Article published online: 2023-10-18

Thermocoagulation in Multiple Targets to Treat Obsessive-Compulsive Disorder Associated with Drug Addiction: Case Report

Termocoagulação de múltiplos alvos para tratar transtorno obsessivo-compulsivo associado à drogadição: relato de caso

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Arq Bras Neurocir

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Abstract

Substance-related disorders are chronic psychiatric conditions defined by substance abuse, and they compromise patients both clinically and functionally. Currently, pharmacotherapy, behavioral therapy, or an association of both are the treatments of choice for obsessive-compulsive disorder associated with drug addiction. However, the refractoriness to treatment, as a result of the high failure rates of these approaches, has led to the need to develop surgical techniques to treat severe cases of substance-related disorders. In the present article, we report the case of a patient who underwent neurosurgery through the stereotactic technique after refractoriness to the conventional treatment for drug addiction. The patient showed sustained improvement in his addiction to drugs. Despite the numerous reports on the effectiveness and applicability of neurosurgery in psychiatric disorders, some concerns regarding stereotactic surgery as a treatment for drug addiction still remain, especially in relation to its efficacy, safety, and ethical implications.

Keywords

- obsessive compulsive disorder
- drug addiction
- thermocoagulation
- case report

Resumo

Transtornos relacionados ao uso de substâncias são condições psiquiátricas crônicas definidas pelo abuso de substâncias, que deixam o paciente comprometido clínica e funcionalmente. Atualmente, a farmacoterapia, a terapia comportamental ou a associação de ambas são os tratamentos de escolha para o transtorno obsessivo-compulsivo associado ao vício em drogas. Contudo, a refratariedade ao tratamento, resultante das altas taxas de fracasso dessas abordagens, tornou necessário o desenvolvimento de técnicas cirúrgicas para tratar casos graves de transtornos relacionados ao uso de substâncias. Neste artigo, relatamos o caso de um paciente submetido a neurocirurgia pela técnica estereotáxica após fracasso do tratamento

Palavras-chave

- transtorno obsessivo-compulsivo
- dependência de drogas
- termocoagulação
- relato de caso

received
November 22, 2021
accepted
March 7, 2023

DOI https://doi.org/10.1055/s-0043-1774747.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

convencional para drogadição. O paciente apresentou melhora sustentada do vício em drogas. Apesar dos inúmeros relatos sobre a eficácia e a aplicabilidade da neurocirurgia em transtornos psiquiátricas, ainda existem certa preocupação a respeito da cirurgia estereotáxica como tratamento para a drogadição, principalmente em relação à sua eficácia, segurança e implicações éticas.

Introduction

Substance-related disorders are chronic psychiatric conditions defined by substance abuse, and they compromise patients both clinically and functionally.[1] Patients affected by these disorders present with intense compulsive cravings for drugs, which persist despite the severe consequences they face because of their addiction.

In addition to the clinical and functional impairment of the patients, the problems associated with addiction are responsible for a huge economic and social burden on society. Even after prolonged periods of withdrawal, a high risk of relapse persists, due to the recall of memories associated with the addictive substance and exposure to stressful situations or those that trigger cravings.[2]

Currently, pharmacotherapy, behavioral therapy, or a combination of both are the main treatments for obsessive-compulsive disorder (OCD) associated with drug addiction.[3] Nevertheless, the high failure rates of these approaches have resulted in refractoriness to the treatments, making it necessary to develop surgical techniques to treat severe cases of substance-related disorders.[1]

In the present article, we report the case of a patient who underwent neurosurgery through the stereotactic technique after failure of the conventional treatment for drug addiction. The article aimed to describe possible treatment targets for OCD associated with drug addiction, as well as their indications and applications.

Case Report

A 25-year-old male patient sought treatment in our service after a 6-year history of drug addiction, which had begun when he was 19 years old. He first smoked cannabis and then started using cocaine. He used these drugs daily, and although the amount was variable, consumption was gradually increasing. The patient reported an attempt to end the dependence without any professional guidance, which resulted in irritability and anxiety during the periods of withdrawal; therefore, he also developed nicotine addiction. The patient made some attempts to quit the drugs by adopting a conservative treatment with the use of antidepressant medication as well as psychological treatment in rehabilitation clinics. As a result, he even went through a six-month period without constant drug use but experienced several relapses.

