Published online: 2020-04-06

Neurosurgical Treatment for Drug Addiction: Systematic Review

Tratamento neurocirúrgico para drogadição: Revisão sistemática

Patrícia Leonardo Magalhães dos Santos[1] Rafaella Oliveira Curti[1] Ledismar José da Silva[1]

[1] Departament of Medicine, Escola de Ciências Médicas, Farmacêuticas e Biomédicas, Pontifícia Universidade Católica de Goiás (PUC-Goiás), Goiânia, GO, Brazil

Arq Bras Neurocir 2020;39(2):116–124.

Address for correspondence Ledismar José da Silva, MSc, Departamento de Medicina, Escola de Ciências Médicas, Farmacêuticas e Biomédicas, Pontifícia Universidade Católica de Goiás (PUC-Goiás), Avenida Universitária 1.440, Setor Universitário, 74605-010, Goiânia, GO, Brazil (e-mail: ledismarsilva@gmail.com).

Abstract

Substance-related disorders are psychiatric conditions that have a worldwide impact. Their multifactorial cycle has been treated pharmacologically and with therapeutic support. However, high refractoriness rates and difficulty to control relapses are among the pitfalls associated with these disorders. Thus, recent studies have shown that deep brain stimulation (DBS) is a promising treatment, with a direct intervention in the neurocircuitry of addiction. The results of the present systematic review of the use of DBS for the treatment of drug addiction show that this surgical procedure can reduce the desire for the drug, and, in some cases, establish abstinence, improve psychiatric symptoms related to mood and quality of life, and reintroduce the patient into the social and family environments. Nevertheless, this approach is still limited to the academic realm, based mainly on case reports, with ethics and therapeutic protocols still to be defined. Further in-depth scientific investigations are required to recommend its clinical application.

Keywords

- substance-related disorders
- deep brain stimulation
- systematic review

Resumo

Os transtornos relacionados ao uso de substâncias são desordens psiquiátricas com impacto mundial. Seu ciclo multifatorial tem sido tratado farmacologicamente e com apoio terapêutico. Entretanto, as altas taxas de refratariedade e a dificuldade no controle das recaídas estão entre os perigos associados com essas desordens. Dessa forma, estudos recentes mostraram que a estimulação cerebral profunda (ECP) é um tratamento promissor, em que é feita uma intervenção direta na neurocircuitaria do vício. Os resultados desta revisão sistemática da literatura sobre a aplicação de ECP no tratamento de dependência química demonstram que este é um procedimento cirúrgico capaz de reduzir o desejo pela droga, e, em alguns casos, estabelecer a abstinência, melhorar os sintomas psiquiátricos relacionados ao humor e à qualidade de vida, e reintroduzir o paciente no ambiente social e familiar. No entanto, esta ainda é uma abordagem limitada ao âmbito acadêmico, baseada principalmente em relatos de casos, com questões éticas e protocolos terapêuticos a serem definidos. É necessário maior aprofundamento científico para que sua aplicação clínica seja recomendada.

Palavras-chave

- transtornos relacionados ao uso de substâncias
- estimulação cerebral profunda
- revisão sistemática

received
October 8, 2019
accepted
December 11, 2019

DOI https://doi.org/10.1055/s-0040-1702976.
ISSN 0103-5355.

Introduction

Substance-related disorders are chronic psychiatric conditions characterized by the recurrent use of elements that cause significant clinical and functional impairment to the patient. They are generally connected to eleven types of drugs: alcohol, tobacco, caffeine, cannabis, hallucinogens, inhalants, opioids, sedatives, hypnotics, anxiolytics, and stimulants.[1] The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) established 11 criteria for substance abuse and dependence, and substance-related disorders are usually diagnosed when two or more of these criteria are met within a period of one year.[2]

In 2005, alcohol was the most prevalent addictive substance, with an estimated 63.5 million cases worlwide.[3] Overall, the estimated prevalence in the adult population was of 18.4% for heavy alcohol use, followed by 15.2% for daily tobacco use, and 3.8%, 0.77%, 0.37%, and 0.35% for the past-year use of cannabis, amphetamine, opioids, and cocaine respectively.[3]

