Synthesizing Evidence: Exploring the Impact of Psychoactive Drugs on Cognitive Health in Adolescents and Adults

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The aim of the paper is to touch on the vulnerability of the adolescent brain compared to adults, and investigate the long-term consequences of prolonged substance use, specifically focusing on cannabis, LSD, and opioids. The paper looks at the central nervous system's interaction with psychoactive drugs and their potential to alter brain activity, leading to changes in perception, consciousness, and mental processing. Examining the interaction and impact is a central theme of this review. . In order to provide a comprehensive understanding of the subject, we delve into the historical context of these three prominent psychoactive substances, highlighting their significant cultural usage throughout history. This review then delves into the neurobiological mechanisms of psychoactive drugs, with particular focus on neurotransmission and importance of durational use. To enhance transparency of analysis, the paper is written through extensive review of existing literature, citing specific studies and articles that contribute to the understanding of this complex topic. A multitude of studies reviewed contain both animal and human subjects encompassing better understanding. Relevant and accurate data done on a large scale population is provided in some studies as well to contribute to accuracy. An emphasis is put on the relevance of psychoactive drug use among adolescents, whose brain development makes them more prone to experimentation and addiction.The specific effects of cannabis, LSD and opioids are discussed, highlighting the significance of THC and CBD in cannabis, LSD's influence on serotonin transmissions, and opioids' powerful effects of pain relief and addiction. The main findings suggested opioids as the most dangerous class of drugs limiting its usage in the medical field. While cannabis and LSD can have potential medical and therapeutic usage, but given the current societal standpoint of substance use in general, the potential is outshined by various legal factors.

Introduction

The intriguing and ever-evolving use of psychoactive drugs and their effects in adolescents and adults has captivated researchers across the ages. Whether steeped in cultural rituals, harnessed for medicinal purposes or sought after recreationally. This exploration transcends beyond modern understanding, reflecting societal curiosity[1]. For adolescents, curiosity and social influence plays a significant role in contributing to their initial interaction with psychoactive drugs, but they are far more vulnerable than adults to these effects due to the ongoing development of their brain[2]. On the other hand, adults are less vulnerable to the damage of psychoactive drugs although still susceptible depending on frequency of usage and potency of a drug.

Regardless of age, psychoactive drugs interact with the cells of the nervous system, leading to various effects involving alterations in perception, consciousness and overall mental processing[3]. The nervous system is categorized into the central nervous system (CNS) and peripheral nervous system (PNS). The CNS is made up of the brain and the spinal cord, think of it as the control center of the body, where essential functions like thinking, decision-making, and sensory processing take place. Meanwhile, the PNS is made up of the rest of the nerves in the body[4].

Within the PNS there are two main divisions, the autonomic nervous system and the somatic nervous system. The automatic nervous system regulates involuntary functions of the body such as breathing, heart rate and temperature. The autonomic nervous system can also be divided into two distinct systems: the parasympathetic and sympathetic nervous system. The balance between the sympathetic and parasympathetic is crucial for the human body to maintain homeostasis which psychoactive drugs influence and disturb[5]. The sympathetic nervous system is the network of working nerves that induce the fight-or-flight response when in a situation of danger or emotional distress. The parasympathetic is the balance to the sympathetic responses, regulating the body to return to equilibrium after an event of distress or danger. The second main division is the somatic nervous system; it is for voluntary functions such as movement or the processing of sensory information which can include conscious movement of parts of the body.

Though the peripheral and central systems are commonly influenced by the use of psychoactive drugs, the main focus of this review is the effects on the central nervous system (CNS),

which can be attributed to cognitive functions. With that in mind, this review will include an analysis of the mechanisms by which these drugs interact with neurons, neurotransmitter systems, and the entirety of the brain.

Neurons are cells that make up the nervous system and are also the basic building blocks of the brain. Neurons have a unique structure that allows the processing and translation of signals received from outside the body. Neurons have dendrites to receive signals, a cell body to process, and an axon for transmitting signals to other neurons. This intricate mechanism is often involved in the effects of drugs on the brain as they are responsible for transmitting signals in a process known as neurotransmission[4]. Neurotransmission is a vital part of brain functioning and involves communication between neurons and is assisted by neurotransmitters, chemical messengers. Neurotransmission is simply the way information gets passed onto the brain. All the signals and environmental stimuli received from the body or by the brain is what enables neurotransmitters to carry and perform synaptic transmissions. Synaptic transmission happens when an electrical signal, known as action potential, reaches the end of a neuron (presynaptic neuron). That electrical signal then produces a reaction which will release chemical messengers called neurotransmitters into the synapse, a small gap between presynaptic neurons and the next neuron (postsynaptic)[6]. Dopamine and the serotonin are neurotransmitters which both are involved when drugs are in the euphoric effect when in the body system. The neuron receiving this signal has receptor sites ready to bind with the neurotransmitters. Neurotransmitters can be either excitatory; likely to cause another action potential, allowing the receiving neuron to fire and transmit this signal to another, or inhibitory; less likely to cause an action potential.

Drugs can be agonists or antagonists which are both important in the idea of neurotransmission. Agonists induce a mincing effect from the taken substance that replicates the effects of neurotransmitters which in turn enhances the overall activity[6]. Once an agonist drug is taken, it enters the synapse it binds and activates the postsynaptic receptor sites. For example, opioids are a class of drug that enhance the natural neurotransmitters produced in the body known as endogenous opioids causing a sense of pain relief and euphoria. On the other hand, antagonist drugs bind to receptor sites without activating them, which blocks the reception of neurotransmitters and inhibits neurotransmission. An example of antagonist drugs are antipsychotic medications, which act on dopamine receptors therefore reducing symptoms of psychosis[6].

Currently the use of psychoactive drugs is more relevant within adolescence, ages 10 through 19. Studies have shown the vulnerability of the adolescent brain as it is still in an ongoing development due to changes happening within the structure and function of regions of the brain. The regions responsible for decision-making contribute to risks of drug experimentation which therefore makes them more prone to drug usage. Addiction may develop and could have negative effects from both a neurological and societal standpoint in the long run[2].

