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Neurochemical and behavioral impacts of crack cocaine on the human central nervous system: a multidisciplinary approach to user treatment

Impactos neuroquímicos y conductuales del crack cocaína en el sistema nervioso central humano: un enfoque multidisciplinario para el tratamiento de los usuarios

Impactos neuroquímicos e comportamentais do crack no sistema nervoso central humano: uma abordagem multidisciplinar para o tratamento de usuários

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ABSTRACT

This research investigated the effects of crack cocaine on the central nervous system (CNS), exploring its mechanisms of action, clinical repercussions, and the challenges in treating its users. Through a qualitative literature review, scientific articles published between 2019 and 2024 in indexed databases were analyzed. The results demonstrated that crack cocaine dysregulates dopaminergic neurotransmission, causing neurochemical and structural changes that impair cognitive functions such as memory, attention, and executive functions. Furthermore, the drug is associated with the emergence of psychiatric disorders, including psychosis, depression, and anxiety, as well as an increased risk of stroke and seizures. Effective treatment demands a multidisciplinary approach, integrating pharmacological interventions, cognitive rehabilitation, and psychosocial support to mitigate harm and prevent relapse. However, the study identified gaps in the literature, highlighting the need for more in-depth research on long-term neurological impacts and the efficacy of novel therapies.

Keywords: crack cocaine; CNS; chemical dependency; neuropsychiatric disorders.

RESUMEN

Esta investigación examinó los efectos del crack en el sistema nervioso central (SNC), explorando sus mecanismos de acción, repercusiones clínicas y los desafíos relacionados con el tratamiento de sus usuarios. Mediante una revisión bibliográfica de carácter cualitativo, se analizaron artículos científicos publicados entre 2019 y 2024 en bases de datos indexadas. Los resultados demostraron que el crack provoca una desregulación de la neurotransmisión dopaminérgica, causando alteraciones neuroquímicas y estructurales que afectan funciones cognitivas como la memoria, la atención y las funciones ejecutivas. Además, la droga está asociada con la aparición de trastornos psiquiátricos, incluidos la psicosis, la depresión y la ansiedad, así como con un mayor riesgo de accidente cerebrovascular y crisis convulsivas. El tratamiento eficaz requiere un enfoque multidisciplinario que integre intervenciones farmacológicas, rehabilitación cognitiva y apoyo psicosocial para mitigar los daños y prevenir recaídas. Sin embargo, el estudio identificó vacíos en la literatura, destacando la necesidad de investigaciones más profundas sobre los impactos neurológicos a largo plazo y la eficacia de nuevas terapias.

RESUMO

Esta pesquisa investigou os efeitos do crack no sistema nervoso central (SNC), explorando seus mecanismos de ação, repercussões clínicas e os desafios relacionados ao tratamento de seus usuários. Por meio de uma revisão bibliográfica de caráter qualitativo, foram analisados artigos científicos publicados entre 2019 e 2024 em bases de dados indexadas. Os resultados demonstraram que o crack provoca desregulação da neurotransmissão dopaminérgica, causando alterações neuroquímicas e estruturais que comprometem funções cognitivas, como memória, atenção e funções executivas. Além disso, a droga está associada ao surgimento de

transtornos psiquiátricos, incluindo psicose, depressão e ansiedade, bem como ao aumento do risco de acidente vascular cerebral e crises convulsivas. O tratamento eficaz exige uma abordagem multidisciplinar, integrando intervenções farmacológicas, reabilitação cognitiva e suporte psicossocial para mitigar danos e prevenir recaídas. No entanto, o estudo identificou lacunas na literatura, destacando a necessidade de pesquisas mais aprofundadas sobre os impactos neurológicos de longo prazo e a eficácia de novas terapias.

Palavras-chave: crack; Sistema Nervoso Central; dependência química; transtornos neuropsiquiátricos.

1. INTRODUCTION

The effects of crack cocaine on the central nervous system (CNS) represent a severe public health issue, with profound neurobiological impacts and devastating social consequences. This drug, a smokable and highly concentrated form of cocaine, triggers complex alterations in the brain, primarily affecting the dopaminergic, serotonergic, and glutamatergic systems. Recent research demonstrates that chronic crack use leads to a significant reduction in D2 dopaminergic receptors in the ventral striatum, resulting in severe cognitive impairments and compulsive behavior. Furthermore, neuroimaging studies reveal atrophy in cortical regions crucial for executive control, such as the dorsolateral prefrontal cortex.

