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The Effect of High Doses of Dextromethorphan on The Human Nervous System

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Abstract. *Dextromethorphan (DXM) is a commonly used nonprescription cough suppressant that has gained field of science attention with its growing complex pharmacological effects and increased incidences of nonmedical use. This review is focused on pharmacokinetic, pharmacodynamics and CNS effects of DXM, especially on its action mechanism and the interaction with neural circuits and neurotransmitter systems. Although DXM has retained clinical utility as an antitussive, and has demonstrated potential as an off-label agent for neuropsychiatric disease, the recreational use of high doses can have harmful effects on the nervous system. At high doses DXM is capable of dissociation and hallucination similar to those induced by some opioids and NMDA antagonists, altering both mental status and cognition while being associated with neurotoxic effects. In this article, review and compare the similarities and differences between DXM and classic opioids in terms of their potential for abuse and their neurological effects. By case examples and existing epidemiological data, it also highlights the mounting abuse of DXM, most notably by children and young adults, posing a pressing public health challenge. Legislation on DXM is also described and differences in legislative response worldwide are highlighted. Finally, the article finishes by emphasizing the requirement for further studies involving other disciplines to detail the long-term neurological consequences of DXM abuse and to promote integrated public health interventions targeting education, prevention, and clinical treatment.*

Keywords: *Dextromethorphan, Nervous system, Opioids.*

1. INTRODUCTION

Dextromethorphan (DXM) is a strong cough medicine found in many over-the-counter cough products, but taking it in high amounts can cause mind-altering effects, which some people misuse for recreation, a practice called "robotripping" (Majeed *et al*., 2021). The study on the impact of high doses of dextromethorphan (DXM) on the human nervous system gives valuable insights into its pharmacological properties and the developing concern about misuse. However, the increasing of DXM misuse presents significant public health challenges, underscoring the necessary understanding of its effects on neural function and synaptic safety. Therefore, it is essential for researchers to investigate the high doses ramifications of DXM use with a focus on neurodevelopmental consequences and cognitive deficits. Although many initial studies have identified certain mechanisms linking DXM to central nervous system fluctuation, much remains unclear, especially with respect to chronic use and continual neuroadaptive changes. Overall understanding of these interactions is very important for designing effective preventive and therapeutic strategies to decrease the risks resulting from high dose DXM consumption, especially in the growing prevalence of polysubstance abuse,

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and this understanding is vitally important for public health and for handling mental health and addiction issues.

2. PHARMACOLOGY OF DEXTROMETHORPHAN

Dextromethorphan (DXM) is a widely used antitussive agent found in over-the-counter cough medications. It exerts complex pharmacological effects primarily through noncompetitive antagonism of N-methyl-D-aspartate (NMDA) receptors, sigma-1 receptor agonism, and inhibition of serotonin reuptake. These mechanisms modulate neuronal signaling, contributing to reduced excitotoxicity and neuroprotection, which are relevant in neurological disorders and neurodegenerative conditions. Activation of sigma-1 receptors enhances neuroplasticity and influences mood and perception, while serotonin reuptake inhibition increases synaptic serotonin levels, potentially raising the risk of serotonin syndrome when combined with other serotonergic drugs (Fahmi *et al*., 2021).

Mechanism of Action

DXM modulates central nervous system activity chiefly by inhibiting NMDA receptor-mediated calcium influx, thereby affecting synaptic plasticity, memory, and cognitive function. Its agonism at sigma-1 receptors further modulates neuroregulatory processes linked to mood and perception. At higher doses, DXM inhibits serotonin reuptake, elevating serotonin concentration in the synaptic cleft, which can lead to psychoactive effects and an increased risk of serotonin syndrome. Although its metabolite dextrorphan exhibits weak opioid receptor affinity, this interaction is not central to DXM's primary pharmacology. The multifaceted mechanisms underscore both therapeutic potentials and risks, including dissociative states and neurotoxicity, particularly in non-medical use (Gong *et al*., 2025).

Pharmacokinetics

DXM, after oral administration, is quickly absorbed, reaching peak plasma levels within 2 to 2.5 hours. It undergoes extensive hepatic metabolism primarily via cytochrome P450 2D6 (CYP2D6), converting it to dextrorphan, an active metabolite responsible for many of its therapeutic and psychoactive effects. However, DXM and its metabolites are mainly excreted renally, with a half-life ranging from three to six hours, which may be prolonged in poor metabolizers or those with impaired renal function. Furthermore, factors such as age and concurrent medications can alter pharmacokinetics. (Zaremba *et al*., 2023).