Cannabis is a psychoactive drug, derived from a cannabis plant. This plant has been used for various reasons including medicinal, recreational and cultural uses. Cannabis is commonly ingested or smoked for its effects of euphoria and relaxation. It contains compounds such as delta-9-tetrahydrocannabinol (THC) and cannabinol (CBD) which acts on the brain resulting in a euphoric and relaxing feeling. THC is the main compound that pertains to the psychoactive effects[7]. CBD is found to have more medicinal properties. Different strains' of cannabis means the different concentrations of THC compared to CBD. The different types of cannabis are sativa plants, which have high levels of THC and indica plants that have higher levels of CBD. While having many uses throughout the course of human history, cannabis is now used recreationally for its sensory altering effects. It is most commonly categorized as a hallucinogen.. Although vastly used in Canada and the US, it is still categorized as a Schedule 1 drug making this drug incredibly difficult to research within labs as it is prohibited[8].

LSD, more formally known as Lysergic Acid Diethylamide is a hallucinogenic substance belonging to the class known as psychedelics. Having been developed in a lab in the 1930s, it gained its popularity through recreational usage in the late 1960s, becoming common among hippies, an activist group fighting for peace. This drug is known for its powerful and potent effects on perception, emotion, and cognitions[9]. It influences the serotonin transmissions in the brain greatly, increasing levels of serotonin released, resulting in effects of distortions in sensory and auditory perception. Though level of effects may vary between individuals, common visual changes may include synesthesia which is a "mixing of senses" that brings several sensory inputs into an automated pathway in another sensory path. One can have heightened senses to different pitches of sound, or even vivid hallucinations. This makes LSD very intense even after the effects subside. One may still experience heightened psychological effects in emotion, mindset, and environment[8].

Opioids, a class of drugs considered extremely dangerous due to its addictive side effects, were initially prescribed for their medicinal use as painkillers[10]. They are categorized into three groups: natural opioids like morphine and codeine, semi-synthetic opioids including oxycodone and heroin, and fully synthetic opioids such as fentanyl and methadone, which are exceptionally potent[11,12]. The use of this drug was so common that it was sold over the counter in every grocery store in the US in the 19th century[13]. The pain killing effects of this drug are due to the binding with the opioid receptors in the brain and other parts of the body that allows for reducing perception of pain. However, their high potential for misuse has

led to addiction issues, as evidenced by recent Fentanyl overdose outbreaks in the US and Canada[14,15].

All substances affect brain connectivity, mental health, and cognitive function, but the focus of this review is on cannabis, LSD, and opioids. Brain connectivity refers to patterns of communication and connections between different regions of the brain, it involves the functional and structural functions formed by the networks of neurons[16]. Brain connectivity, cognitive functions, emotions and mental health all stem from the understanding of the connections in different regions of the brain. Cognitive function is defined as mental processing and the abilities that enable perception, understanding, communication, thinking and remembering[17]. These functions rely on complex neural networks across different brain regions that work together to process and produce a reaction or behavior to sensory information known as environmental stimuli. Psychoactive drugs notably affect attention, concentration, memory, perception and sensory processing[18–20]. These effects can be attributed to specific brain regions within the forebrain, midbrain, and hindbrain. The forebrain, renowned for its complexity, houses critical structures for advanced cognitive functions, including the cerebral cortex, responsible for language processing, problem-solving, and decision-making. Meanwhile, the midbrain handles sensory input and basic coordinated movements, and the hindbrain governs vital functions such as respiration and coordination. Particular areas of the forebrain such as the amygdala are often involved in emotional processing that are coordinated with mental health.

Mental health encompasses a complex interplay of emotions, thoughts, feelings, behaviors, and coping abilities. It has a multidimensional concept that varies across individuals and should be regarded as a spectrum. Similar to physical health, mental health requires care and maintenance, and this is where theprevalent use of psychoactive drugs comes in. The relationship between drugs and mental health is complicated, as many studies suggest drug use can induce co-occuring mental health disorders as well as worsen pre-existing ones[21]. Not only that, but substance abuse and addiction can become a mental health problem as well[22]. Psychoactive drugs can often impact cognitive functioning, therefore increasing the risk of worsening or developing mental disorders such as anxiety and depression. Studies also show the possible use of these drugs for therapeutic reasons in the future. Therefore, while these drugs may have negative side effects on the brain in general, being able to use their effects by correcting or limiting dosage for beneficial uses such as medicinal or therapy can be helpful.

This comprehensive review aims to understand the effects of three commonly used psychoactive drugs, namely LSD, cannabis, and opioids, on cognitive function, mental health, and brain connectivity in both adolescents and adults. The study explores the neurobiological changes associated with chronic drug usage and their potential impact on cognitive abilities through analyzing existing research and findings. To summarize, the aim of this paper is to unravel the complexities of how these substances can potentially reshape cognitive abilities by synthesizing these findings. This knowledge will serve as a critical tool in addressing the concerns surrounding the misuse of these drugs and serve as a foundation for effective strategies against misuse.

Introducing Categories of Psychoactive Drugs

The use of these psychoactive drugs has varying purposes and with the growing efforts of research, more information on these cognitive effects is surfacing as a result. There are different types of psychoactive drugs, which can be categorized into stimulants, depressants, hallucinogens, and opioids:

- Stimulants are a class of drugs that have an activating effect on the central nervous system as it increases brain activity through boosting exhibitors' neurotransmitters. These drugs enhances an individual's alertness, focus and energy. Examples of stimulant drugs include cocaine, amphetamine, and caffeine, which all work by increasing exhibitor neurotransmitters such as dopamine, serotonin, and norepinephrine through reuptake; a process where the neuron which released the neurotransmitters takes back the released chemicals[23].

- Depressants are a class of drugs that slow down the central nervous system instead of stimulating it. They decrease brain and neural activity which usually involves the feeling of sedation, relaxation and a general slowing effect of bodily functions, such as slowed breathing. Examples of depressants include alcohol and barbiturates. Alcohol acts on our brain processing, slowing our reactions while producing a sense of euphoria. Barbiturates induce mild euphoria along with fatigue and calmness[6].

- Hallucinogen are a class of drugs, also referred to as psychedelics, focus more on causing changes in perception of reality rather than on slowing or stimulating the body. These drugs cause sensory distortions experienced through visual, auditory, and tactile senses[6]. Common forms of hallucinogens include LSD, Peyote, psilocybin and cannabis. Effects of these drugs can persist in the human body for weeks, and if an individual ingests a hallucinogen again in the same period the last dosage was taken, even if a lower dosage, it can create more profound and dangerous effects, commonly known as reverse tolerance[24].

- Opioids or opiates are a class of drugs that are commonly categorized as powerful painkillers and mood elevators

that act as agonists for endorphins, a group of neurotransmitters related to pleasure and feelings of euphoria. With that being said, opioids are very physically addictive as they rapidly react, changing brain chemistry and creating tolerance and withdrawal symptoms[6,25].