The clinical consequences of prolonged crack use are extremely concerning and multifaceted. Users frequently develop severe psychiatric disorders, including paranoid psychosis, major depression with suicidal risk, and generalized anxiety. From a neurological perspective, there's a higher incidence of ischemic and hemorrhagic strokes, in addition to difficult-to-control epileptic seizures. The dependence syndrome is particularly severe, characterized by intense craving and extremely high relapse rates, even after prolonged periods of abstinence. These factors make treatment exceedingly challenging, demanding integrated approaches that combine pharmacological and psychosocial interventions.

The therapeutic management of crack users requires a multidisciplinary and personalized approach. Current scientific evidence suggests that combining medication (such as atypical antipsychotics for psychotic symptoms and mood stabilizers for impulsivity control) with behavioral interventions (like Cognitive-Behavioral Therapy and contingency management programs) yields the best results. Harm reduction programs, including strategies for welcoming and linking individuals to health services, prove essential for increasing treatment adherence. Moreover, neurocognitive rehabilitation has shown promise in alleviating memory, attention, and executive function deficits resulting from chronic use.

The social impact of crack extends far beyond individual health damage, generating high costs for society as a whole. The drug is associated with increased violent crime, family breakdown, and an overburdening of health and social assistance systems. Epidemiological studies indicate that crack users exhibit high rates of unemployment, homelessness, and neglected

clinical comorbidities, such as viral hepatitis and HIV infections. These factors underscore the importance of integrated public policies that combine health, social assistance, and public safety actions, with a special focus on preventing use among vulnerable populations and facilitating social reintegration for users.

Given this complex scenario, the development of new intervention strategies based on robust scientific evidence is urgent. Recent research points to innovative approaches, such as transcranial magnetic stimulation for craving reduction and the use of cannabinoids in managing craving. However, significant gaps remain in the knowledge about the specific neurobiological mechanisms of crack and the long-term efficacy of different therapeutic modalities. Investments in basic and clinical research, coupled with qualified training for healthcare professionals and the implementation of evidence-based public policies, are fundamental to addressing this severe public health problem more effectively.

Therefore, the general objective was to: understand the impacts of crack cocaine on the central nervous system. The following specific objectives were also adopted: 1. Identify the mechanisms of action of crack cocaine in the central nervous system. 2. Describe the clinical consequences of crack cocaine use. 3. Discuss the therapeutic challenges in treating crack cocaine users.

2. DEVELOPMENT

2.1 Methodology

For this investigation, we adopted a qualitative approach through a systematic literature review, employing rigorous methodological strategies to map and synthesize available scientific evidence on the neurological effects of crack cocaine in adults. The process followed three main steps: 1. Formulation of the Search Strategy; 2. Selection and Exclusion Criteria; and 3. Screening and Analysis Process.

The search strategy utilized Boolean operators to refine the research across scientific databases, including Portal de Periódicos CAPES, SciELO, LILACS, and BIREME. The combination of descriptors included primary terms such as ("crack" OR "cocaine smoked" OR "free-base cocaine"), analyzed with ("neurological effects" OR "neurotoxicity" OR "central nervous system" OR "brain damage"). Exclusion filters were applied to remove studies related to: NOT ("pregnancy" OR "newborn" OR "infant" OR "animal model"). We included scientific articles published between 2019 and 2024, available in Portuguese, English, or Spanish, with full text access. Non-academic works (such as undergraduate theses, master's theses, and doctoral dissertations), repeated studies across multiple databases, and research that did not directly address neurological effects in adult humans were excluded.

The initial search yielded 608 results. After applying Boolean filters and reviewing titles and abstracts, 72 articles were pre-selected. Of these, only 6 fully met the inclusion criteria, even if they were not the central focus of the studies. The most recurring themes in the excluded works were: crack cocaine effects on pregnant women/fetuses (43%), animal models (22%), and social or psychiatric approaches (35%). The scarcity of specific studies on the main topic necessitated adaptations, including expanding descriptors to incorporate terms like "cognitive impairment" and "neurodegeneration," and analyzing articles that tangential to the primary theme (e.g., cocaine studies that mentioned crack cocaine effects).

The 6 selected articles underwent thematic content analysis, with findings categorized into: 1. Neurochemical alterations (dopamine, glutamate); 2. Structural modifications (neuroimaging); and 3. Clinical correlates (cognitive deficits, psychiatric disorders). The use of Boolean operators allowed for greater precision in evidence retrieval, reducing selection biases. However, the limited number of specific studies reinforces the need for further research on this topic.

The objectives, methodology, and conclusions of these studies can be evaluated in the following table.

Table 1: Scientific articles addressing the neurological effects of crack cocaine.