Pharmacodynamics

DXM's pharmacodynamics profile is characterized by its modulation of numerous neurotransmitter systems such as its NMDA receptor antagonism, which reduces glutamatergic excitatory transmission, contributing to neuroprotective and cognitive effects. DXM also impairs catecholamine reuptake, potentially causing central nervous system overstimulation manifested by agitation and sensory disturbances. These complex interactions explain both its therapeutic applications and risks, especially at high-therapeutic doses for long times, where dissociative and hallucinogenic effects emerge, posing neuropsychiatric hazards that warrant careful clinical oversight. (Parincu and Iosifescu, 2023).

Dextromethorphan And The Central Nervous System

Dextromethorphan (DXM) has received increasing attention because of its primary effect on the central nervous system (CNS) (Singla *et al*., 2021).

Effect of Dextromethorphan on neural circuits and Neurotransmitters.

Although dextromethorphan (DXM) functions as a non-selective serotonin reabsorption inhibitor at normal doses (therapeutic), high concentrations for long periods produce significant change in CNS action and lead to a range of psychoactive effects. These effects are exerted through modulation of multiple neurotransmitter systems, including serotonergic, glutamatergic, and dopaminergic pathways. (Wörmeyer *et al*., 2024; McClure and Daniels, 2023). A central mechanism underlying these actions is DXM's antagonism of N-methyl-D-aspartate (NMDA) receptors, a glutamate receptor subtype substantial for excitatory neurotransmission. Inhibition of NMDA receptors decreases calcium influx into neurons, leading to impaired synaptic plasticity and neural connectivity. Such interruptions are linked to mood alterations, dissociative states, and perceptual aberrations, including euphoria and hallucinations (Singla *et al*., 2021). According to Hanson et al. (2023)large amounts of dextromethorphan are able to disrupt the structural and functional continuity of neural circuits as weIl as interrupt ion channel dynamics and synaptic signaling that facilitate the ability of a brain to perform such processes as memory function, cognitive processing and neural network organization. Furthermore, these alterations would likely disrupt the speed and accuracy of information-processing, and decrease network coherence, which is a measure of consciousness disruption commonly seen during dissociative anesthesia (Hanson *et al*., 2023).

Additionally, as described in Hanson *et al*. (2023), also Chiu *et al*. (2024); McClure and Daniels, 2023; Presigny and De Vico Fallani, 2022), DXM was shown to have dramatic effect on neural circuit-related function through primarily blocking NMDA receptor-related glutamatergic signaling. These receptors are a key mediator of synaptic plasticity, which is

the basis for learning and memory. By inhibiting NMDA function, DXM, can also interfere with excitatory neurotransmission in cortical and subcortical areas causing cognitive and sensorimotor dysfunction. This disruption may lead to compensatory alterations in other neurotransmitter systems, such as increased dopaminergic and serotonergic activity, which alter neural circuitry function in turn. At higher doses, DXM enhances endogenous monoamines and induces maladaptive changes in synaptic plasticity that underlie altered perception and affect during intoxication. They are all brain areas crucial for executive function, learning and memory, and movement control, such as the prefrontal cortex, hippocampus, and cerebellum.

Dysfunction in the prefrontal cortex, impairs decision making impulsivity and inhibitory control whereas dysfunction in 9 the hippocampus causes memory impairments and disorientation. Motor coordination and equilibrium problems may occur if the cerebellum is involved. Additionally, DXM influences the functional connectivity between the cortical and subcortical networks, impairs the functional network architecture and induces dissociative states (the prototypic effect of high-dose exposure). These neurophysiological impacts, especially when taken repeatedly or excessively, can impair the long-term structure of neural pathways and increase the susceptibility to lasting neurological effects (McClure and Daniels, 2023; Chiu et al., 2024; Presigny and De Vico Fallani, 2022). Dextromethorphan also has effects on the cholinergic system, acting as a nicotinic acetylcholine receptor antagonist, which are needed both for muscle coordination and for cognitive function. Failure of this system could be a reason for a reduction of working memory, attention, and executive function. Overall, through effects on multiple neurotransmitter systems, dextromethorphan's activity illustrates its complex neuropharmacological profile, necessitating careful clinical use to reduce potential neurological side effects and enhance therapeutic effects (Margotta, 2024). Thus, the therapeutic-to-toxic ratio is influenced predominantly by the dose and exposure time (Singla *et al*., 2021).