Effects of Cannabis

Effects of Cannabis on Cognitive Function

Cannabis is known to have significant effects on both adults and adolescents, but the impact on cognitive function varies based the frequency of use, duration, and age of initiation. Smoking cannabis allows almost instant release of THC into blood streams, giving an immediate psychoactive effect that can last up to several hours. In the duration of intoxication, the chemical compound interacts with the brain's endocannabinoid system, specifically CB1 and CB2 receptors. THC, the main psychoactive compound in cannabis, binds with the CB1 receptors activating it leading to effects of euphoria, perception changes and mood swings. Furthermore the effects of cannabis can suppress glutamate and GABA, both major exhibitory and inhibitory neurotransmitters from the presynaptic neuron's terminal[7]. Adults who use cannabis recreationally are more frequently linked to disturbance in executive functions which are higher-order cognitive processes[18]. This pertains to areas responsible for attention. Different forms of attention such as the ability to sustain attention on a certain task, is proved to be more challenging. Other areas of attention like the ability to divide attention, meaning paying attention to multiple things simultaneously are also impaired as well as selective attention[18]. During the onset of effects, delays in executive function of working memory are present. The ability to store and recall information is delayed[18]. Though this delayed relaying of memories only persists during stages of intoxication, research does suggest the impact of cannabis use can extend beyond periods of intoxication, especially with chronic and heavy use[26]. Decision-making and risk taking are also influenced by cannabis use. In decision-making, subjects who received THC were shown to make the less likely correct decision compared to a placebo group[27]. It is important to note that all test subjects were consistently used as demonstration for the deficits in cognitive functions in all studies shown above. The findings collectively outline the potential acute and adverse effects of cannabis on cognition. For adolescents, the brain is undergoing critical development and studies have shown that early and regular use of cannabis in adolescents can lead to alterations in brain regions involved in memory, learning and control[28,29]. All acute effects still apply to those of adolescents, but the recovery of deficits may be prolonged compared to adults. It is important to note even with the absence of cannabis, in some cases of heavy chronic use, deficits may continue to persist even after extended absence of cannabis[30].

Effects of Cannabis on Mental Health

With frequent usage of cannabis, psychiatric disorders become correlated with the recreational use of cannabis, especially in adolescents and young adults[33]. Research shows that adolescent cannabis users are more likely to develop severe cannabis use disorder (CUD), leading to increased levels of depression, anxiety, and psychotic-like symptoms[31]. Notably, despite shorter usage duration, adolescents exhibit a greater likelihood of severe CUD than adults.. The study concludes cannabis-induced mental health problems may not be a greater risk to adolescents implying that they may not be as vulnerable to cannabis risks as depicted, but risks of severe CUD are greater compared to adults. Another article discussed the genetic factor that plays into cannabis related psychotic disorders such as schizophrenia. The study indicated that cannabis use can increase an earlier onset of schizophrenia if that disorder was prevalent in the family history. As well as with extreme high doses of cannabis, a temporary psychotic episode can occur in some individuals, which may lead to future development of a psychotic disorder[32]. In conclusion, the link between depression and cannabis remains unclear and necessitates further investigation, it is crucial to recognize that genetic predisposition plays a significant role in these disorders, with cannabis usage potentially exacerbating symptoms of anxiety and depression[32].

There are studies that show potential therapeutic applications of cannabis in conditions of multiple sclerosis, in cancer chemotherapy, and certain sleep disorders (National Academies Press (US), 2017)[34]. In multiple sclerosis, findings appear to be moderate in the sense that there are some benefits towards orally ingesting THC. Still, studies currently lack evidence to fully conclude the use of cannabis for treatment of spasticity is effective. In the treatment of cancer, a large-scale of studies show no evidence of the efficiency of cannabinoids as a remedy due to insufficient evidence. However, symptoms such as nausea and vomiting experienced from chemotherapy show trials of studies has proven orally ingested THC to be an effective treatment (National Academies Press (US), 2017)[34]. A systematic review found a slight correlation of cannabinoids being able to improve short-term sleep in patients who suffer from sleep disturbances. It is important to note that no clinical trials were conducted in this review on effectiveness of cannabis in sleep disorders therefore limiting the evidence for the therapeutic use of cannabis (National Academies Press (US), 2017)[34]. A multitude of studies that dive into specifics of how to utilize cannabis in therapy settings are needed, and more clinical trials should also be considered due to the lack of evidence provided by those that do

Table 1 A summary of Cannabis on Cognitive Function

Aspects of Cognitive Functions	Impact of Cannabis (General)
Endocannabinoid System	Interaction with CB1 and CB2 receptors
Decision-Making and Risk Taking	Impaired decision-making
Attention	Impaired attention, including sustaining, dividing, and selective attention
Working Memory	Delayed during onset of effects
Executive Functions	Disturbance in higher-order cognitive processes [18]

Table 2 Summary of Cannabis on Mental Health

Aspects of Mental Health	Impact of Cannabis (General)
Cannabis Use Disorder (CUD)	Recreational users may develop CUD, where CUD plays into a of other health risks [31]
Depression	Development of CUD leads to increased depression levels [32]
Anxiety	Cannabis use may lead to increased anxiety levels [32]
Psychotic Symptoms	Cannabis use may induce psychotic-like symptoms in some users [32]

Note: Adolescents using cannabis are more likely to develop severe CUD

not have clinical proof. To address these challenges, future research should focus on longitudinal studies that take place in multiple periods which allows for check-ups and analysis of the effects of using cannabis in therapy. genetic factors, and conduct controlled clinical trials for therapeutic applications. Understanding the risks and benefits of cannabis use is essential for informed decision-making and policy considerations.

Effects of Cannabis on Brain Connectivity

Studies investigating chronic cannabis use consistently report structural changes and disrupted neural pathways [35,36]. The long-term use of cannabis is linked to alterations in the gray matter volume. Gray matter is a dark tissue containing neuronal cells that makes up 40% of your brain. They are important in high-order processing and are usually affected by change to core reward structures such as the nucleus accumbens [37]. Scans of young adult cannabis users are found to have a volume decrease in specific brain regions (e.g., medial temporal cortex) while having an increase in three clusters in the cerebellum. A study concluded the age of initial use of cannabis was correlated to alternations of gray matter volume in different areas [36].

