics carry a risk of neurotoxicity and dependence in non-clinical contexts. The opioid crisis highlights how urgently comprehensive strategies that prioritize both medical regulation and psychosocial support are needed to combat addiction. Despite the promise of new pharmacological treatments like opioid and cannabinoid agonists, there are still many obstacles in the way of a long-lasting recovery. To lessen the negative social and economic effects of recreational drug abuse, a comprehensive approach that includes prevention, early intervention, and specialized treatment programs is critical for protecting global health and fostering recovery.

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References:

1. McCormack M, Measham F, Wignall L. The Normalization of Leisure Sex and Recreational Drugs: Exploring Associations Between Polydrug Use and Sexual Practices by English Festival-Goers. *Contemp Drug Probl*. 2021;48(2):185-200. doi:10.1177/00914509211009901
2. Hussain CM, Rawtani D, Pandey G, Tharmavaram M. Chapter 7 - Raman spectroscopy in forensic science. In: Hussain CM, Rawtani D, Pandey G, Tharmavaram M, eds. *Handbook of Analytical Techniques for Forensic Samples*. Elsevier; 2021:109-128. doi:10.1016/B978-0-12-822300-0.00007-0
3. Edwards S. Chapter 4 - Reinforcement principles for addiction medicine; from recreational drug use to psychiatric disorder. In: Ekhtiari H, Paulus M, eds. *Progress in Brain Research*. Vol 223. Neuroscience for Addiction Medicine: From Prevention to Rehabilitation - Constructs and Drugs. Elsevier; 2016:63-76. doi:10.1016/bs.pbr.2015.07.005
4. What is the Definition of Addiction? Default. Accessed January 26, 2025. https://www.asam.org/quality-care/definition-of-addiction
5. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/withdrawal. February 2, 2011. Accessed January 26, 2025. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/withdrawal
6. Schwenker R, Dietrich CE, Hirpa S, et al. Motivational interviewing for substance use reduction - Schwenker, R - 2023 | Cochrane Library. Accessed January 26, 2025. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008063.pub3/full
7. Nawi AM, Ismail R, Ibrahim F, et al. Risk and protective factors of drug abuse among adolescents: a systematic review. *BMC Public Health*. 2021;21(1):2088. doi:10.1186/s12889-021-11906-2
8. Panlilio L, Goldberg S, Justinova Z. Cannabinoid abuse and addiction: Clinical and preclinical findings. *Clin Pharmacol Ther*. 2015;97(6):616-627. doi:10.1002/cpt.118
9. Passie T, Seifert J, Schneider U, Emrich HM. The pharmacology of psilocybin. *Addict Biol*. 2002;7(4):357-364. doi:10.1080/1355621021000005937
10. Bates MLS, Trujillo KA. Use and abuse of dissociative and psychedelic drugs in adolescence. *Pharmacol Biochem Behav*. 2021;203:173129. doi:10.1016/j.pbb.2021.173129
11. Coussens NP, Sittampalam GS, Jonson SG, et al. The Opioid Crisis and the Future of Addiction and Pain Therapeutics. Accessed January 26, 2025. https://jpet.aspetjournals.org/article/S0022-3565(24)26881-6/fulltext
12. Aj K, Dm L. Cannabis use, abuse, and withdrawal: Cannabinergic mechanisms, clinical, and preclinical findings. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/33891706/
13. Me S, Jl G, Va R, Yl H, B LF. The endocannabinoid system as a target for addiction treatment: Trials and tribulations. *PubMed*. Published online 2017. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/28564576/
14. R S. Cannabinoids and the endocannabinoid system in reward processing and addiction: from mechanisms to interventions. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/33162767/
15. Marandure BN, Mhizha S, Wilson A. "Spice Was Made, by the Devil Himself": A Thematic Analysis of the Experience of an Addiction to Synthetic Cannabinoids. *J Psychoactive Drugs*. 2023;55(3):321-329. doi:10.1080/02791072.2022.2083534
16. N S, Lh P. Endocannabinoid-mediated synaptic plasticity and addiction-related behavior. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/21669214/
17. Zd C. Adverse Effects of Synthetic Cannabinoids: Management of Acute Toxicity and Withdrawal. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/27074934/
18. N N, D V, R S, P S, M S, J M. The synthetic cannabinoid withdrawal syndrome. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/23609214/
19. S C, Ja F, Mj B, et al. Clinical withdrawal symptom profile of synthetic cannabinoid receptor agonists and comparison of effects with high potency cannabis. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/34533608/
20. Mackie K. Cannabinoid Receptors: Where They are and What They do. *J Neuroendocrinol*. 2008;20(s1):10-14. doi:10.1111/j.1365-2826.2008.01671.x
21. Urits I, Charipova K, Gress K, et al. Adverse Effects of Recreational and Medical Cannabis. *Psychopharmacol Bull*. 2021;51(1):94-109.