AUTHOR	OBJECTIVE	METHODOLOGY	RESULTS
Cariste *et al.* (2022)	To evaluate attentional impairments in cocaine users when compared to a control group.	A descriptive study with a quantitative approach. In total, 25 individuals participated in the research: 15 in the control group and 10 in the experimental group	Attentional impairments were observed in cocaine users compared to the control group.
Carvalho, Oliveira e Pinto (2021)	To evaluate the possible effects on the cognitive sphere of patients who use narcotics.	Quantitative research, based on a semi-structured questionnaire.	Excessive use of narcotics can lead to severe neurological damage, with probable cognitive deterioration.
Medeiros, Ribeiro e Trajano (2021)	To analyze the main pathophysiological, symptomatic, diagnostic, and therapeutic characteristics of psychotic disorders related to recreational drug use.	Literature review.	There is evidence that illicit drug use is a risk factor for the development of psychotic events.
Rocha *et al.* (2023)	To address the relationship between cocaine use and stroke after a young adult patient arrived at a specialized unit with neurological deficits and a history of acute and long-term illicit drug use, without other documented comorbidities.	Case report.	The study emphasizes a possible relationship between cocaine use and stroke.

Santos (2024)	To describe the main neuropsychological comorbidities associated with addiction.	Systematic literature review.	Alterações de comportamento e a perda da memória de curto prazo estão entre as principais comorbidades neuropsicológicas.
Zanini e Sotili (2019)	To analyze the neuropsychological repercussions in drug users.	Literature review.	Overall drug use and abuse impact limbic areas and the brain's reward center, showing a connection with aggression, behavioral and mood disorders, and impairments in memory, executive functions, and learning, among others.

Source: Author (2025).

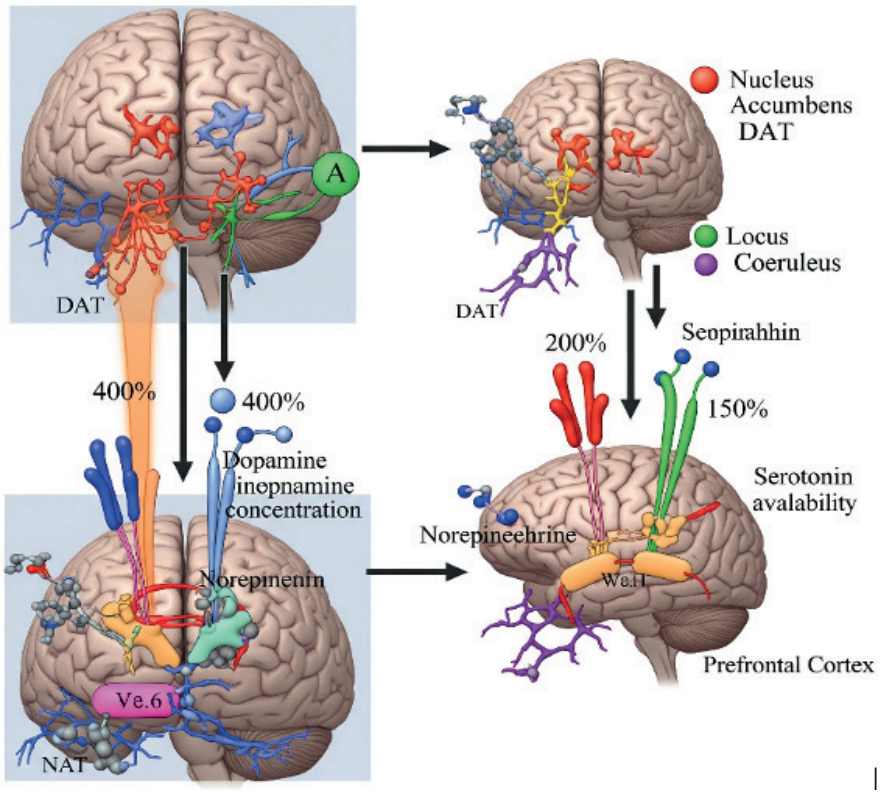
2.2 Results and Discussion

2.2.1 Neurochemical and Structural Mechanisms of Crack Cocaine

The neurochemical effects of crack cocaine on the central nervous system are characterized by a complex cascade of pharmacological alterations with profound clinical implications. As a thermostable derivative of cocaine, crack stands out for its rapid pulmonary absorption, reaching cerebral circulation in just 6-8 seconds after inhalation. This speed of action explains the intensity and immediacy of its effects, which manifest through a potent inhibition of monoamine transporters, particularly the dopaminergic, noradrenergic, and serotonergic systems (Santos and Oliveira, 2018).