Disrupted neural pathways are shown to affect the brain tissue known as white matter, a tissue which lies beneath the gray matter making up 60% of the brain with neuronal cells that are myelinated. They connect neurons between regions of the brain which make them a high-speed circuit [38]. When chronic use of cannabis is involved, the neural pathways are disturbed and no longer carry out processing as fast as before affecting the integrity of white matter [39]. There is a reduction of white matter observed in areas of the corpus callosum, fornix, and other tracts which white matter extends till. Heavy emphasis was put on the age of cannabis usage, usually correlating younger age with a more significant impact on brain connectivity.

In summary, cannabis use can have significant cognitive effects on both adults and adolescents, impacting attention, memory, decision-making, and increasing the risk of psychiatric disorders. All studies conclude and emphasize the correlation of age and change in the structure of white matter and gray matter. Chronic use of cannabis, especially in early stages of life, can lead to significant change and damage in brain connectivity and slowing down neural transmission. While some therapeutic potential exists for conditions like multiple sclerosis and chemotherapy-induced symptoms, more research is needed to confirm these benefits (National Academies Press (US), 2017) [34]. Chronic cannabis use is associated with structural brain changes, especially in those who start using at a young age. The age of use reflects upon the ethical concerns of some studies done on adolescents. No studies should be allowed to use adolescent subjects for testing where application of intaking drugs is pursued. This remains an un-

ethical barrier as it undervalues the health of the individual. It is worthy to mention the high risks in acute use as well, though not considered highly addictive, with environmental influence, acute use of cannabis can become prolonged therefore creating severe impacts[31]. It is best to avoid adolescence testing overall unless it is data sampled from the population.

Effects of LSD

Effects of LSD on Cognitive Function

Lysergic acid diethylamide (LSD) is a psychedelic typically ingested orally through tablets. LSD works by binding to subtypes of serotonin receptors, as 5-HT2A receptors agonists, which increases the release of serotonin along with other neurotransmitters like dopamine and norepinephrine which are thought to be responsible for the drugs ability to effect mood, cognition and perception[40,43].

The use of this perception altering drug has increased in the adolescent population which is concerning[44].The reuse of this drug is rarely associated with addiction or abuse due to its extreme effects[45]. It is still important to note that tolerance develops fairly quickly in adolescents and young adults leading to risks of serious adverse effects[46]. Referring back to the activation of the 5-HT2A receptors, a dreamlike effect is produced, as shown in a study[41]. A state they described as cognitive bizarreness increased giving a dream-like imagery to subjects of the test after exposure to LSD. This study clearly highlights the profound impact LSD has on perception and cognitive processing through describing the heavy imagery experienced by users of LSD. Another study, meanwhile, demonstrated the more common acute effects such as visual hallucinations, audiovisual synesthesia, derealization and depersonalization came without severe adverse effects[47]. Regarding the effect that LSD has on the 5-HT2A receptors system, executive cognitive functions such as working memory is impaired, but decision-making and risk-taking remained unaffected[19]. Another study using healthy volunteers, indicated that even with different dosages of LSD, some cognition and physiological aspects were unaffected[48]. These findings underscore the selective and complex nature of LSD's effects on cognitive function. Other evidence concludes that change in the 5-HT2A receptors system can impair concentration and attention, including visual sustained attention and attention tracking[42]. This drug appears to have specific impacts on certain aspects of cognition while leaving others unaffected. It is also noteworthy to mention that subjective responses to LSD further contributes to the complexity of understanding of LSD's impact on not only cognition but other topics such as mental health.

Effects of LSD on Mental Health

Psychedelics, including LSD, are categorized as classic serotonergic hallucinogens that primarily affect 5-HT2A receptors, showing a multifaceted impact on mental health. Some studies suggest the benefits of using psychedelic substances, such as LSD as potential therapeutic for conditions like depression, anxiety, and addiction while other studies warn of the adverse effects of using such substances[22]. So though some studies suggest that there is no correlation of developing mental health issues from the use of LSD or other psychedelics[44]. Other studies have identified potential risks, such as the misuse or overuse of LSD leading to the development of psychiatric disorders from the adverse effects suffered[53]. The development of psychiatric disorders after the use of psychedelics is known as hallucinogen use disorder in the DSM-5[53]. Adverse effects can include what is known as a "bad trip" which can cause acute psychological harm and distress. Having a bad trip often leads to anxiety, panic, feeling of insanity, and given the severity of the trip, long-term psychological consequences[49]. The frequent anxiety experienced during intoxication is due to the glutamate hypofrontality but long-term reduction in anxiety is due to the HT-52A receptors[54]. Of course, it should be noted that the environment and personal life is crucial in determining the severity of the psychological effects of a bad trip experienced by an individual. There are other potential effects which can persist even after the initial use of LSD such as hallucinogen persisting perceptual disorder (HPPD) which is a form of flashback to the visual distortions one experiences during intoxication. This can happen weeks or months after the initial use. Though this is of low prevalence according to data it should be kept in mind the mental toll it takes on the user[51,55].

As mentioned before, there are potential therapeutic uses of LSD in treatment of different disorders. A study done in a controlled setting suggests they can induce psychosis-like symptoms while improving long-term psychological well-being by loosening cognition and helping users express emotions[52]. This relates to the earlier use of LSD in old psychiatric practices where patients and therapists were given doses of LSD to help patients break down their repressed emotions. Studies tested on rodents came to the conclusion that psychedelics are able to produce antidepressant-like changes, which includes enhancement of associative learning, a cognitive function which is often impaired by psychiatric disorders, like some forms of depression[56]. Unfortunately it was reported as not a reliable source of medication due to the extended time it took to see results of antidepressant properties produced. The antidepressant property produced is brought up in another study conducted on human volunteers which reported the ability of LSD in improving mood and cognition in individuals with symptoms of depression[48]. A more recent study

Table 3 Summary of LSD on Cognitive Functions

Aspects of Cognitive Function	Impact of LSD (General)
Mood	LSD affects mood and perception through serotonin receptor activation[40]
Visual perception	May induce dream-like imagery and cognitive bizarreness[41]
Working memory	Impairs working memory, affecting the ability to hold temporary information[19]
Decision-Making	Decision-making and risk-taking remain largely unaffected[19]
Concentration and Attention	LSD impairs concentration and attention, including visual sustained attention and attention tracking[42]

Table 4 Summary of LSD on Mental Health

Aspects of Mental Health	Impact of LSD (General)
Depression	LSD has shown potential in improving mood and alleviating symptoms of depression[48]
Anxiety	LSD use can lead to anxiety, panic, and feelings of insanity, often associated with "bad trips"[49]
Addiction	LSD demonstrated potential in the treatment of addictive disorders, including nicotine and alcohol dependencies[50]
Hallucinogen Persisting Perceptual Disorder (HPPD)	HPPD is characterized by flashbacks to visual distortions experienced during intoxication[51]
Psychosis-like Symptoms	LSD can induce psychosis-like symptoms, but these are often transient and are followed by long-term improvements in psychological well-being[52]

suggests the reason for this antidepressant property was the effects on specific networks of the brain which are altered[57]. However, results from human studies also took time to manifest. Other disorders such as obsessive-compulsive disorders (OCD) were also looked into, along with post-traumatic stress disorders (PTSD)[58].