Pharmacological treatment is currently the therapy of choice to interrupt the multifactorial cycle of the disease, in addition to personal and family therapeutic support.[4] However, high failure rates in this approach have resulted in treatment refractoriness, defined as drug use for more than three years associated with at least three unsuccessful pharmacological treatments.[5,6] Therefore, in cases of extreme severity, deep brain stimulation (DBS) may be indicated for patients diagnosed with substance-related disorders.[4]

Therefore, the present systematic review aimed to critically describe researches involving DBS for the treatment of substance-related disorders that reflect relevant and current scientific contributions to a topic still underexplored.

The Neurocircuitry of Addiction

The neurobiological basis of this disorder is well-defined by the reward system, which is composed of the dopaminergic mesolimbic and mesocortical pathways. The ventral tegmental area is simultaneously connected with the limbic system and the prefrontal, orbitofrontal, and anterior cingulate cortices.[7] Both the mesolimbic and mesocortical pathways include the release area of dopamine, the neurotransmitter responsible for triggering feelings of pleasure and euphoria. In addition, these pathways act in parallel and interact with other structures, such as GABAergic, glutamatergic, and serotonergic neurons. The key role of the nucleus accumbens (NAc) in the limbic and motor interface is to integrate cognitive and affective information such as hippocampal contextual, amygdala emotional, and reward-guided behaviors of the prefrontal cortex.[8] The use of psychoactive substances leads to the artificial stimulation of this neurocircuitry at different intensities, depending on the chemical compound. Motivation for the continuous use of the drug occurs, therefore making it indispensable for the survival of the patients.[9]

The natural history of addiction is described from controlled and occasional use to complete substance dependence. Based on this, the patient goes through three phases, which are not necessarily isolated, that make up a cycle: the first one is the phase of compulsion and intoxication; the second, is of withdrawal and negative effect; and the third, is of preoccupation and anticipation.[10] To be considered good, treatments for substance addiction have to effectively provide intervention in these three phases, preventing the activation of specific neuronal pathways and their consequent clinical and behavioral characteristics.[11] A promising technique is DBS, which acts in the neuronal source of the disease in a reversible way. Hence, this surgical procedure has been investigated as more effective than other treatments for substance-related disorders.[12]

Methods

The present study is a systematic review of the application of DBS for the treatment of substance-related disorders. It was performed by two independent researchers, and was based on the methodological protocol recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[13] The electronic databases consulted were: the National Center for Biotechnology Information (NCBI), Medical Literature, Analysis, and Retrieval System Online (MEDLINE), Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, and Portal de Periódicos da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, in Portuguese). The search descriptors used were retrieved from the medical subject headings (MeSH): *Deep Brain Stimulation*; *Addiction*; and *Substance-Related Disorders*. They were combined in each database using the following Boolean operators: *Deep Brain Stimulation* AND *Substance-Related Disorders*; and *Addiction* AND *Substance-Related Disorders*. The search started in October 2018 and ended in August 2019.

For the selection of the studies, the following inclusion criteria were chosen: 1) DBS treatment in patients diagnosed with substance-related disorders with no restriction regarding gender, age, ethnicity, or substance; 2) experimental human studies and case reports; and 3) studies in English, Spanish, or Portuguese.

The exclusion criteria were: 1) animal studies and literature reviews; 2) studies addressing other psychiatric disorders, without drug addiction as the focus; 3) studies that included non-DBS surgical treatments; 4) articles that did not have enough information; 5) clinical trials that were discontinued or that had no results; and 6) duplicate studies.

Initially, the articles were evaluated based on the inclusion and exclusion criteria, and by reading their titles and abstracts. After that, the selected articles were read in full and included in the study.

During data extraction, the following parameters were arranged in a standardized way: authors, year of publication, surgical target, sample size, drug of abuse, type of study, DBS parameters, laterality, adverse effects, period of follow-up, and outcomes.

