

Cocaine, a Form of Self-Medication

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Received: January 20, 2022; **Published:** March 30, 2022

Abstract

Cocaine use has increased significantly over the past decade, making the absence of treatments targeting this addiction an important issue in recent years. In 1983, the improvement of cocaine dependence was described for the first time with the use of psychostimulant medication, commonly used in the treatment of hyperactivity and attention disorder (ADHD).

ADHD is one of the most common disorders in childhood and its symptoms usually persist into adulthood and tend to occur with other disorders, such as substance use disorders. Adults with ADHD are at a greater risk of developing substance use disorders, with cocaine being the most abused substance, causing a feeling of tranquillity, which leads to the possibility of the self-medication hypothesis.

Methylphenidate and cocaine share a similar mechanism of action, differing mainly in the time of onset and the half-life, which makes these types of stimulating drugs promising for the treatment of cocaine addiction.

Keywords: Cocaine; ADHA; Dependency; Methamphetamine; Self-Medication

“When I started using cocaine, it calmed me down”.

In 1983 Khantzian described a case of a woman with extreme dependence on cocaine use who simultaneously presented symptoms of what we now know as attention deficit hyperactivity disorder. This patient was treated with methylphenidate and her condition improved. She was followed up for 30 years, with no relapse to cocaine use. A few years later, two additional cases were described of individuals who also responded favorably to psychostimulant treatment. For reasons still unknown, these promising data were ignored for more than a decade, being studied again only years later [1,2].

Cocaine is an alkaloid of the *Erythroxylon coca* bush and in ancient times the leaves of this bush were chewed for invigorating purposes. The psychostimulant effects result from the inhibition of catecholamine reuptake, with greater expression of dopamine. Cocaine prevents dopamine from being recycled, leading to the accumulation of large amounts in brain circuits, between nerve cells, interrupting their normal communication. Currently, it is the most used illicit stimulant substance in Europe, and its dependence is considered one of the most debilitating and lethal addictions [3].

Physiologically, the deregulation of these various brain circuits is responsible for the addictive nature of these substances. Dopaminergic dysregulation is responsible for the appearance of tolerance and withdrawal, hyperactivity in the prefrontal cortex and amygdala,

a consequence of glutamatergic dysregulation, responsible for the compulsive pattern characteristic of addiction disorders, and, finally, GABAergic dysregulation, with a decrease in GABA in the pallidum. ventral is associated with seeking behavior [3,4].

Methylphenidate is also a psychostimulant substance, structurally related to amphetamines and acting in the same brain region as these. Its effect occurs through the direct stimulation of alpha and beta-adrenergic receptors and indirectly through the release of dopamine and noradrenaline at synaptic terminals [2,4].

The clinical condition that we currently call attention deficit hyperactivity disorder (ADHD) was first described by Still in 1902 in restless, impulsive, and inattentive children as “Minimal Brain Injury Syndrome”. This syndrome was thought to be secondary to encephalitis lethargica caused by the influenza virus. In 1937, Bradley administered to a group of these children benzedrine, a stimulant drug initially used as a nasal decongestant, with amphetamine in its composition, demonstrating apparent effectiveness. In 1960 Connors and Isenberg raised the etiological hypothesis of dopamine [2,5,6] deficit.

ADHD is currently described as a neurobehavioral disorder and according to the DSM-V is characterized by “a persistent pattern of inattention and/or hyperactivity and impulsivity that interferes with functioning or development”. The diagnosis is based on the presence of six or more functionally harmful symptoms of inattention and hyperactivity-impulsivity, which are present in two or more different environments, and that several of these symptoms are present before the age of twelve [5,7].

This neurobehavioral disorder is one of the most common in childhood and is present in up to 18% of children and adolescents, with the majority maintaining harmful symptoms in adulthood, affecting 2.5% to 4% of adults in the general population. This disorder is present in 10 to 24% of adults seeking treatment for substance use disorders [2,8].

Several studies suggest that ADHD is 5 to 10 times more common among individuals with alcohol and other substance use disorders. It appears that 14% of children diagnosed with ADHD between 15 and 17 years of age develop problems related to alcohol abuse or dependence as adults. It is also verified that analyzing alcohol consumption in children (average age 14 years), 40% of them have a diagnosis of ADHD compared to 22% without a diagnosis of this disorder. Regarding alcohol consumption in young adults (average age of 25 years) they have the same probability of consumption of alcohol as adults without this diagnosis, however, those diagnosed with ADHD were more likely to consume alcohol in excess [8,9].

As previously described, adults with ADHD have a higher risk of developing substance use disorders, with cocaine being the most commonly abused substance, raising the possibility of the self-medication hypothesis. Some cocaine users with ADHD symptoms initially obtain a therapeutic effect, however, with continued consumption, responses to use are increasingly negative [5,8,10].

The psychopharmacological treatment indicated for ADHD is based on psychostimulants, such as methylphenidate, which acts by blocking the reuptake of dopamine and noradrenaline in the nucleus accumbens, also known as the brain’s reward center. Stimulation and activation of the motor inhibitory system in the orbital-frontal-limbic axis develop, leading to an increase in the inhibition of impulsivity and consequently improvement in executive functioning. Sharing a similar mechanism of action, methylphenidate and cocaine differ mainly in time of onset of action and half-life [2,11,12].

A major concern with agonist therapies in substance use disorders is their potential for abuse. It is known that one of the factors that most contribute to the development of addiction and drug abuse is how quickly a substance increases dopamine levels, so the faster dopamine levels increase, the greater the potential for abuse. In studies carried out it was found that the drug of trade name Ritalin (methylphenidate hydrochloride) takes about an hour to increase the levels of dopamine in the brain. In comparison, inhaled cocaine only takes a few seconds. Given this time difference, this risk of abuse or undue diversion to recreational uses is mitigated, in the case of methylphenidate, by the use of long-lasting formulations, without rapid absorption and elimination [2,11].

Currently, on the market there are different formulations of methylphenidate, which differ in the time of onset of action and half-life, acquiring the denominations of immediate or prolonged release. It is important to refer to lisdexamfetamine dimesylate, which is a pharmacologically inactive prodrug. After oral administration, lisdexamfetamine is rapidly absorbed from the gastrointestinal tract and requires enzymatic hydrolysis that results in a slow rise in the serum level of dexamphetamine which is responsible for the drug's activity, providing a possibly reduced potential for diversion or abuse. In a comparative study of the oral and intranasal routes of drug administration, it was found, counter-intuitively, that the rate of elevation of the serum level of dexamphetamine in either route of administration was identical, also decreasing the potential risk of abuse [13].

Conclusion

When we are faced with substance use disorders, namely psychostimulants such as cocaine, it is important to note the importance of collecting a detailed clinical history, with a special focus on development during childhood and adolescence and how consumptions began in this way as its effects.

A large percentage of patients with drug use disorders presented symptoms of undiagnosed ADHD in the past, and it is not possible to exclude the maintenance of symptoms, as many of these persist into adulthood. These patients usually describe a paradoxical feeling of calm and tranquility with cocaine use, which is one of the reasons why they continue to use cocaine.

Although these effects have been described since 1983, the treatment of this dependence with dopamine agonists is still controversial given the potential for abuse. However, with the emergence of new formulations with the longer onset of action and longer half-life, this potential is reduced, translating into a possible therapeutic option in the treatment of addictions.

Conflict of Interests

The authors declare that they have no conflict of interest.

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Volume 13 Issue 4 April 2022

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