The patient had a history of depression, attempted suicide, and hypothyroidism. A psychiatric assessment was performed, and he was diagnosed with OCD associated with drug addiction. The patient filled out the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), a non-diagnostic scale to evaluate the severity of obsessive-compulsive symptoms, with scores ranging from 0 to 40, and he reached a total score of 16.

In 2019, the medical team and the patient's family, in consensus and following the protocol of the Brazilian Federal Council of Medicine, opted for the surgical procedure. Throughout the 30 days of drug withdrawal before the surgery, the patient presented nervousness, anxiety, and insomnia. He underwent thermocoagulation using a stereotactic technique, targeting the anterior limb of the internal capsule, the subgenual area, the nucleus accumbens, and the cingulate gyrus. Bilateral ablation of multiple targets was performed using an electrode with a 4-mm exposed tip at 70°C for 60 seconds.

In the first four months after the surgery, the patient underwent monthly follow-ups with our neurosurgery team, with subsequent follow-ups every three months, and then every six months. Another psychiatric evaluation was performed four months after surgery, when the patient was assessed once more using the Y-BOCS, with a total score of 3. The craving for cocaine ceased shortly after the surgical procedure. Nonetheless, the addiction to nicotine remained. Improvements in quality of life, sleep, and social, family, and professional functioning were observed since the first postoperative month. Although the patient reported slow reasoning and difficulty in articulating ideas in the first three postoperative months, his cognitive functions, especially memory, learning, and planning started showing improvement from three months onwards. He lost 20 kg after surgery but had no other major side effects.

The collection of data about the case was performed with the authorization of the patient, after he signed the Informed Consent Form, which was submitted to and approved by the Ethics in Research Committee of Pontifícia Universidade Católica de Goiás (CAAE: 39924920.6.0000.0037), following national and international guidelines.[4,5]

Discussion

Since ancient times, numerous attempts have been made to treat mental illnesses surgically. Trephination of the human skull, the oldest known neurosurgical procedure, has been used as part of the treatment of psychiatric disorders.[6,7] The first published account of an ablative surgery to treat psychiatric patients was made by Burkhardt in 1892.[8] Nevertheless, the popularization of neuropsychosurgery (NPS)

only occurred in 1935, with António Egas Moniz and Pedro de Almeida Lima, who performed the first frontal leucotomy, aiming to treat psychiatric patients with depression, anxiety, and aggressiveness.[7] Walter Freeman and James Watts further refined the leucotomy technique, enabling a more precise location of the lesion using anatomical landmarks.[9] Despite the effectiveness of the surgery, its indiscriminate application, associated with the emergence of pharmacological drugs, led to prejudice against leucotomy and the consequent decline in neurosurgical treatments for psychiatric disorders starting in the 1950s.[8,9]

As stereotactic surgery improved, the therapeutic targets have gradually become more precise.[10] In stereotactic surgical procedures, small lesions are created in specific targets, modifying neuronal activity without damaging the nervous system.[11] The selection of target points to be injured during the NPS procedure for the treatment of psychiatric disorders was greatly influenced by the description of the limbic system as the essence of human emotions.[12,13] As a consequence of the improvements in stereotactic techniques, the medial thalamic nucleus, the hypothalamic nucleus, and the amygdaloid nucleus, which make up the limbic system, and are considered the biological determining center of individual conduct, have become surgical targets for psychiatric disorders.[10]

Stereotactic neurosurgery as a treatment for drug addiction was first used between the 1960s and the 1970s.[11] Substance-related disorders are characterized by psychological and physical dependence.[14] Drug addiction is associated with OCD, a mental illness that is caused by a dysfunction in the dopaminergic inhibitory system, and its symptoms are the most important characteristics in chemically dependent people with psychological dependence.[14,15]