Results

Study Selection

The electronic search resulted in 141 articles, 118 of which were excluded after reading the titles and abstracts, and 2

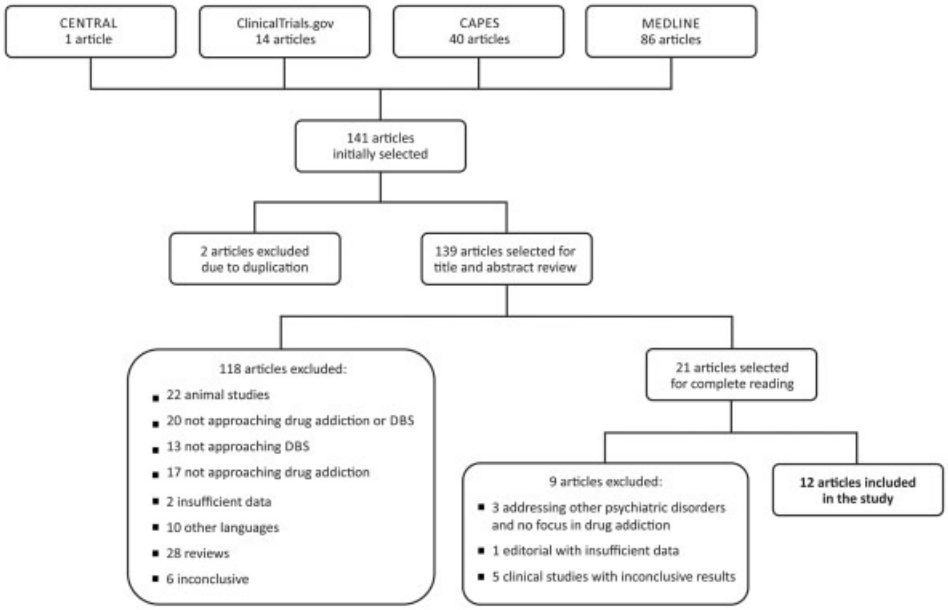

Fig. 1 Study selection for the systematic review.

were duplicates. Therefore, 21 articles were selected for a full-text reading. After reading them, 9 articles were excluded, and 12 were included in the present systematic review for a final analysis (►**Fig. 1**).

Study Characteristics

The 12 articles selected are summarized in ►**Table 1**. They have an experimental character, with surgical approach using DBS for the treatment of patients that have shown to be refractory to clinical treatment for substance abuse.

The samples of the studies were limited, with a minimum of 1 and a maximum of 8 patients per study, totaling 21 subjects. A predominance of male patients was observed (90%), and their ages ranged from 22 to 69 years. This diagnosis was more common around the third decade of life (58%), and most cases involved long-term users (71.42%), with an average period of drug use between 20 and 30 years.

Substance-related diagnoses included disorders regarding the use of heroin (62%), alcohol (33%), and cocaine (5%), and 1 study analyzed patients who used multiple drugs, including alcohol, heroin, amphetamine, and benzodiazepines, but it focused on heroin.[14] Nicotine was not considered a drug to be treated in the selected studies; however, patients who also used nicotine in association with any other of the aforementioned drugs obtained an additional reduction or cessation of use of this substance after DBS.[15–19]

The treatment using DBS in all studies was composed of steps, from planning electrode implantation to obtaining the results in the follow-up. In of all the studies included in this systematic review, the surgery planning phase was performed employing the stereotactic technique for the anatomical location of the surgical target. The NAc was the preferred surgical target in all of the treatments, and, in addition to it, some studies have also addressed the anterior arm of the internal capsule (50%),[15,20–24] the bed nucleus of the stria terminalis (8%),[22] the ventral capsule (8%), and the ventral striatum (8%).[19] In these areas, bilateral quadripolar electrodes were implanted and later connected to an electrical stimulation generator implanted in the thoracic region. Some studies have stipulated a time interval between implantation and activation of electrode stimulation. In 33% of the studies included, the activation took place after one week;[16,20,21] in 25%, after two weeks;[19,23,24] and, in most of them (42%), DBS was activated on the same day of surgery.[14,15,17,18,22,25]

The DBS parameters were individualized according to the patient, with the frequency ranging from 130 Hz to 185 Hz, with a predominance of 130 Hz, the pulse width ranging from 90 µsec to 275 µsec, with a predominance of 90 µsec, and the amplitude ranging from 1 V to 6 V, with a predominance of the the 2.5-4.5 V interval. The DBS parameters were adjusted and optimized over time according to each patient's therapeutic response.