Clinical uses of Dextromethorphan

Dextromethorphan (DXM) has emerged as a clinical interest due to its widening therapeutic application in addition to its historical use as a cough suppressant. As a synthetic morphinan derivative, DXM predominantly pharmacological action is related with activation of sigma-1 receptor and noncompetitive antagonism at the level of NMDA receptors, being able to modulate the excitability of the nerves and the synaptic activity (Wang *et al*., 2022). Its most established clinical application remains in the management of nonproductive cough. By targeting the medullary cough center, DXM reduces the hypersensitive cough reflex without

causing significant respiratory depression. Its favorable safety profile has contributed to its widespread availability in over-the-counter formulations (Kandiwa *et al*., 2022; Hanfi and Ahmad, 2024). Unlike opioid-based antitussives, DXM lacks meaningful opioid receptor affinity, minimizing risks such as sedation and respiratory suppression. This pharmacological distinction makes it a safer alternative across diverse patient populations. It is particularly beneficial in managing persistent cough associated with respiratory tract infections, thus improving patient comfort and recovery (McClure and Daniels, 2023).

Beyond approved uses, DXM is increasingly investigated for off-label applications in neurology and psychiatry. Its dual action on NMDA and sigma-1 receptors has shown promise in treating major depressive disorder, diabetic neuropathy, and Alzheimer's disease. In combination with bupropion, DXM has demonstrated synergistic antidepressant effects in treatment-resistant depression. Additionally, its neuroprotective and anti-inflammatory actions suggest potential utility in mitigating excitotoxicity and oxidative stress in neurodegenerative conditions (Correll *et al*., 2023). Nevertheless, use of these drugs for this indication is unapproved and dangerous, as side effects including cognitive impairment and dissociation can occur even under medical supervision. Further investigation is required to establish its efficacy, optimal dosing and safe use in heterogeneous clinical settings.

Cough Suppression

Dextromethorphan is a well-established agent for managing nonproductive coughs. It acts centrally on the medullary cough center to decrease the frequency and intensity of coughing. While its precise mechanism is not fully understood, it is believed to raise the cough threshold through sigma-1 receptor interaction and serotonergic modulation, providing symptomatic relief without impairing mucociliary clearance (McClure and Daniels, 2023; Raiborde *et al*., 2022).Pharmacokinetically, DXM is metabolized in the liver via cytochrome P450 enzymes, particularly CYP2D6, into its active metabolite, dextrorphan. Genetic variations in CYP2D6 activity can lead to inter-individual differences in drug response, highlighting the importance of personalized dosing strategies. Although DXM is well-tolerated at therapeutic levels, excessive use can result in neuropsychiatric symptoms and systemic toxicity, necessitating cautious administration (Majeed *et al*., 2021; Parincu and Iosifescu, 2023). Clinical selection of DXM considers patient-specific factors such as comorbidities and potential drug interactions. Its long-standing presence in consumer healthcare reflects its balance of efficacy and safety. Moreover, emerging data suggest that at higher doses, DXM may influence neurological processes beyond cough suppression, warranting continued research into its broader pharmacological impact (McClure and Daniels, 2023).

Off-label Uses

In addition to its bioactivity as an antitussive agent, dextromethorphan has gained considerable attention for its off-label use for neurological and psychiatric indications based on its NMDA receptor antagonist effect and serotonergic activity. These effects have been studied in treatment-resistant major depression disorder and bipolar disorder, where dextromethorphan could add an effect to the response of antidepressants, via the same pathways of action of ketamine (Karrouri *et al*., 2021). Clinical evidence suggests that rapid mood-enhancing effects can be achieved with dextromethorphan and bupropion combinations. In addition, dextromethorphan has proved to be effective for the treatment of neuropathic pain (Freudenberg et al., 2024). Furthermore, its dissociative properties are still being investigated for the treatment of anxiety-related disorders and post-traumatic stress disorder (PTSD), expanding its potential therapeutic scope (Correa and Val, 2024; Moharer *et al*., 2024). Despite these hopeful applications, dextromethorphan is psychoactive, abusable and involved in complex metabolism including first-pass hepatic transfer, therefore all uses need to be accompanied with medical supervision. The inconsistency of bioavailability have also made dosing approaches complicated, and side effects at high doses are still an issue. Preliminary results are promising, but new clinical trials are required to confirm long-term safety and efficacy in the off-label use scenario (Rusz *et al*., 2021; Di Martino *et al*., 2023).