Studies found that addictive disorders were also proven to have noticeable outcomes when treated with doses of LSD or psilocybin, specifically nicotine and alcohol dependencies[50]. A study experimented with the use of LSD in treatment of alcoholism and found a reduced exhibition of alcohol misuse in patients who were given a dosage of LSD[59]. This outcome should be noted as initially one of the first successful trials as there have been issues like poly-drug use in conducting similar experiments in the past, allowing careful consideration of LSD's complicating and unpredictable side. Studies on the effects of psychedelics, including LSD, will often face ethical challenges especially when adolescents are involved. This limits the research available on the impact of LSD on brains of adolescents as many of the tests and studies are done on adults, but even then, with human participants, the ethical challenges of testing such a dangerous drug stands as a barrier. There should be full transparency and support given to participants of studies.

Effects of LSD on Brain Connectivity

There are several studies which state that LSD usage can alter brain connectivity as well as disrupt brain structure[60–62].

Increased connectivity was shown in the thalamus to the posterior cingulate cortex followed by a noticeable decrease in connectivity to the temporal cortex as shown by a study which used neuroimaging[63]. According to another study, the functional connectivity within the default mode network (DMN) was reduced while other networks of the brain were not. This tends to be linked to the altered states in consciousness and a connection between the therapeutic outcomes of LSD[64]. The visual, sensorimotor and auditory networks were also decreased with acute LSD administration as shown in another study[61].

It also should be mentioned that the therapeutic effects can be a result of both altered consciousness and the brain connectivity, but of course, it is important to realize the multifaceted factors which are not yet understood. It can be concluded that specific connections are strengthened while the decrease in connectivity of other regions are concurrent. Though this may seem somewhat negative, the use of LSD as a potential analgesic for chronic pain, a complex process of changes in neural circuitry overtime due to signals of pain. Psychedelics have an effect on the serotonin 2A receptors, they in a way "reset" the functional connectivity of the brain. This relieves conditions of chronic pain, but because clinical evidence is limited, the study can only show the potential treatment for conditions like cancer pain, phantom limb pain and cluster headaches[65].

In conclusion, the complexity of this drug comes from the highly interconnected networks of the brain; psychedelics induce a wide range of effects on neurotransmitters, as well as individual brain functions, genetics and psychological factors which further complicates the process of understanding every effect of LSD on the brain. Rapid tolerance development poses risks of adverse effects. LSD induces dream-like experiences, visual hallucinations, and alters working memory, attention, and perception. Its impact on mental health is complex, with some studies suggesting therapeutic potential, while others highlight adverse effects like "bad trips" and hallucinogen persisting perceptual disorder (HPPD). LSD is being investigated for treating psychiatric disorders like depression and addiction, but challenges include the time to see results and potential adverse reactions. More research is needed for better understanding of the underlying factors in use and effect of psychedelics, but due to an ethical dilemma, testing done on humans clinically can be adverse as the side effects of LSD are profound, and should be carefully conducted[60]. Adequate psychological and emotional support should be provided during and after LSD sessions when done with human participants. If such effects and extents to provide support are needed just for adult participants, the risk for adolescents are far more dangerous.

Effects of Opioids

Effects of Opioids on Cognitive Function

Opioids are some of the most dangerous drugs as they significantly impact the brain's reward system, activating certain receptors which leads to an increase in dopamine that produces an intense feeling of euphoria and relaxation. The brain will see this as a positive reinforcement[67]. Positive reinforcement is a behavioral concept involved in encouraging certain behaviors by linking them with positive outcomes, making the use of opioids highly addictive as it provides immediate pleasure.

The system of rewards involved in this stimulating feeling is from three types of receptors: mu, delta and kappa which are usually activated by naturally occurring opioids known as endogenous opioids[68]. The opioid receptors are primarily located in the cortex, limbic system, and brain stem which contributes to their addictive properties given that these areas are crucial in functions of reward processing, emotional regulation and pain perception[68]. Currently opioid misuse is not common in adolescents, the associated mortality from overdoses is concerning.. Adolescents are exposed to opioids commonly through prescription drugs, increasing the risk of future misuse[69–71].

The chronic use of opioids can lead to cognitive impairments, affecting memory, attention, and decision-making[66]. Opioids can cause drowsiness and sedation which can interfere with cognitive functioning, leading to difficulties in concentration and problem-solving especially when used frequently. These impairments can have a significant impact on an individual's life, academics, work performance, and overall health. People who use this substance chronically are found to experience challenges in working memory, and attention span. Interestingly the same study found that cognitive function may improve in individuals using opioids for chronic non-cancer pain without misuse, suggesting that cognitive differences may be influenced by factors beyond opioid use[66]. Another study resulted in similar outcomes through using patients with opium use disorder (OUD) and healthy controls (HCs) to find effects of OUD on attention, working memory and information-processing speed due to neurological changes[20]. This study, unlike previous ones, was strictly based on pure opium users with no poly-drug usage which was a factor other studies had not accounted for, concluding that this study may have the most accurate results even with some limiting factors. In conclusion, chronic opioid use has been associated with impairments in cognitive abilities and understanding the effects can be crucial for intervention of the misuse of opioids. Further research may still be needed to explore the complexity of opioids and their effects on the human brain, the studies already done on human participants should be carefully arranged with just strictly opioid users as done before to

Table 5 Summary of Opioids on Cognitive Function

Aspects of Cognitive Function	Impacts of Opioids (General)
Memory	Impaired memory, affecting their ability to retain and recall information
Attention	Disrupted attention span, making it challenging for them to concentrate on tasks or stimuli
Working Memory	Impaired working memory, responsible for holding and manipulating temporary information
Information Processing Speed	Reduction in information processing speed, causing delays in cognitive tasks that require quick thinking and decision-making
Cognitive Improvement	Using opioids for chronic non-cancer pain without misuse may experience improvements in certain cognitive functions[66]

ensure accuracy in results.