Neurosurgery has emerged as a therapeutic measure for substance dependence based on the understanding of the neurocircuitry of drug addiction and its recognition as a psychiatric disorder. As stereotactic procedures for drug addiction treatment evolved, multiple targets have been tested. Leucotomy was the first stereotactic neurosurgery used to treat substance dependence.[11] Subsequently, hypothalamotomy was reported as a surgical treatment for chemical dependency because it increased the patients' self-control. Nonetheless, it also produced serious side effects, such as amnestic syndrome, ophthalmic disorder, and vegetative crisis.[11,14]

Currently, NPS has gained ground in the treatment of psychiatric illnesses due to refractoriness to the conventional treatment, defined as the use of drugs for more than three years and at least three unsuccessful treatments.[16] The essential criteria used for the indication of neurosurgery in OCD include a diagnosis of at least five years; previous use of at least three serotonin reuptake inhibitors (clomipramine, mandatorily) and two effect enhancers at the maximum recommended doses for at least 12 weeks; a minimum of 20 hours of behavioral therapy; and rates of symptomatic improvement in the Y-BOCS lower than 25%.[17]

The theoretical foundation that supports the targets of surgical interventions in OCD is functional neuroimaging findings.[17] Resting computed tomography (CT) of patients with OCD shows increased activity in the orbitofrontal gyrus, cingulate gyrus, and caudate nucleus, unlike the images of patients without the disease. Furthermore, a normalization of activity is observed in these regions after clinical therapy in individuals who respond to conventional treatments.[18]

Although the drugs involved in substance-related disorders have different chemical structures and target sites, the main mechanism that culminates in drug addiction is the reward system.[19] In the 1950s, James Olds and Peter Milner discovered that, when stimulated, certain areas of the brain, identified as reward centers, provided a feeling of pleasure. Due to its numerous receptors for the neurotransmitter dopamine, known as the "pleasure molecule," the limbic system and the nucleus accumbens have become the main representatives of these centers.[20]

Psychoactive substances increase the discharge of dopamine in the nucleus accumbens, decreasing neuronal inhibition, thus causing the activation of the reward system. Dopaminergic neurons are projected from the ventral tegmental area to the ventral striatum (including the nucleus accumbens), septal nuclei, amygdala, and prefrontal and cingulate cortices. In addition to activating the reward system, drugs cause an increase in dopamine release in the amygdala, which strengthens the relationship between the rewarding characteristics of the substances and the exteroceptive sensations.[14]

The nucleus accumbens in the limbic system is responsible for the integration involving cognitive and affective information and reward-driven behaviors from the prefrontal cortex. Psychoactive substances stimulate this neurocircuit and the continuous use of the drugs become essential for the survival of the patients.[21]

In the natural history of addiction, the patient goes through three stages that make up a cycle: the first is the "binge/intoxication" phase, the second is the "withdrawal/negative affect" phase, and the third is the "preoccupation/anticipation" (craving) phase.[22] To be considered effective, addiction treatments must ensure successful interventions during all these phases to avoid behavioral responses.

The brain circuitry involved in the long-term chronic effect of drug addiction includes, in addition to the reward effect regulators, circuits involved in learning and memory, as well as those in charge of processing and storing substance-induced rewarding stimuli. Therefore, the hippocampus, amygdala, limbic system, and cerebral cortex play important roles in the neurocircuitry of substance-related disorders.[19]

In the patient of the present case report, the thermocoagulation targets were the nucleus accumbens, anterior limb of the internal capsule, cingulate gyrus, and subgenual area. These targets were chosen after an analysis of the patient's clinical history, self-reported behavior, and psychiatric assessment. However, no consensus has already been reached on the best targets to be chosen for the surgical treatment of OCD associated with drug addiction.