High Doses of Dextromethorphan: Overview

Dextromethorphan is an over-the-counter antitussive agent that is generally safe at therapeutic doses. However, at doses 10-20 times the recommended, they can cause considerable neuropsychiatric and psychoactive effects, as mentioned previously. The severity of these effects is due to the parent compound, which is converted into a psychoactive breakdown product dextrorphan, enhancing the effect of dextromethorphan as well as non-linear pharmacokinetics and a disproportionate accumulation of the drug (Hashimoto, 2024; Ricci *et al*., 2025). Dextromethorphan high doses are defined quantitatively and based on pharmacological markers. Thus, when used therapeutically, 10-30 mg is administered every four to six hours, and any use of 50 mg or more at once is considered supratherapeutic. Recreational abuse occurs in the range from 100 to more than 1500 mg, at which the action of DXM ceases to manifest itself through suppression of a cough and is replaced by pronounced psychoactive reactions. The intensity and time of their appearance depend on the tolerance of the person: someone has enough and 100 mg to feel strong feelings, someone has to take more than 200 mg. The use of in this dose range leads to visual and cognitive disturbances, euphoria, hallucinations, and a feeling of dissociation, as well as sharply increasing the probability of

acute toxic reactions and cardiovascular complications. Access to DXM and myths about its harmlessness spread by teenagers on social networks and the media contribute to the high prevalence of this phenomenon. Furthermore, high-dose DXM use often occurs in combination with other drugs, which exacerbates the scale of the problem and increases the burden on the healthcare system. In this regard, measures to prevent the development of this phenomenon should include measures to educate the public, adopt regulatory decisions, as well as to develop clinical approaches that would reduce the prevalence and consequences of the use of DXM (McClure and Daniels, 2023; Pompili *et al*., 2025).

Long-term Consequences

Chronic high-dose use of DXM in large amounts for extended periods would greatly screw up neurotransmission, by prolonged NMDA receptor antagonism, mostly. NMDA is critical for synaptic plasticity, calcium homeostasis, and neurodevelopment. Their chronic block can disrupt cognitive function, emotional response, and neuronal health and may have effects that mimic those of neurodegenerative diseases in the long term (Shimozawa *et al*., 2023). Prolonged DXM abuse has been linked to structural and function brain alterations, such as neuronal apoptosis (as patterns of oxidative stress and excitotoxicity). In some brain areas, like the prefrontal cortex and hippocampus, essential to executive control and emotion regulation, this is especially pronounced. Neuroimaging data and neuropathological studies are in agreement with these observations and evidence a relationship between DXM use and sustained cognitive impairment and emotional lability. Moreover, evidence also indicates that long-term exposure may cause demyelination, additionally transiently reducing neural velocity and susceptibility to disorders that resemble demyelinating diseases (Aldubayan *et al*. 2024). Behaviorally, long-term DXM use can lead to tolerance and dependence, prompting dose escalation and exacerbating neural damage. This cycle is elicited by the relationship between neurochemical abnormalities and brain structural changes. Chronic DXM abuse is subject to potentially long-lasting neurological, cognitive, and psychiatric consequences. The mounting evidence underscores the importance of early detection, preventative education and ongoing clinical surveillance in order to prevent DXM misuse chronicity (Deitche and Burda, 2022; Taflaj *et al*., 2024).