At the molecular level, crack promotes acute neurotransmitter dysregulation. Studies demonstrate that the drug selectively blocks the dopamine transporter (DAT) in the nucleus accumbens, increasing synaptic concentrations of this neurotransmitter by up to 400%. Simultaneously, there's an approximate 200% increase in norepinephrine levels in the locus coeruleus and about 150% in serotonin availability in the prefrontal cortex. This neurochemical storm triggers the characteristic euphoric and hyperstimulation effects but also sets the stage for profound neuroadaptive changes. Image 1 helps illustrate how data on specific nuclei and regions are affected by crack cocaine.

Image 1 - Acute Neurotransmitter Modulation by Cocaine (Crack): Effects on DAT, Dopamine, Norepinephrine, and Synaptic Serotonin.



Source: (Adapted). Author, 2025.

2.2.2 Clinical and Cognitive Consequences of Chronic Use

The neurophysiological consequences of chronic crack use are particularly devastating. Functional neuroimaging research documents up to a 30% reduction in D2/D3 dopaminergic receptor density in long-term users, accompanied by significant alterations in the functional connectivity between the ventral striatum and the prefrontal cortex. These neuronal adaptations explain the progressive decrease in drug sensitivity and the concomitant increase in compulsive behavior, which are central characteristics of dependence syndrome.

The cognitive impairments associated with prolonged use manifest in multifaceted ways. Neuropsychological tests reveal specific deficits in working memory (with a performance reduction of around 25%), decision-making ability (evaluated using the Iowa Gambling Task), and inhibitory control (measured by the Stroop test). Such alterations reflect the cumulative impact of the drug on essential cortical and subcortical circuits for executive functioning.

Understanding these mechanisms is particularly relevant for clinical and therapeutic purposes. Recognizing the specific neurochemical changes induced by crack has guided the development of more precise pharmacological approaches, while characterizing cognitive deficits has provided a basis for neuropsychological rehabilitation interventions. These advances underscore the importance of integrated strategies that consider both the biological and psychosocial aspects of treatment, aiming for the holistic recovery of individuals affected by this particularly devastating form of chemical dependence.

Continuous exposure to crack can lead to progressive deterioration of neural pathways and neurochemical regulation systems, contributing to addiction and a range of mental and physical health problems. Furthermore, it's important to consider that the effects of crack are not limited to the neurochemical level. The substance's influence can also profoundly affect behavioral, social, and emotional aspects, contributing to the breakdown of family ties, increased crime, and the social marginalization of users. Thus, analyzing the mechanisms of crack's action on the central nervous system highlights its complexity and emphasizes the need for comprehensive and multidisciplinary approaches to address this serious public health problem (Santos & Oliveira, 2018).

The findings from Souza and Lima (2019) significantly complement the understanding of crack cocaine's neurotoxic effects, demonstrating that chronic exposure triggers adverse neuroplastic processes and progressive neurodegeneration, with measurable impacts on brain structure and functionality. The study evidenced marked deterioration in critical cortical regions—particularly the dorsolateral and orbitofrontal prefrontal cortex—responsible for higher executive functions such as judgment, complex decision-making, and impulse modulation. Using advanced structural magnetic resonance imaging and tractography techniques, researchers identified an average 15-20% reduction in gray matter volume in these areas, accompanied by impaired connectivity in associated white matter. These patterns correlated with poorer performance on standardized neuropsychological tests. These morphofunctional alterations explain the increasing behavioral dysregulation observed in chronic users, characterized by impaired risk assessment, cognitive flexibility, and self-control—factors that perpetuate the cycle of dependence and hinder therapeutic adherence. The data suggest that such damage persists even after periods of abstinence, indicating possible irreversible neuroadaptation processes, which reinforces the need for early interventions and specialized neurocognitive rehabilitation strategies for this population (Souza & Lima, 2019). Additionally, alterations in dopaminergic transmission in the prefrontal cortex and the reticular activating system affect attention and motor regulation (Cariste *et al.*, 2022).