Before and after DBS, the patients were followed and analyzed in different ways regarding their responses to the new treatment. All studies applied different types of scales to the patients during the pre- and postoperative periods to measure the clinical evolution of the chemical dependence and the neuropsychiatric symptoms. The main instruments applied were: the Symptom Checklist 90, the Obsessive Compulsive Drinking Scale, the Alcohol Urge Questionnaire, the Alcohol Dependence Scale, the Visual Analogue Scale, and the Desire for Drug Questionnaire. Other ways to evaluate patients were through hospitalizations, during outpatient consultations, telephone calls, family interviews, and blood and/or urine toxicology tests.

The follow-up of all of these patients ranged from 3 months to 8 years, with an average of 2 years, and 5 of them were lost to follow-up. The first patient was lost because of relocation due to a new job, whereas the second and third ones died from alcohol-related causes;[18] the fourth patient died from heroin

Table 1 Literature review of DBS studies on drug addiction

Target	Sample (n)	Drug	Type of study	Stimulation parameters	Laterality	Adverse effects	Follow-up period	Results	Reference
Nucleus accumbens	3	Alcohol	Case report	130 Hz, 90 µsec, 3.5–4.5 V	Bilateral	Transient hypomania (patient 2)	12–18 months	All patients lost their desire for alcohol and began to enjoy life	Müller et al.[15]
Nucleus accumbens	1	Alcohol	Case report	130 Hz, 120 µsec, 5.5 V	Bilateral	Obsessive compulsive traits	1 year	Significant reduction in drug use and improvement in cognitive control deficits	Kuhn et al.[25]
Nucleus accumbens	1	Heroin	Case report	145 Hz, 120 µsec, 0.8–2.5 V	Bilateral	Mild confusion and urinary incontinence, both with full recovery within 12 hours	6 years	Abstinence; returned to work; further reduced cigarette consumption; improved memory scales, IQ, and symptoms of depression and anxiety	Zhou et al.[16]
Nucleus accumbens	1	Alcohol	Case report	130 Hz, 90 µsec, 3.5 V	Bilateral	Transient hypomania	2 years	Abstinence; reduction in desire for alcohol; improved behavioral control during decision-making	Heldmann et al.[20]
Nucleus accumbens and internal capsule	1	Heroin	Case report	180 Hz, 90 µsec, 3.5 V	Bilateral	–	6 months	After dorsal electrode stimulation, reduction in heroin use on weekends, and then cessation for 6 months, except for a 14-day relapse	Valencia-Alfonso et al.[21]
Nucleus accumbens	5	Alcohol	Case series	130 Hz, 90 µsec, 3.5–4.5 V	Bilateral	Transient hypomania (patient 2)	2 years	Patient 1: abstinence; returned to work; patient 2: abstinence; returned to work; patient 3: relapses; reduction in consumption; patient 4: abstinence in the beginning; later relapses at 16 months; electrode dislocation after 2.5 years; patient 5: relapses and reduction in consumption	Voges et al.[17]
Nucleus accumbens	2	Patient 1: heroin, alcohol and amphetamine; Patient 2: heroin, amphetamine, and benzodiazepine	Case report	130–140 Hz, 90–120 µsec, 4.5–5 V	Bilateral	Patient 2: epileptic seizure 2 days after surgery, but with a history of epileptic seizures	2 years	Both patients abandoned the use of heroin permanently, and showed an improvement in the symptoms of depression-anxiety, and increased quality of life according to perception scales. Both increased the occasional use of other psychotropic drugs due to boredom or coexisting social/private problems	Kuhn et al.[14]

(*Continued*)

Table 1 (*Continued*)