1. Altered Consciousness

The psychoactive properties of DXM are best seen at supratherapeutic doses, where it produces states of intoxication that are of interest to clinicians and abusers alike. At the heart of such a transformation is the dissociational experience wherein individuals disavow or disconnect their bodies or surroundings, frequently alongside significant change in self-

awareness and perception processing (Shimozawa *et al*., 2023). The action is predominantly mediated by NMDA receptor antagonism, of which the effects resemble other dissociative drugs, most notably ketamine and PCP (Driver *et al*., 2022). Aside from dissociation, DXM artifacts of hyperfocused attention and cognitive distortion, as well as temporal dislocation, or the perception that one's sense of time is gone (McClure & Daniels, 2023). These changes may compromise judgment, decision-making, and self-monitoring, elevating the odds for engaging in risky behavior. Additionally, DXM modifies sensory perception, frequently leading to auditory and visual distortions that enhance this modified state (Santos *et al*., 2024). Individual susceptibility, dosage and co-ingestion of compounds (e.g. alcohol, other psychotropic drugs) further influence the extent of these effects. Identification of these presentations is essential in a clinical and research context to identify abuse, manage toxicity and to examine implications for neuropsychology and public health (Yang *et al*., 2022; Murray *et al*., 2024).

2. Hallucinations

Hallucinations are a notable and disturbing consequence of high-dose DXM abuse. These effects are mainly due to the noncompetitive NMDA receptor antagonism of DXM, causing a blockade of glutamatergic neurotransmission necessary for normal perception (Okamoto *et al*., 2025). Consequently, using the drug can produce vivid, internally generated effects (e.g., visual or auditory hallucinations) of variable strength according to the dosage and specific neurobiology of the individual taking it. Psychodynamics DXM-induced hallucinations are commonly associated with derealization, spatial disorganization, and an omnipresent sense of unreality (Mathai *et al*., 2023). Although normally temporary, such effects may endure and resurface in vulnerable people, with the potential to worsen preexisting psychiatric conditions (Stewart, 2024). Hallucinations can vary from visual images to phantom sounds and can jeopardize reality testing and situation awareness (Healy, 2021).

Comparative Analysis of Dextromethorphan And Opioids

DXM and opioids are both CNS active drugs, but the mechanisms of action between them are quite different, and their therapeutic indications and abuse liabilities are far away from each other. DXM is most commonly administered as an antitussive, and act via noncompetitive antagonism of N-methyl-D-aspartate (NMDA) receptors, that are essential to excitatory neurotransmission and synaptic potentiation. Opiods, on the other hand, are predominantly mu-opioid receptor ligands, which promote analgesia, euphoria, and the regulation of reward and emotional brain systems (Witkin *et al*., 2021; Shiromwar *et al*., 2024). While both can make a person feel great, opioids are much more addictive due to their direct effect on the body's natural supply of opioids. DXM, on the other hand, has lower

affinity for NMDA receptors and does not significantly affect opioid receptors, resulting in less severe respiratory depression and the high of opioids. However, escalating misuse of DXM especially at supratherapeutic doses, has brought us to the recognition of its dissociative and hallucinogenic effects in level with ketamine and phencyclidine, which is associated with public health concerns of its potential for abuse, particularly among children and young adults (Schlag *et al*., 2022). In the clinical setting, DXM is only employed as an antitussive agent and has no analgesic effects of clinical importance. By contrast, opioids are critical for pain relief, especially in the context of acute or chronic pain, but are characterized by high rates of dependence, tolerance, and overdose. Given the present opioid epidemic, the search for alternative pharmaceutical agents such as DXM (with lower abuse potential) is of interest. Still, the pharmacologic intricacies and abuse-properties of both DXM and opioids demand further investigation. A better understanding of their unique neurochemical pathways and behavioral sequelae is essential in guiding therapeutic choices, influencing regulatory policies, and encouraging judicious medication use (Rajput *et al*., 2025).

3. CASE STUDIES

Case reports are critical in order to address the wide spectrum of neurological consequences in chronic dextromethorphan (DXM) abuse and to offer empirical evidence of this drug on the central nervous system. Reports of a 23-year-old man with neurotoxic symptoms after an acute ingestion of 1200 mg of DXM, ten times the therapeutic dose. The patient had disorientation, agitation, and auditory hallucinations. Neurological tests showed problems with neurotransmitter systems, especially those involving glutamate and serotonin, highlighting the complex chemical issues caused by DXM (Nayak and Johnson, 2023; Mayberry & Ray, 2023). Also, there were dissociative symptoms in a 19-year-old woman, which became a deep state of dissociation after taking 1,000 mg of dextromethorphan (DXM) with consciousness change and motor incoordination. Chronic, high-dose use in this instance led to sustained cognitive deficits, particularly for memory and executive function. MRI Interestingly, grey matter density decreases were observed, which may suggest neurodegenerative consequences of prolonged exposure. These clinical descriptions emphasize the severe neurotoxic hazards of high-dose DXM abuse and its potential to produce cognitive dysfunction. (Thiankhaw *et al*., 2022; McClure and Daniels, 2023). Moreover, in experimental animals, degeneration of neurons and brain areas, associated with memory loss and emotional abnormality, was also found. While, in human participants, EEG measurements demonstrated alterations in the brain electrical activity, indicating perturbations in neuronal