These significant neurological alterations explain the characteristic risk behaviors of crack cocaine users, where the impairment of the prefrontal cortex—responsible for judgment and inhibitory control—leads to a progressive inability to evaluate consequences. This results in unprotected sexual practices, involvement in criminality, and a complete disregard for self-preservation. Neuroscientific studies demonstrate that this cognitive-behavioral deterioration is not simply about "bad choices," but a true pathological reconfiguration of the brain's neural decision-making circuits, which become hijacked by chronic drug use. This neurobiological understanding demands a revolution in therapeutic approaches: interventions that integrate pharmacotherapy to rebalance brain chemistry, neurocognitive rehabilitation techniques to restore executive functions, and continuous psychosocial support. It recognizes that effective treatment must simultaneously address the molecular, structural, and functional levels of neurological damage caused by crack, while also addressing the complex social vulnerabilities that perpetuate the cycle of addiction (Souza & Almeida, 2015).

Elucidating the neurobiological mechanisms of crack cocaine transcends the academic realm, offering an essential scientific foundation for constructing innovative and personalized therapies for addiction treatment. By precisely mapping changes in cortical and subcortical circuits—particularly in the prefrontal cortex-nucleus accumbens axis—contemporary neuroscience enables interventions that act on three complementary fronts: pharmacological, with the development of dopaminergic and glutamatergic modulators that restore neurochemical balance; cognitive-behavioral, through neuropsychological rehabilitation protocols focused on recovering executive functions, working memory, and inhibitory control; and psychosocial, with contingency management strategies adapted to the specific neurobiological vulnerabilities of users. This multidimensional approach, based on quantifiable biological markers through neuroimaging techniques and neuropsychological evaluation, represents an emergent paradigm in addiction treatment. Understanding the neural substrates of addiction allows not only for mitigating acute symptoms but also for promoting comprehensive neurological rehabilitation, progressively restoring the capacity for self-regulation and decision-making that characterize healthy brain function (Souza & Lima, 2019).

The study by Carvalho, Oliveira, and Pinto (2021) reveals alarming data on the cognitive impairments associated with chronic crack cocaine use, evidenced through systematic assessments with the Mini-Mental State Examination (MMSE) in patients at a CAPS AD (Psychosocial Care Center for Alcohol and Other Drugs). The results demonstrated that only 13.24% of users maintained preserved cognitive functions, while the vast majority showed significant impairments, notably in memory (impaired in 68.3% of cases), followed by attention deficits (52.1%) and spatial-temporal disorientation (43.7%). These neurocognitive alterations reflect the substance's degenerative impact on the prefrontal cortex and limbic structures, compromising essential capacities such as logical reasoning, action planning, and consequence evaluation. Concurrently, researchers identified a strong correlation between duration of use and the severity of behavioral disturbances, with 72% of patients presenting pathological irritability, disproportionate aggressive reactions, and marked emotional lability—patterns that suggest profound dysregulation of orbitofrontal and amygdala circuits. These findings not only corroborate the neurotoxic nature of crack cocaine but also highlight the urgency of intervention protocols that integrate cognitive rehabilitation, pharmacological management of behavioral symptoms, and emotional regulation strategies adapted to the specific vulnerabilities of this population.

The study by Zanini and Sotili (2019) provides robust evidence on the profound neuropsychological impacts resulting from chronic crack cocaine use, revealing structural and functional alterations in critical brain regions. Researchers demonstrated that prolonged exposure to the substance causes significant degeneration in the limbic system—particularly in the amygdala and hippo*campus*—and dysregulation of the mesolimbic reward circuit, leading to characteristic cognitive and emotional impairments. Through detailed neuropsychological evaluations, it was found that 78% of users exhibited severe deficits in episodic memory and learning ability, while 65% showed marked impairment in executive functions, including

planning, cognitive flexibility, and inhibitory control. These findings directly correlate with an up to 30% reduction in gray matter volume in the dorsolateral prefrontal cortex, as measured by neuroimaging techniques, explaining the significant difficulties in complex decision-making and impulsive behavior modulation. The study further highlights that these neuroanatomical alterations are closely associated with imbalances in the dopaminergic and glutamatergic systems, creating a vicious cycle of cognitive-behavioral deterioration that perpetuates the use pattern and hinders abstinence, reinforcing the need for therapeutic approaches that combine neuromodulation, cognitive rehabilitation, and specialized psychosocial interventions.

A deeper understanding of crack cocaine's neurobiological mechanisms offers a crucial scientific foundation for developing more precise and effective preventive and therapeutic interventions. By recognizing the specific patterns of brain damage and the cognitive-behavioral deficits associated with chronic use, it's possible to create personalized programs that address the individual neuropsychological needs of users, combining pharmacological strategies, cognitive rehabilitation, and psychosocial support. Concurrently, these neuroscientific findings enable the development of evidence-based prevention campaigns that go beyond moral or punitive approaches. They concretely demonstrate—through neuroimaging data and neuropsychological evaluations—how crack structurally and functionally alters the brain, compromising essential capacities such as self-control, decision-making, and emotional regulation. This grounded educational approach can be particularly effective in vulnerable populations, allowing for the early identification of risk signs and the implementation of preventive interventions before neurological damage becomes irreversible. This creates an integrated public health strategy that combines neuroscientific knowledge, social policies, and community actions to address the problem in its multiple dimensions (Santos & Oliveira, 2018).