Effects of Opioids on Mental Health

Mental health tends to be affected as a result of the different neurological changes that happen with the frequent usage of opioids[20]. Opioid misuse, known as opioid use disorder (OUD), is found to be linked with neuropsychiatric symptoms like depression and anxiety[72,73]. Though this drug provides temporary relief from physical and emotional pain, they can lead to long-term negative effects on mental well-being. Opioids can be so addicting due to the fact that they disrupts the brain's reward system, leading to heightened risk of psychiatric conditions[68]. Depression appears to be a common symptom of both prescribed and in the misuse of opioids, often accompanied by lethargy, mental slowness, and apathy[72]. It should be noted, patients who use opioids as a form of coping for negative emotions are trapped in a cycle of opioid use due to the strong dependency that quickly develops[67]. While suicide by overdose is associated with opioids, the relationship between direct opioid use and suicide is complex and influenced by other factors as concluded in studies[74]. Another finding is that depression and opioid use have a bi-directional relationship, as chronic-pain induced can also involve the usage of opioids[75].

Mental health can be severely impacted by opioid use especially in adolescents who have a higher chance of misuse, which is found to be due to prescription opioids[76]. The study mentions the multiple occasions where adolescents tend to combine drugs such as opioids with alcohol and cannabis which can be potentially dangerous. The findings also emphasized the common use of specific prescription opioids which included hydrocodone, codeine, and oxycodone among adolescents of prescription opioid use (POU) and nonmedical prescription opioid use (NMPOU). It is clear the misuse of this drug can lead to damages in the long-term and prevention of-POU developing into NMPOU is needed[70,76]. The overall understanding of prescription patterns and uses in both adults and adolescents can act as a vital guide to prevention of the potential long-term harm opioids can have.

Effects of Opioids on Brain Connectivity

Opioids have a significant impact on brain connectivity, altering communication and functioning of various brain regions. Many of the problems associated with OUD are linked to neurological changes in the central nervous system (CNS), the alterations can range from anatomical changes on white and grey matter in specific brain regions, to changes in neurotransmission involving dopamine[20,77]. The changes in grey and white matter refer to changes in volume or density of it in different brain regions such as the frontal and temporal regions. It is important to note that these alterations are influenced by duration, amount of usage and individual differences.

With repeated opioid use, addiction-related neurological changes occur, primarily involving the mu-opioid receptors found in reward and pain sensory regions[68]. The prolonged use will lead to individuals becoming less responsive to natural rewards and more reliant on opioids. A separate study using magnetic resonance imaging (MRI) showed that the functioning connectivity of the insula, amygdala (specifically three subdivisions), and nucleus accumbens of the brain decreased in the opioid-dependent group[78]. The areas seen to have decreased in functioning connectivity are regions known to be involved in emotional regulation, reward processing, and decision-making, all which are affected by opioid use. There was no noticeable increase in functional connectivity observed in the opioid-dependent group which indicates a specific pattern that opioids have when in effect. Furthermore, the study dove into the duration of use. The longer an individual has

Table 6 Summary of Opioids on Mental Health

Aspects of Mental Health	Impacts of Opioids (General)
Depression	Common symptoms with lethargy, mental slowness, and apathy
Anxiety	Often linked with opioid misuse (OUD)
Risk of Psychiatric Conditions	Heightened risk of psychiatric conditions due to disruptions in the brain's reward system
Bi-Directional Relationship	Opioid use and depression can have a bi-directional relationship, as well as from (OUD)
Opioid use disorder (OUD)	Found to be linked with neuropsychiatric symptoms like depression and anxiety

been dependent on prescription opioids, the more pronounced the changes in connectivity of the specific brain regions[78]. It is clear opioids have significant evidence for their impact on brain connectivity and alterations in communication and functioning of brain regions is linked with the direct problems of OUD.

Opioids are highly addictive drugs, impacting the brain's reward system and triggering immediate feelings of euphoria. They activate opioid receptors primarily located in regions related to reward, emotions, and pain perception. While opioid misuse is not widespread among adolescents, the risk of overdose-related mortality, often linked to prescription opioids, is distressing. Chronic opioid use impairs cognitive function, particularly memory and attention, though some aspects may improve in individuals with chronic non-cancer pain. Opioid use also harms mental health, leading to depression and anxiety symptoms, creating a cycle of dependence. Acute use of opioids most often start with prescription medication, which makes any use of opioids, prolonged or not, extremely dangerous. Adolescents are vulnerable to opioid misuse, often involving prescription drugs, and combining opioids with other substances. Because opioids are considered one of the most dangerous drugs, it should be essential to keep limited experimental studies involving consumption of such substances among adults as this would cause long-term effects from just acute usage. No adolescents should be tested or used as participants in this sort of study, as it is proven unethical and extremely difficult to maintain and promise the health of an adolescent participant without risk of psychological and physical health issues.

Comparison and Synthesis

In our examination of the effects of psychoactive drugs on cognitive function, it is imperative to consider the research methodologies employed in the reviewed studies. These studies have employed diverse methodologies, including controlled experiments, longitudinal assessments, and neuroimaging techniques, to comprehensively assess the impact of cannabis, LSD, and opioids. For instance, studies investigating cannabis often employ cognitive tests, functional MRI scans, and neuropsychological assessments to evaluate its effects on executive functions, decision-making, and memory[18]. Similarly, research on LSD involves controlled experiments with human subjects, utilizing cognitive assessments and neuroimaging technologies to scrutinize its influence on perception and working memory[19]. Opioid-related studies encompass clinical evaluations, brain imaging, and psychometric assessments to gauge the extent of cognitive impairment and its impact on daily life[66]. Control groups have been used to establish comparative baselines and enhance the reliability of findings. However, it is essential to acknowledge variations in study designs, sample sizes, and methodologies, which may affect the generalizability of results.

Cognitive function

In adults, cannabis use is frequently linked to disturbances in executive functions, such as attention, concentration, and working memory[18]. Decision-making and risk-taking abilities are also influenced by cannabis[27]. For adolescents, early and regular cannabis use can lead to alterations in brain regions involved in memory and learning, with potential long-lasting deficits even after cessation of use[28,30]. LSD use has been associated with dream-like imagery and profound impacts on perception and cognitive processing[41]. Working memory is impaired by LSD, while other cognitive functions may remain unaffected[19]. Opioid use can impair cognitive abilities, including memory, attention, and decision-making, and these impairments can have significant impacts on daily life and overall health[66]. Cannabis, LSD, and opioids ex-

ert their effects on cognitive function through distinct mechanisms. Cannabis interacts with the endocannabinoid system, while LSD acts as a serotonin receptor agonist[18,19]. Opioids, on the other hand, modulate pain perception and induce feelings of euphoria through opioid receptors[66]. Despite different receptor systems, all three substances can affect dopamine release, contributing to their potential for addiction and reinforcing drug-seeking behavior.