22. Zou S, Kumar U. Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. *Int J Mol Sci*. 2018;19(3):833. doi:10.3390/ijms19030833
23. Bahji A, Meyyappan AC, Hawken ER, Tibbo PG. Pharmacotherapies for cannabis use disorder: A systematic review and network meta-analysis. *Int J Drug Policy*. 2021;97:103295. doi:10.1016/j.drugpo.2021.103295
24. Werneck MA, Kortas GT, de Andrade AG, Castaldelli-Maia JM. A Systematic Review of the Efficacy of Cannabinoid Agonist Replacement Therapy for Cannabis Withdrawal Symptoms. *CNS Drugs*. 2018;32(12):1113-1129. doi:10.1007/s40263-018-0577-6
25. Connor JP, Stjepanović D, Budney AJ, Le Foll B, Hall WD. Clinical management of cannabis withdrawal. *Addiction*. 2022;117(7):2075-2095. doi:10.1111/add.15743
26. Nd V, Gf K, At M. Neurobiologic Advances from the Brain Disease Model of Addiction. *PubMed*. Published online 2016. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/26816013/
27. Tr K, Tp G. The neurobiology of opioid dependence: implications for treatment. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/18567959/
28. Al S, Cl D, Tr K. Opioid dependence treatment: options in pharmacotherapy. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/19538000/

29. Rp M, J K, C B, M D. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/15266465/
30. Kosten TR, Baxter LE. Review article: Effective management of opioid withdrawal symptoms: A gateway to opioid dependence treatment. *Am J Addict*. 2019;28(2):55-62. doi:10.1111/ajad.12862
31. Shah M, Huecker MR. Opioid Withdrawal. In: *StatPearls*. StatPearls Publishing; 2025. Accessed January 26, 2025. http://www.ncbi.nlm.nih.gov/books/NBK526012/
32. M P, Sm B, M H, T M. Corrigendum to "National record linkage study of mortality for a large cohort of opioid users ascertained by drug treatment or criminal justice sources in England, 2005-2009" [Drug Alcohol Depend. 146 (2015) 17-23]. *PubMed*. Published online 2015. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/28965977/
33. Rj V, Nd V. Untangling the complexity of opioid receptor function. *PubMed*. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/30250308/
34. Se N, Jk W, Ra L. Opioids and Chronic Pain: An Analytic Review of the Clinical Evidence. *PubMed*. Published online 2021. Accessed January 26, 2025. https://pubmed.ncbi.nlm.nih.gov/35295493/
35. Maia LO, Daldegan-Bueno D, Fischer B. Opioid use, regulation, and harms in Brazil: a comprehensive narrative overview of available data and indicators. *Subst Abuse Treat Prev Policy*. 2021;16(1):12. doi:10.1186/s13011-021-00348-z
36. Shulman M, Wai JM, Nunes EV. Buprenorphine Treatment for Opioid Use Disorder: An Overview. *CNS Drugs*. 2019;33(6):567-580. doi:10.1007/s40263-019-00637-z
37. A dual-receptor model of serotonergic psychedelics: therapeutic insights from simulated cortical dynamics | bioRxiv. Accessed January 26, 2025. https://www.biorxiv.org/content/10.1101/2024.04.12.589282v1
38. 3-Methoxy-Phencyclidine Induced Psychotic Disorder: A Literature Review and an 18F-FDG PET/CT Case Report. Accessed January 26, 2025. https://www.mdpi.com/1424-8247/17/4/452