Target	Sample (n)	Drug	Type of study	Stimulation parameters	Laterality	Adverse effects	Follow-up period	Results	Reference
Nucleus accumbens, bed nucleus of the stria terminalis, and anterior limb of the internal capsule	1	Cocaine	Longitudinal, double-blinded, cross-sectional, randomized case-control	Right hemisphere: 150 Hz, 150 µsec, 3–4 V; left hemisphere: 150 Hz, 150 µsec, 2.5–3 V	Bilateral	Unpleasant feeling of heat, sweating, redness, metallic taste, decreased libido, and transient weight gain	2.5 years	Significant drop in the severity of the dependence and control over cocaine use and craving	Gonçalves-Ferreira et al.[22]
Nucleus accumbens	5	Alcohol	Case series	130 Hz, 90 µsec, 3.5–4.5 V	Bilateral	Transient hypomania (patient 2)	8 years	Patient 1: abstinence for 8 years; works as a craftsman; denied craving for alcohol; patient 2: abstinence for 6 years, until losing contact with the study by relocation; graduated in nursing; patient 3: relapses; reduction in consumption; denied desire for alcohol; died due to non-DBS related cause; patient 4: abstinence in the initial 16 months of DBS, with later relapses; electrode dislocation after 2.5 years of DBS; depressive symptoms due to external causes; died after 4 years of the DBS because of a non-DBS related cause; patient 5: relapses; reduction in consumption; depressive symptoms due to external causes	Müller et al.[18]
Nucleus accumbens and anterior limb of the internal capsule	7	Heroin	Open-label pilot	145–185 Hz, 180–249 µsec, 2.0–3.3 V	Bilateral	Hypomania, insomnia, anxiety and dizziness; all of these symptoms were transitory	40 months	None of the patients showed immediate changes in their desire for the drug. Four patients had better mood and more vigor. After one month, significant decrease in the visual scale of drug dependence. The other three patients showed better mood and more vigor. Four patients were abstinent for 40, 35, 23, and 21 months. Two patients relapsed 7 and 10 months after surgery. One patient was	Ge et al.[23]

Table 1 (*Continued*)

Target	Sample (n)	Drug	Type of study	Stimulation parameters	Laterality	Adverse effects	Follow-up period	Results	Reference
								lost to follow-up after 3 months	
Ventral capsule and ventral striatum	1	Heroin	Case report	90–174 Hz, 90–275 μsec, 3.5–5.5 V	Bilateral	Transient hypomania	3 months	Initial decrease in cigarette consumption, improved insomnia, decreased heroin dependence, and return to work. Gradual increase in the desire for the drug and frequent relapses 2 months after DBS. Later death due to overdose	Zhang et al.[19]
Nucleus accumbens and anterior limb of the internal capsule	8	Heroin	Open-label pilot	130–185 Hz, 150–240 μsec, 1.5–7 V	Bilateral	Dizziness when stimulation greater than 5 V; difficulty sleeping; feeling hot; agitation; irritability; sweating; increased voice, palpitation; fever; headache; all of these symptoms were transitory	24 months	Five patients remained abstinent for more than 3 years, 2 relapsed (patients 5 and 8) after abstinence for 6 months, 1 (Patient 6) was lost to follow-up after 3 months of DBS. Reduction in the scales that assessed the degree of drug dependence and desire, improved quality of life, and relief of neuropsychiatric symptoms in patients who remained abstinent	Chen et al.[24]

overdose, even after increasing readjustments in the DBS parameters for relapse correction and difficult control of hypomania;[19] and the fifth patient was lost to follow-up after three months of DBS due to unknown causes.[23]

Regarding the results obtained, ~ 48% of the patients were abstinent,[16,17,20,21,23–25] and the others had relapses (52%), but for shorter periods and less frequently than before the surgical treatment. Among the relapsed patients, only one had a desire for the drug,[19] whereas the others reported lack of desire. The main reasons for the relapses were related to psychosocial problems such as interpersonal conflicts, boredom, and a non-compensating social environment. Another factor that influenced relapses was the reduction in pulse generator battery power over the years of treatment, with clinical improvement after replacement with a new one.[14,17]