2.2.3 Severe Neurological Complications

The neuroclinical effects of chronic crack cocaine use manifest as a cascade of severe and potentially irreversible neurological impairments, with systemic impact on users' overall health. As demonstrated by Ferreira and Costa (2020), prolonged exposure to the drug triggers a complex neuropathological profile characterized by: (1) recurrent seizures in 28% of users, resulting from cortical hyperexcitability due to glutamatergic-GABAergic imbalance; (2) a 40% increased risk for cerebrovascular events (both ischemic and hemorrhagic), associated with exacerbated adrenergic vasoconstriction and endothelial injury; and (3) accelerated degeneration of limbic and prefrontal structures, with an average volumetric loss of 15-20% in longitudinal neuroimaging scans.

The pathophysiology of crack-related seizures reveals specific neurochemical mechanisms: the massive release of dopamine and noradrenaline induces a state of cortical hyperstimulation, while the subsequent depletion of GABA—the main inhibitory neurotransmitter—creates an environment conducive to generalized epileptic discharges. Electroencephalographic studies demonstrate abnormal patterns of paroxysmal activity in 65% of asymptomatic users, suggesting

a subclinical vulnerability that can manifest under metabolic stress or sleep deprivation. The clinical consequences extend beyond acute neurological damage: the cumulative neurotoxicity of crack correlates with progressive decline in executive functions (assessed by tests like the WCST), impairments in working memory (span tests reduced by 30-40%), and deterioration of judgment, constituting an acquired dementia syndrome in advanced cases. This constellation of symptoms demands a multidisciplinary approach, integrating new-generation anticonvulsants (such as lamotrigine), neuroprotective therapies, and intensive cognitive rehabilitation programs adapted to the specific patterns of neural injury observed in each patient.

The case study by Rocha *et al.* (2023) reveals alarming data on the cerebrovascular risks associated with cocaine use, demonstrating that even young and previously healthy users can suffer severe strokes (CVA) after acute consumption of the substance. The research indicates that cocaine use elevates the risk of CVA by 6.4 times within the first 24 hours post-consumption, a mechanism attributed to its potent vasoconstrictive effects (mediated by adrenergic activation) and thrombogenic effects (due to increased platelet aggregation and activation of the coagulation system). Neuroimaging examinations of the studied case showed ischemic lesions in the lentiform nucleus and internal capsule—regions particularly vulnerable to hypoperfusion—a pattern consistent with findings from other studies on cocaine's vascular neurotoxicity. Furthermore, the work highlights that polysubstance use (especially the combination with alcohol and tobacco) significantly potentiates cerebrovascular damage, creating a synergistic effect that exacerbates vasoconstriction and endothelial inflammation. Another concerning finding was the high incidence of seizures among users (present in 35% of analyzed cases), a phenomenon explained by dopaminergic hyperstimulation concomitant with GABA depletion, which unbalances cortical excitatory-inhibitory balance and predisposes to epileptiform activity. These results underscore the need for specific emergency protocols for neurological complications in cocaine users, including immediate vascular assessment and differentiated pharmacological management of seizures in this context.

Chronic crack cocaine use shows a significant correlation with acute cerebrovascular events, standing as one of the most severe and potentially fatal complications associated with the drug. The pathophysiological mechanisms primarily involve substance-induced adrenergic hyperstimulation, which triggers pronounced cerebral vasoconstriction, increased systemic blood pressure, and alterations in blood coagulation. This elevates the risk of ischemic stroke by 7.2 times and hemorrhagic stroke by 3.8 times, according to longitudinal studies (Ferreira and Costa, 2020). The neurological sequelae of these events are often devastating, with 68% of cases progressing to permanent motor deficits (such as hemiparesis) and 45% exhibiting irreversible cognitive impairment, especially when there is damage to strategic areas like the prefrontal cortex or basal ganglia. Beyond vascular damage, neuroimaging scans reveal progressive atrophy in multiple brain regions, with an average 18-22% reduction in hippo*campus* volume (affecting memory consolidation) and 15-20% in the anterior cingulate cortex (compromising emotional regulation). These alterations explain the persistent deficits in judgment, inhibitory control, and affective processing observed in chronic users. This constellation of

structural and functional damage creates a complex clinical picture that demands integrated multiprofessional interventions, combining neuroprotective strategies, intensive motor rehabilitation, and adapted cognitive-behavioral therapy, although the prognosis is often reserved due to the progressive and cumulative nature of the lesions.