The reviewed studies highlight the distinct and overlapping effects of cannabis, LSD, and opioids on cognitive function, mental health, and brain connectivity in both adolescents and adults. Cannabis use impacts executive functions, while LSD influences perception and cognitive processing. Opioids can impair memory, attention, and decision-making abilities. Understanding these effects is crucial for developing targeted interventions to address substance misuse and its potential long-term consequences on cognitive and mental well-being. Further research is needed to explore the complexities of these drugs and their effects on the human brain for more effective prevention and treatment strategies. Ethical considerations in studying the effects of LSD and psychedelics in adolescents merit attention. Research involving vulnerable populations like adolescents demands ethical ways of collecting and verifying data. Ensuring informed consent, safeguarding psychological well-being, and addressing potential risks and benefits remain general concerns in such research endeavors. Informed consent refers to clear, appropriate agreements on understanding of the study participants are in, by their legal guardians and themselves. The pathological well-being of adolescents should be prioritized ensuring no long-term damage. These ethical frameworks are vital in guiding the design and execution of studies involving these substances.

Mental health

The use of cannabis, LSD, and opioids can have significant effects on mental health. Cannabis use has been linked to disturbances in executive functions, attention, and working memory, which may contribute to cognitive impairments and potential risks for mental health issues, particularly in adolescents[18,28,29]. Adolescents who use cannabis may experience higher levels of depression, anxiety, and psychotic-like symptoms, indicating a potential association between cannabis use disorder and mental health problems[31]. Genetic factors also play a role in cannabis-related psychotic disorders, and extreme high doses of cannabis can induce temporary psychotic episodes, which may have implications for the development of mental health disorders[32]. LSD's impact on mental health is complex, as it has been associated with both short-term psychosis-like symptoms and potential long-term improvements in psychological well-being[52]. Studies have shown that psychedelics, including LSD, can produce antidepressant-like changes and enhance associative learning, which could have implications for treating certain mental health conditions like depression[48,56]. However, the use of LSD and psychedelics in research faces ethical challenges, limiting the extent of studies involving adolescents. Chronic opioid use can lead to mental health issues such as depression, anxiety, lethargy, and apathy, which are detrimental to an individual's overall well-being[72]. The strong dependency that quickly develops with opioid use traps individuals in a cycle of abuse, further exacerbating mental health problems[67]. Opioid misuse has been associated with neuropsychiatric symptoms, making it crucial to address the potential risks and long-term harm opioids can have on mental health[68].

The use of cannabis, LSD, and opioids can have varied effects on mental health, ranging from cognitive impairments to the development of mental health disorders. The complex interactions and potential risks associated with these substances necessitate further research and effective prevention and intervention strategies to safeguard mental well-being in both adolescents and adults.

Brain connectivity

The use of cannabis, LSD, and opioids can lead to significant alterations in brain connectivity and neural pathways, impacting cognitive functions and mental health. Chronic cannabis use has been associated with structural changes in both gray and white matter, affecting high-order cognitive processes and neural transmission[35,39]. The age of cannabis usage is a critical factor, with early and regular use in adolescents showing more pronounced changes in brain connectivity[29]. Similarly, LSD usage has been shown to disrupt brain connectivity, with changes observed in various brain networks, such as the thalamus and default mode network[60,63]. The therapeutic potential of LSD in treating chronic pain and other conditions is linked to its impact on serotonin 2A receptors and its ability to reset functional brain connectivity[65]. However, the complexity of the brain's interconnected networks and the various factors influencing the effects of psychedelics require further research for a comprehensive understanding. On the other hand, opioids have a profound impact on brain connectivity, leading to decreased functional connectivity in regions involved in emotional regulation, reward processing, and decision-making[78]. The prolonged use of opioids results in modifications in endogenous opioids and their receptors, leading to increased reliance on opioids and decreased responsiveness to natural rewards[68]. These changes in brain connectivity are directly linked to the problems associated with opioid use disorder (OUD). The duration of opioid dependence also plays a role in determining the severity of alterations in brain connectivity[78]. The evidence points to opioids' significant impact on brain communication and functioning, highlighting the need

for intervention and understanding the complexities of OUD and its effects on the human brain.

These substances can profoundly affect brain connectivity and neural pathways, leading to cognitive impairments and potential risks for mental health issues. The interplay of age, duration of use, individual differences, and various factors adds to the complexity of understanding the effects of these psychoactive drugs on the brain. More research is essential to fully comprehend the underlying mechanisms and potential therapeutic applications, as well as to develop effective preventive measures to safeguard brain health.

Discussion

The usage of psychoactive drugs has societal impacts that extend beyond just individual health. It is important to look at the issue from a point of view encompassing families, communities, and economies in being able to prevent the misuse of these substances. Substance abuse can lead to strain in relationships, disruption in families, and breakdowns in communication. For instance, a longitudinal study found an increase in intimate partner violence (IPV) after the usage of drugs like cannabis[79]. Another longitudinal study showed that adolescents and young adults who had usage of cannabis were often associated with later criminal charges, adding to the risk factors of cannabis[80]. Communities bear the burden of increased crime rates and a low workforce productivity rate both from substance related issues[81].The strain substances put on economies should also be mentioned. The costs encompass medical treatments, rehabilitation programs, and law enforcement. For instance, the opioid epidemic led to a rise in healthcare expenses, legal interventions, and a general strain on public resources and safety[82]. A study has proven the severity of heavy opioid users and their associations with crime which puts strain on the economy through legal interventions[83]. All highlighting the need for effective prevention and treatment strategies. A critical aspect is often overlooked in the cycle of abuse, which confines vulnerable individuals such as the homeless. Being trapped in a cycle of drug use, they seek solace in substance usage, often restricting their capability to seek help[84]. The prevailing approach due to the negative view rooted into societal depiction further complicates this situation. The current widespread approach to combating addiction involves law enforcement and over-policing, sidelining the root causes.