In total, 3 patients from different studies[14,19,21] increased the use of drugs after DBS. In one study, the patient was abstinent for 2 months after surgery, and then had several relapses, with persistent desire for the opioid and withdrawal symptoms. This required progressive adjustments of the stimulation parameters, with no therapeutic success, and the patient eventually died from overdose.[19] In another study, a patient referred increased use of amphetamines secondary to reduced heroin use, which was the study's target drug, due to the need to maintain weight.[14] In a third study, a patient reported an increase in temporary drug use during ventral stimulation of the medial electrodes, but after switching to the dorsal position, the patient reduced the consumption.[21] Improvements in the psychological scores were observed in all of the studies that used them, especially the scales that evaluated craving and symptoms of depression and anxiety. This progress helped some patients return to work after years and reestablish social bonds.[15,17–19,23,24]

However, DBS is a treatment susceptible to adverse effects, present in ~ 70% of the patients, although most of them are transient and easily corrected by changing the stimulation parameters. The main immediate side effects reported were: transient hypomania,[15,17,18,20,23,24] sensation of warmth,[23] excessive sweating, decreased libido,[22] mild mental confusion, urinary incontinence,[16] transient obsessive traits,[25] transient weight gain,[22] insomnia, anxiety, dizziness, and speech disorders.[23,24] The immediate effect that was considered the most severe was convulsive seizure, but the patient had already had them before surgery.[14] The major long-term symptoms were weight gain,[16] hypomania,[19] and a slight decline in memory.[24]

Two studies had surgical complications.[18,24] In one of them, a patient had caudoventral migration of the electrodes of ~ 10 mm in relation to the initial implantation limits, and needed to undergo a reimplantation.[18] In the other, one patient had a slight intracranial hemorrhage adjacent to the lead implantation without neurological repercussion.[24]

In some studies, the DBS surgical treatment was complemented with pharmacological and/or non-pharmacological therapies. In two of them, a pharmacological treatment was used;[14,21] in one study, the patients were provided with routine psychiatric consultations;[18] and, in two other studies, the patients were provided with weekly psychotherapy sessions.[19,22] In one study, the patients were encouraged to participate in support groups, but the modality was not standardized as a complementary therapy.[17]

Discussion

Substance-related disorders are considered major health problems worldwide. They are chronic conditions characterized by the continuous use of a drug despite the harm caused by it, leading the individuals to have cognitive, behavioral, and physiological symptoms.[2]

In this systematic review, 21 people with drug addiction were analyzed, and there was only one female patient.[14] The average age was around the third decade of life, and the main substance of abuse was heroin, followed by alcohol. All of the patients had a long history of drug abuse refractory to clinical treatment.

In an attempt to treat the disease, several case studies have been conducted to better understand the DBS of the NAc, most of which resulted in decreased drug use.[12] Nonetheless, experimental studies with greater scientific impact should be performed, since only a few have been performed and published so far.

Among the studies analyzed, only one was a longitudinal, double-blind, cross-sectional, randomized case-control study. This study on the treatment of refractory cocaine dependence was divided into 3 phases, and had a follow-up of 2.5 years.[22] Two open-label pilot studies outlined clinical trials in which 8 and 7 patients were followed for 24 and 40 months respectively.[23,24] The greater methodological rigor applied in these cases produced enriched data and better standardized results, effectively contributing to the dissemination of knowledge about the procedure.

Deep brain stimulation is emphasized as an innovative alternative for the treatment of drug addiction. It consists of an adjustable, reversible, non-destructive intervention.[26] Electrodes are stereotaxically implanted, directly remodeling the neurocircuitry of addiction by providing electrical pulses.[4] In the present review, all patients underwent this type of treatment.

The main surgical target was the NAc because of the relevance of its role in the reward circuit. The studies selected here also demonstrated the protagonist role of this structure in DBS, as it seems to be the most promising and safe focus for addictive behaviors.[5,26]

The parameters of stimulation were individualized per patient. The values chosen were based on pre-established standards found in the literature, adjusted throughout the studies, and optimized according to the therapeutic response of each patient.