39. Nawaz S, Althwanay AM, B EMAMC, et al. Therapeutics Uses of Psychedelics in patients with psychiatric disorders A Systematic Review. *J Int Med Grad*. 2024;1(1). doi:10.56570/jimgs.v1i1.155
40. New Psychoactive Substances (NPS), Psychedelic Experiences and Dissociation: Clinical and Clinical Pharmacological Issues | Current Addiction Reports. Accessed January 26, 2025. https://link.springer.com/article/10.1007/s40429-019-00249-z
41. Shafique H, Demers JC, Biesiada J, et al. (R)-(-)-Ketamine: The Promise of a Novel Treatment for Psychiatric and Neurological Disorders. *Int J Mol Sci*. 2024;25(12):6804. doi:10.3390/ijms25126804
42. Frontiers | Editorial: Perspectives on new fast-acting antidepressants. Accessed January 26, 2025. https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2024.1430990/full
43. Sedway JA, Opler MGA, Citrome L. Antidepressant medications have evolved in terms of speed of onset of efficacy: How can we best measure antidepressant treatment response? *Curr Med Res Opin*. 2024;40(4):701-703. doi:10.1080/03007995.2024.2323638
44. Liechti ME. Modern Clinical Research on LSD. *Neuropsychopharmacology*. 2017;42(11):2114-2127. doi:10.1038/npp.2017.86
45. Hallucinogen Persisting Perception Disorder: Etiology, Clinical Features, and Therapeutic Perspectives. Accessed January 26, 2025. https://www.mdpi.com/2076-3425/8/3/47
46. Sabé M, Sulstarova A, Glangetas A, et al. Reconsidering evidence for psychedelic-induced psychosis: an overview of reviews, a systematic review, and meta-analysis of human studies. *Mol Psychiatry*. Published online November 27, 2024:1-33. doi:10.1038/s41380-024-02800-5
47. Disorders due to Substance Use: Hallucinogens and MDMA-Related Substances | SpringerLink. Accessed January 27, 2025. https://link.springer.com/referenceworkentry/10.1007/978-3-030-42825-9_94-1
48. Costa G, Gołembiowska K. Neurotoxicity of MDMA: Main effects and mechanisms. *Exp Neurol*. 2022;347:113894. doi:10.1016/j.expneurol.2021.113894
49. Ketamine and phencyclidine: the good, the bad and the unexpected - Lodge - 2015 - British Journal of Pharmacology - Wiley Online Library. Accessed January 26, 2025. https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bph.13222
50. Spangler DC, Loyd CM, Skor EE. Dextromethorphan: a case study on addressing abuse of a safe and effective drug. *Subst Abuse Treat Prev Policy*. 2016;11(1):22. doi:10.1186/s13011-016-0067-0
51. PCP and Ketamine Toxicity Treatment & Management: Medical Care, Consultations, Long-Term Monitoring. Published online January 30, 2024. Accessed January 28, 2025. https://emedicine.medscape.com/article/1010821-treatment
52. LSD Toxicity Medication: Benzodiazepines, Antihypertensives. Accessed January 26, 2025. https://emedicine.medscape.com/article/1011615-medication?form=login&anfErr=true&anfErrHint=true&client=205502&urlCache=aHR0cHM6Ly9lbWVkaWNpbmUubWVkc2NhcGUuY29tL2FydGljbGUvMTAxMTYxNS1tZWRpY2F0aW9uIzM_Zm9ybT1mcGYmc2NvZGU9bXNwJnN0PWZwZiZzb2NpYWxTaXRlPWZhY2Vib29r&reg=1