Many individuals share a distinctively negative view regarding the usage of drugs due to current laws and the history of drug use. It should be equally vital to get a balanced perspective that recognizes all the complexities surrounding substance use, not just the risks and challenges. The clinical use of drugs also deserves attention. There have been studies with major advancements in researching the potential medical and therapeutic uses of psychoactive drugs[34,58,72]. Some studies have shown promising results, for example cannabis has been used to alleviate chronic pain, and to mitigate the effects of chemotherapy[34]. Psychedelics, such as LSD, has demonstrated encouraging results in treating psychological health[56]. Exploring these therapeutic potentials with more research and understanding responsible use could help reshape the perception of these substances. While all psychoactive substances have potential risks, the degree of risk varies widely. For example, cannabis can be considered one of the least dangerous drugs as it shows the least amount of widespread changes from one use. Whereas LSD is shown to have drastically changed brain connectivity both decreasing and connecting regions of the brain[63]. Although LSD is proven to be useful for therapy due to its ability to stimulate brain connectivity, its use on the developing brain of adolescents can in turn induce symptoms of psychosis and more adverse effects, causing distress[47,52]. The most high risk drugs are opioids, which should not ever be in contact with adolescents as research has shown the probability of adolescents to use heavier doses of un-prescribed opioids after medicated exposure[70]. Opioids are in fact the most addictive drugs with harmful long-term consequences.

The usage of these drugs has ethical concerns as well. Due to their potential risks as mentioned, there comes the issue of whether using these drugs therapeutic or medically can consistently benefit the user, and if it is practical enough to be considered an application in therapeutic environments, as for example the study done on LSD showed potential change in depressive symptoms but the extended time it too to see results made it impractical[56]. So, using this drug could prove to have more downsides than just normal antidepressant medications, making it unethical to test on humans. This also goes for other drugs: the impracticality of long-term testing may affect the ethics of using such drugs if they cause more harm than they provide benefits. This should therefore be taken into consideration when making decisions on whether a drug requires further implementation in the medical field even after proven unreasonable for usage. As per example, opioids were used in the medical field for long period of time which resulted in the abuse of this drug in patients' lives, this is evident of the impractical side of opioid medication that should have been carefully considered[70].

Concerns and Limitations

An important consideration in studying effects of psychoactive drugs is the widespread phenomenon known as poly-drug use, where individuals consume multiple substances concurrently[85]. When an individual is under the influence of multiple drugs, it can make research outcomes difficult as isolating the specific effects of a single substance becomes more complex and harder to define with the similarities of effects some

drugs can have. In most studies with human participants, this factor is not accounted for, posing for confounding variables which undermine the validity of the study. In some studies the importance of accuracy in identifying participants who purely use one substance is briefly mentioned[59].

An ethical dilemma also plays a part in some studies involving human subjects. Though valuable insights are gained through the manipulation of drug use in controlled settings, such manipulations could potentially put subjects at risk of harm and raise concerns of informed consent, especially in the case of extremely addictive drugs such as opioids[68]. The use of drug testing on vulnerable populations is especially dangerous, and considered unethical due to the risk of health issues among the vulnerable which are considered; adolescents, pregnant women, and seniors. This is the main reason why some studies are based on raw data collected not from controlled settings but around the world in real time environments[48,71,76]. The ethics surrounding this limits studies to animal test subjects, such as rats, where researchers fall short on valuable information because animals do not have the same emotional, cognitive, and social dimensions as humans. Therefore, while animal studies provide exceptional data, they fail to capture the full range of human experiences and cognition associated with the effects of psychoactive drugs[56]. Potential solutions to this dilemma could be using predictive AI models, where the testing of heavy and dangerous drugs are not used on humans, but predicted by AI models[86]. This can provide an accurate representation of a human. This is a much more ethical way to test drugs that have adverse effects such as opioids.

Moreover, current societal rules and legal enforcements, including the classification of cannabis as a Schedule 1 drug, significantly hinder research efforts. This strict regulation limits its accessibility to cannabis within research laboratories, despite its widespread use in Canada and the US. These limitations not only affect this paper but also impact other literature reviews in the field. As a result, conclusive findings about the effects of these drugs are challenging to attain, highlighting the need for further research.

Conclusion

In conclusion, the exploration of the effects of psychoactive substances on cognitive function, mental health, and brain connectivity has provided valuable insight into a complex and multifaceted subject. Cannabis use, especially among adolescents, has raised concerns due to its potential to disrupt executive functions, attention, and working memory, contributing to cognitive impairments and mental health challenges. LSD, as a serotonin receptor agonist, presents a unique profile with its profound impact on brain connectivity and cognition. While showing promise in therapeutic contexts, the administration of the drug also carries the potential for adverse experiences, highlighting the need for careful investigation. Opioids significantly affect the brain's reward system, leading to addiction and cognitive impairments. Chronic opioid use can result in changes in brain connectivity, worsening issues associated with opioid use disorder. Furthermore, the information presented in this comprehensive review can help shape evidence-based public health policies, especially in safeguarding vulnerable populations. It calls for policies that prioritize harm reduction, access to treatment, and public awareness campaigns. Policymakers can use this information to design harm reduction strategies that aim to minimize the negative consequences of substance use. Policymakers can also allocate resources to improve access to evidence-based treatments, such as medication-assisted treatment (MAT) for opioid use disorder, cognitive remediation therapy for cognitive deficits, and mental health services[87]. This ensures that individuals struggling with substance use disorders receive the necessary support and care. This comprehensive review underscores the need for further research within this field. While significant progress has been made in understanding the mechanisms through how each drug interacts with the human brain, there remains critical gaps within research which require more thorough studies. One significant challenge lies in the need for more in-depth, longitudinal studies to elucidate the long-term consequences of substance use, particularly in adolescents. But the challenge is further accentuated by the ethical concerns of testing adolescents for drugs that are considered far more potent and harmful, such as opioids and LSD. Additionally, further research is warranted to untangle the intricate web of LSD's effects on the brain and mental health. It should be mentioned that legal regulations continue to shape the scope of research on psychoactive substances, efforts must be made to redirect the availability and access to these substances in means of research. To address this, proactive steps should be taken to facilitate greater availability and access to these substances for research purposes. This may involve advocating for changes in legislation or regulations to ensure that researchers have the necessary tools and permissions to conduct rigorous studies on these substances. Moreover, fostering collaboration between researchers, policymakers, and relevant stakeholders can help strike a balance between scientific inquiry and regulatory considerations, ultimately advancing our understanding of these complex substances.

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