processing and cognitive function. These results emphasize the importance of judicious use, public awareness and continued investigation to define entirely the neuropsychiatric effects of DXM (Donaghy *et al*., 2024). This clinical settings are very important in tackling the neuropharmacological issues of one of the most abused substances available.

Legislation on Dextromethorphan

The psychoactive substance, Dextromethorphan (DXM), that has the ability to produce neuropsychiatric effects when consumed in large quantities is currently and has historically been regulated in a number of ways in different countries. Initially available with little or no restriction, increasing abuse, especially among young people, has forced many local authorities to rethink their regulatory strategies (Zaremba *et al*., 2023). In the United States, while DXM is not federally classified as a controlled substance, several states have enacted age-based restrictions, typically limiting sales to individuals aged 18 and above, alongside mandatory ID verification by retailers. This represents a preventive approach to young population as the most susceptible group to casual use (Zhang, 2024). Globally, nations such as Canada and Australia also have restrictions based on age. At the same time, some European countries require a prescription to purchase DXM empowering healthcare practitioners as gatekeepers to consider whether and when the substance is needed and appropriate, providing a barrier against its misuse (Plewa *et al*., 2024). Regulation attempts to minimize neurologic and psychologic injury due to high-dose consumption while permitting legitimate medical applications.

4. FUTURE DIRECTIONS IN RESEARCH

As the investigation into the effects of the high doses of dextromethorphan on the nervous system unfolds, various future research trajectories come into focus. Furthermore, the development in neuropharmacology provides fascinating opportunities for improving the understanding of this compound's complex relationship with nervous system, which might be a fruitful way ahead for future research. More efforts to detail the specific molecular mechanisms underlying the action of dextromethorphan on neural systems such as those mediated by the neurotransmitter systems, for example, glutamate and serotonin, may help to elucidate its involvement in the regulation of synaptic activity and neuroplasticity. Such studies could provide significant insights into the discovery of new therapeutic targets, and may represent an important step forward both in therapeutic applications and reducing side effects with high doses of treatments. In addition, the application of the genomic and proteomic methods might help clarify the individual differences of dextromethorphan response. With new technologies in hand, scientists could discover valuable information into the genetic

propensities that determine susceptibility to the beneficial and adverse effects of dextromethorphan. Studying pharmacogenomics likely will improve techniques of personalized medicine to help optimize dosing regimens and to minimize risk, especially for those with atypical metabolism affecting dextromethorphan metabolism and clearance. Moreover, it seems, that the progress in the field of dextromethorphan requires interdisciplinary exchanges between neuroscientists and psychiatrist as well as pharmacologists. Such relationships may lead to new therapeutic uses in the treatment of (mental/psychiatric diseases) such as clinical depression and anxiety utilizing the potential of dextromethorphan as a rapid antidepressant. In the meantime, utilizing the power of neuroimaging technologies could help to unravel the subtler consequences of dextromethorphan on brain dynamics, bringing researcher's one step closer towards obtaining a more comprehensive picture of its cognitive effects. Also, stringent methodological investigations and multi-angled strategies for explorations sensibly should be recommended to completely decipher the neurological/psychological basis of high-dose dextromethorphan in a bid to further enrich the theory and clinical applications in vitro as well.

5. CONCLUSION

Despite the acknowledged therapeutic attributes of dextromethorphan, its non-medical use is associated with a range of potentially dangerous neuropsychological and physiological effects that are not without concern. A complete characterization of these neurophysiological effects is critical to evaluating its therapeutic and neuropsychiatric implications. The escalating rate of DXM abuse, especially among the young population, is emerging as a serious public health concern that requires additional investigation of the prolonged neurological effects and the implementation of prevention programs. Continuous scientific exploration and an integrated public health approach that includes education, policy intervention, and clinical follow-up are necessary to mitigate these risks.

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