Anterior capsulotomy is based on the disconnection of fibers that connect the orbitofrontal cortex and the limbic

system, located between the caudate nucleus and the putamen. Although this surgical intervention can cause side effects such as weight gain, fatigue, and headache, it generally yields results that are more satisfactory and causes fewer side effects compared with procedures in other brain regions.[23]

The cingulate gyrus has been described as an important point for ablative lesions when aiming to interrupt obsessive thinking connected to substance abuse.[11,14] It is an indicated target for the treatment of affective diseases, chronic anxiety states, OCD, as well as drug addiction.[8] Anterior cingulotomy, first suggested by John Fulton, consists of a bilateral lesion of the anterior cingulate with the objective of interrupting the connection of the cingulate cortex, the orbitofrontal cortex and the limbic system, thus blocking the reward system. The subgenual area is located in the cingulate cortex as a narrow band in the caudal portion of the subcallosal area. It is important in the regulation of emotional responses and, consequently, its ablation especially helps control the emotional state of intense desire for the effects of drugs.[24]

In a clinical study conducted in China,[25] the authors reported that, for the first time, ablation of the nucleus accumbens successfully alleviated drug addiction and simultaneously decreased the relapse rate. The mesolimbic dopaminergic system plays an important role in the reward mechanisms of the brain and the functions of the nucleus accumbens. Therefore, thermocoagulation of the nucleus accumbens leads to the blockade of this circuit, which prevents both the craving for drugs and the relapses.[26]

The possible complications of ablative stereotactic surgeries for the treatment of OCD associated with drug addiction are generally nonspecific, including those not related to the functions of the target area, such as fever, headache, urinary incontinence, and epilepsy. Nevertheless, some specific complications, closely related to the function of the injured targets, such as personality changes, memory complaints, affective disorders, and paraphilias may also occur. The rates of both types of complications do not exceed 5%, and they usually disappear gradually after the appropriate management.[19]

Nowadays, current stereotactic neurosurgery results in less severe adverse events and complications.[17] The patient in the case herein reported presented a mild and transient complication of slow reasoning during the first three months after the neurosurgical procedure, and he remained addicted to nicotine. Interestingly, the patient lost 20 kg in the postoperative period, contradicting the trend of weight gain after NPS.[27]

After the stereotactic surgery, the patient showed sustained improvement and did not have any relapses, corroborating literature data.[1,17,19] The Y-BOCS, used to assess the severity of his OCD symptoms, was applied pre- and postoperatively, and the score of the patient decreased by over 80% postoperatively, evidencing that the stereotactic procedure led to an important improvement in his symptoms.

Despite numerous reports[9,11,14] on the effectiveness and applicability of NPS in psychiatric disorders, certain concerns regarding stereotactic surgery as a treatment for drug addiction remain, especially in relation to its safety and efficacy. One of the concerns is related to the permanent injuries caused by the stereotactic technique,[14] performed in areas of the brain that mediate drug addiction, as well as mood, natural reward, and motivation.[11]

Establishing specific surgical methods for each psychiatric disorder, with more precisely targeted lesions, lower rates of complications, and absence of personality and cognitive adverse effects are the biggest challenges for the future of NPS, and they may be the answers to questions about the safety of the procedure. Ethical issues and the prejudice against psychiatric neurosurgeries date back to the period of lobotomies,[8] raising questions about whether written informed consents were signed by the patients or even if independent reviews were performed before the treatments.[11]

Stereotactic surgery remains a potential treatment for drug addiction, as contemporary pharmacological and behavioral treatments do not cure this condition.[11] Currently, this surgical technique, which has already been proven to be a viable option with excellent results in carefully selected cases, is indicated only for patients who are refractory to the clinical treatment.[28]

Finally, neuromodulation for mental illnesses needs to focus on the approach for the selection of targets and will probably incorporate multiple targeting methods. Patient specificities should not be underrated, and an individualized symptom- and patient-directed approach is necessary.[9]

Conclusion

Given the large biopsychosocial impact of substance-related disorders, their treatment attracts considerable scientific interest. Considering the current lack of evidence that cognitive or pharmacological treatments promote the cure of drug addiction, in addition to their high relapse rates, neurosurgery is a potential therapeutic option for OCD associated with drug addiction. Nowadays, despite its proven efficacy and few side effects, its application is limited to cases refractory to conventional treatments. Therefore, further studies that address stereotactic surgery using multiple targets for the treatment of OCD associated with drug addiction are needed.

Conflict of Interests

The authors have no conflict of interests to declare.

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