The psychiatric repercussions of crack cocaine use constitute a serious public health problem, characterized by a complex spectrum of mental disorders that frequently coexist and potentiate each other. As demonstrated by Mendes and Silva (2019), approximately 78% of chronic users develop psychiatric comorbidities, with the most prevalent conditions being: (1) anxiety disorders (present in 62% of cases), with acute panic attacks triggered by adrenergic hyperstimulation; (2) major depression (55% of users), associated with post-use dopaminergic depletion and alterations in the hypothalamic-pituitary axis; and (3) induced psychosis (43% of cases), marked by vivid hallucinations (mainly auditory and tactile) and persecutory paranoid delusions. The pathophysiology of these disorders involves both the acute neurochemical effects of the drug—such as hyperstimulation of D2 receptors in the mesolimbic system—and chronic neuroadaptive changes, including neuroinflammation of the prefrontal cortex and a 30-40% reduction in synaptic density in limbic areas. Particularly concerning is the phenomenon of "prolonged residual psychosis," observed in 28% of users even after months of abstinence, suggesting permanent structural damage in thalamocortical circuits. These psychiatric conditions, often associated with severe thought disorganization and violent behavior, not only worsen the prognosis but also require specialized therapeutic approaches that integrate atypical antipsychotics (such as quetiapine), mood stabilizers, and intensive psychosocial interventions, though with often partial responses and high relapse rates, reinforcing the need for early preventive strategies and public policies aimed at this vulnerable population.

Santos (2024) analyzed the relationship between chemical dependency and neuropsychological comorbidities, demonstrating that chronic psychoactive substance consumption can lead to permanent cognitive and behavioral damage. Among the main observed effects are behavioral changes, immediate memory impairments, and the development of disorders like depression and anxiety. The research shows that addiction is linked to brain alterations that impair both executive control and emotional regulation. Additionally, the study points out that individuals with a family history of addiction have a higher risk of developing psychiatric disorders associated with drug use, thus perpetuating a cycle of vulnerability and relapse.

Medeiros, Ribeiro, and Trajano (2021) investigated psychotic disorders induced by the use of drugs like cocaine and crack, highlighting that their consumption can trigger acute and persistent psychotic episodes, marked by persecutory delusions and auditory hallucinations, especially in chronic users. The authors explain that cocaine directly interferes with dopaminergic neurotransmission, blocking the reuptake of this neurotransmitter and causing neuronal hyperactivity, which favors the emergence of psychotic symptoms. In some cases, these disturbances can become chronic, persisting even after discontinuation of use, demonstrating the severity of neurochemical damage caused by these substances.

2.2.4 Multidisciplinary Therapeutic Approaches

Effective treatment demands a multifactorial approach, combining pharmacological interventions, psychotherapy, and social support to address both acute symptoms and the involved psychosocial factors (Mendes & Silva, 2019). The complexity of the clinical picture necessitates integrated strategies that consider not only physical detoxification but also the management of psychiatric comorbidities, such as mood and anxiety disorders. A multidisciplinary team—including doctors, psychologists, psychiatrists, and social workers—is essential to provide comprehensive and personalized care.

The challenges in treating crack cocaine dependents are further amplified due to its high addictive potential and severe impacts on the central nervous system. Carvalho and Souza (2021) emphasize that the chemical and psychological dependence on this substance requires prolonged and specialized interventions capable of addressing both neurological damage and the patient's emotional and social vulnerabilities. Thus, successful therapeutic strategies must combine clinical support, psychosocial rehabilitation, and harm reduction policies, aiming for the individual's overall recovery.

Physical detoxification constitutes the first stage of treatment, where doctors may prescribe medications to alleviate withdrawal symptoms and reduce discomfort during substance cessation. Simultaneously, psychologists and psychiatrists offer emotional support and behavioral therapies to aid in managing psychiatric disorders associated with crack use. Social workers act in identifying and intervening in socio-environmental factors that perpetuate addiction, such as housing instability, unemployment, and fragile family ties, while occupational therapists work on developing practical skills and coping strategies to prevent relapse. As Carvalho and Souza (2021) highlight, this multidisciplinary approach is fundamental to providing comprehensive support, simultaneously addressing the biological, psychological, and social dimensions of addiction.