It is noteworthy that although nicotine was not considered a drug to be treated in the aerticles selected for the present review, patients who also used this substance reported reduction or cessation of use after DBS.[15–19] Similarly, other psychiatric disorders such as obsessive compulsive disorder, Tourette syndrome, and anxiety disorder were also acting in parallel with substance-related disorders.[27–29]

Abstinence was a response to treatment in 48% of the patients. The other patients had transient relapses driven by unfavorable biopsychosocial triggers, considered negative symptoms in the studies. This manifestation is controversial since the patients no longer have the typical desire for the drug. It is assumed that drug addiction added to its neurotoxic effects may cause irreversible brain damage in relapse-associated circuits.[17]

Although most studies indicated reduced drug use and craving, three patients from different studies increased drug abuse after DBS.[14,19,21] One patient reported increased amphetamine use secondary to reduced heroin use due to the need to maintain weight.[14] It is interesting to analyze the reason for a decrease in the consumption of the target drug, while no reduction in the use of parallel drugs was achieved, since DBS acts in the same neurological circuit. Preclinical studies, based on the theory of activation of extracellular signal-regulated kinase, assume that each drug has a distinct type of activation, both in terms of anatomical location and intensity.[30,31]

A patient required progressive adjustments to the stimulation parameters with no therapeutic success, and died from overdose.[19] In this case, it is important to discuss how long the patients benefit from DBS. In a study addressing the feasibility, efficacy, and safety of DBS for drug addiction, the authors noted that the inclusion of drug addicts in studies involving DBS is less successful than that of patients with obsessive compulsive disorder. This is motivated by the fact that the former do not accept the disease, deny its severity, do not consider it an addiction, and some of them are afraid of the surgical procedure.[32]

No life-threatening conditions occurred in any of the studies included in the present systematic review. The adverse effects reported by the patients analyzed are targets of studies in other psychiatric disorders, which focus on behavioral and personality-related effects ranging from hypomania to suicide. Although they were transient and were corrected after changing the parameters of the DBS stimulation, attention should be paid to them given that, in some situations, they might be life-threatening. Therefore, in order to provide an early diagnosis for these conditions, it is important to apply self-assessment scales.[33–37] In the studies reviewed, dependence and self-assessment scales were applied before and/or after DBS as ways to assess the therapeutic response. A decrease in values was registered, especially in scales that evaluated dependence, desire, obsession-compulsion, and depressive-anxious symptoms.

In the joint approach of the patient, the drug, and the environment tripod,[38] it is important to reinsert people into their social groups through complementary treatments such as psychotherapy and family therapy. In the present review, a small sample was submitted to associated alternative therapies;[14,17–19,21,22] consequently, it was not possible to analyze their real impact on post DBS follow-ups. However, in a group of patients only submitted to psychiatric support, this lack of complementary treatments was negatively perceived. One of the patients had several relapses due to depression because of the death of his brother, and another one started undergoing psychotherapeutic treatment 24 months after DBS due to marital problems that also led to a depressive condition.[17]

Some limitations should be considered in the present review. First, most of the selected studies are case reports that were not double-blinded, lacked a control group, and had restricted samples and variable follow-up periods. Second, since DBS is a treatment based on experimental studies conducted in a university environment, no guidelines are available to assist the professionals during its execution, and each service adopts its own consensus.[5] Third, the patient's mental ability to choose therapy is discussed, and this responsibility is often assumed more by the family than by the patients themselves. Finally, in most studies, the multidisciplinary approach was neglected. Deep brain stimulation should not be considered an isolated treatment, but part of a multicenter approach for the potential enhancement of the results.

Conclusion

Substance-related disorders have a strong biopsychosocial impact. Pharmacological treatment associated with cognitive behavioral therapy, which is considered the gold standard for this treatment, is effective regarding detoxification, but ineffective in terms of relapse control.[39] Therefore, DBS appears as a promising therapy, although this technique has some limitations related to its indication and the management of the patient after it. Additionally, this surgical procedure is still in an experimental stage, requiring further in-depth studies so that its clinical application can be recommended.

Conflict of Interests
The authors have no conflict of interests to declare.

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