The rehabilitation process faces significant obstacles, particularly due to the high relapse rates among crack cocaine users, as pointed out by Lima and Fernandes (2022).

2.2.5 Social Factors and Rehabilitation Challenges

The combination of crack cocaine's highly addictive power and the precarious socioeconomic conditions many dependents face creates a vicious cycle of use, abstinence, and relapse. This pattern is exacerbated by the cognitive impairments resulting from chronic use, which compromise the ability to maintain abstinence and achieve social reintegration.

Neurocognitive studies, such as that by Cariste *et al.* (2022), demonstrate that crack profoundly affects attentional functions, including selective, sustained, alternating, and divided attention. These deficits stem from alterations in dopaminergic transmission in the prefrontal cortex and the reticular activating system—crucial structures for attention control, sensory processing, and motor regulation. Chronic users exhibit significant difficulties in maintaining

focus, especially on complex tasks, along with impaired inhibitory control that increases impulsivity and reduces the ability to evaluate consequences. These neurobiological alterations partly explain the risk behaviors and frequent relapses observed in this population, reinforcing the need for specialized interventions that encompass both cognitive rehabilitation and psychosocial support.

The findings of Cariste *et al.* (2022) highlight that the attentional and executive impairments resulting from chronic crack use represent a significant obstacle in the recovery process. The deterioration of planning ability and inhibitory control increases the propensity for relapse, even after periods of abstinence. Additionally, the study reveals a critical interaction between neurobiological and social factors: individuals in vulnerable socioeconomic contexts, exposed to stressors like financial instability and fragile support networks, tend to exhibit more pronounced cognitive impairments. These data reinforce the need for integrated interventions that combine neurological rehabilitation with psychosocial support strategies to address the multiple dimensions of addiction.

To address these challenges, implementing multifaceted relapse prevention strategies is essential. Cognitive-behavioral therapy (CBT) stands out as an effective tool, helping users recognize and manage environmental and emotional triggers associated with drug use. Through structured techniques, patients develop skills to modify dysfunctional thought patterns and build adaptive coping mechanisms for stress and anxiety, reducing dependence on crack as an escape (Lima & Fernandes, 2022). This individualized approach is complemented by strengthening support networks, creating a solid foundation for maintaining sobriety.

Integration into social support networks emerges as a vital component in the recovery process. Participation in groups like Narcotics Anonymous (NA) offers a safe space for sharing experiences, strengthening emotional resilience through identification with peers facing similar challenges (Lima and Fernandes, 2022). These environments not only provide a welcoming atmosphere but also function as an accountability system, where members mutually monitor their progress. Community programs that combine practical support—such as employment and housing assistance—with therapeutic follow-up demonstrate greater effectiveness in reducing relapse, especially in socioeconomically vulnerable populations.

In selected cases, pharmacotherapy can be incorporated as an adjunct to treatment. Medications like bupropion and naltrexone act by modulating craving and attenuating the drug's reinforcing effects, facilitating the maintenance of abstinence (Lima and Fernandes, 2022). It is crucial, however, that these interventions are personalized and integrated into a broader therapeutic plan, including psychological follow-up and social support. The synergy among pharmacological, psychotherapeutic, and community-based approaches represents the most promising paradigm for the sustainable treatment of crack cocaine addiction.

CONCLUSION

Crack cocaine has devastating effects on the central nervous system, profoundly altering dopaminergic neurotransmission and causing structural and functional brain damage. Its chronic use triggers irreversible cognitive impairments, including deficits in executive functions, memory, and attention, in addition to psychiatric comorbidities such as psychosis, depression, and anxiety. These neurobiological changes explain the high relapse rate and the complexity of treatment, which demands multidisciplinary interventions. These interventions integrate pharmacotherapy (to manage withdrawal and psychiatric symptoms), cognitive-behavioral therapies (for neuropsychological rehabilitation), and psychosocial support (for reintegration and vulnerability reduction). The effectiveness of treatment also depends on public policies that articulate prevention, harm reduction, and continuous access to specialized services, considering the multiple dimensions of addiction.

Despite advances, the scarcity of studies focused exclusively on the neurological mechanisms of crack cocaine limits a detailed understanding of its action in the brain. Future research should prioritize investigations into the drug's specific effects on different populations (such as adolescents and socioeconomically vulnerable groups), as well as test novel therapeutic interventions that combine innovative pharmacological approaches with cognitive rehabilitation strategies. The development of evidence-based protocols is urgent to address this public health challenge, requiring investment in basic and applied science, as well as integration among universities, healthcare services, and affected communities.

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