STIMULATORY PROCEDURES OF BRAIN IN TREATMENT OF ADDICTION

Original Research Article

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ABSTRACT

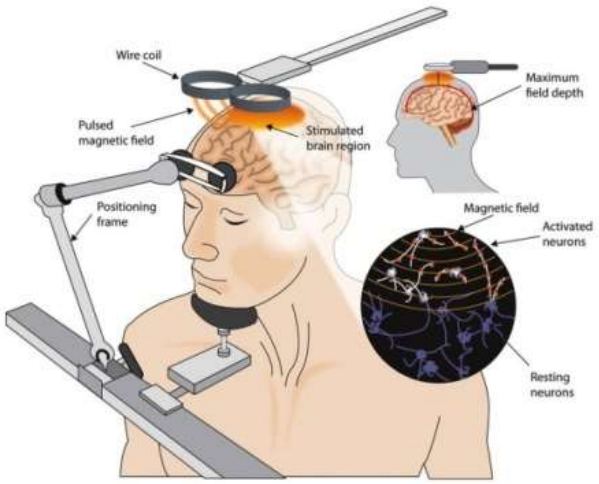
The saying once an addict always an addict is one that many people believe is true, but this does not always have to be the case. Drug addiction does not mean that your life is ruined, or that you will always be an addict. If you have a problem with drugs or alcohol you do not have to just learn to live with the issue. Deep brain stimulation has been put forward as a potential "cure" for intractable drug addiction. The history of neurosurgical treatment for psychiatric disorders suggests that we should be cautious in prematurely advocating invasive neurosurgical procedures on the basis of such limited evidence. Further research is required in people treated for other neurological or psychiatric disorders before trials in addicted populations can be justified. Localized stimulation of the human brain to treat neuropsychiatric disorders has been in place for over 20 years. Although these methods have been used to a greater extent for mood and movement disorders, recent work has explored brain stimulation methods as potential treatments for addiction. The rationale behind stimulation therapy in addiction involves re-establishing normal brain function in target regions in an effort to dampen addictive behaviors. In this review, rationale and studies investigating brain stimulation in addiction including transcranial magnetic stimulation and transcranial direct current stimulation and deep brain stimulation are added. Overall, these studies indicate that brain stimulation has an acute effect on craving for drugs and alcohol, but few studies have investigated the effect of brain stimulation on actual drug and alcohol use or relapse. Stimulation therapies may achieve their effect through direct or indirect modulation of brain regions involved in addiction, either acutely or through plastic changes in neuronal transmission. Our analysis of the literature suggests that the NAc is currently the most promising DBS target area for patients with treatment-refractory addiction. The medial prefrontal cortex (mPFC) is another promising target, but needs further exploration to establish its suitability for clinical purposes. We conclude the review with a discussion on translational issues in DBS research, medical ethical considerations and recommendations for clinical trials with DBS in patients with addiction.

Keywords : brain stimulation, neuropsychiatric, medial prefrontal cortex, DBS, medial prefrontal cortex (mPFC). rams.

I. INTRODUCTION

Deep brain stimulation (DBS) is a neurosurgical intervention in which implanted electrodes deliver electrical pulses to stereotactically targeted areas of the brain. It has been used as treatment for movement disorders for over 20 years1 and has recently shown promising results as experimental treatment of psychiatric disorders such as obsessive–compulsive disorder (OCD), Tourette syndrome and depressive disorder. A wide range of other possible applications for DBS have been suggested over the last years[6, 7, 8]—one of which is addiction. The reasons to consider DBS as an intervention for addiction are threefold. (1) Preclinical studies and case studies have reported promising results for DBS as a treatment for addiction. [7] (2) The recent understanding of neural pathways that are affected in addiction has created a new range of possibilities for treatments that directly target and normalize affected brain circuits. And (3) new effective interventions are needed for patients who do not benefit from current treatments, since addiction is a chronic relapsing brain disorder seriously affecting both individual and public health.[12] A substantial numbers of patients suffer multiple relapses and show a chronic course of the disorder despite several treatments: abstinence rates after 1 year of completing treatment are about 30–50%.[12, 13]

A well-documented rationale for the choice of the target area in the brain is required in order to investigate the effectiveness, safety and feasibility of DBS in treatment-refractory addiction[8]. Therefore, the objective of this review is to find the most promising target area for DBS in addiction. Original published reports on empirical studies about DBS in addiction in humans were considered[5]. In the first step, a search was conducted using various terms for 'addiction' and 'deep brain stimulation'. In the second step, the reference lists of all papers from the first step were screened for additional articles fitting the inclusion criteria.



Transcranial Magnetic Stimulation

II. CASE FOR CAUTION

1. Addiction does not usually follow an inexorable path to severe disability and death; it is generally more amenable to pharmacological and psychotherapeutic treatment, so drastic remedies are less justifiable[10]. In fact, many of the failures of addiction treatment are due to inadequate access to well-run and optimally provided forms of existing treatments; a situation that could be exacerbated by an increased use of deep brain stimulation to treat drug addiction.

2. The history of neurosurgical treatment in psychiatry cautions against uncritically accepting "positive results" from uncontrolled and often selectively reported clinical case series. Deep brain stimulation has also been reported to *induce* addictive behavior in some cases [13]. And while ablative neurosurgery for heroin addiction reduced drug use in some patients in the short term, subsequent long-term follow-up found that it carried significant side effects and was not as effective as first thought.

3. Deep brain stimulation is often described as a "reversible" alternative to neurosurgery, but it is nonetheless an invasive intervention that carries significant risks [4]: Insertion of stimulating electrodes can cause serious infections and produce cognitive, behavioral, and emotional disturbances [15]. It can also produce irreversible psychosocial changes that can be harmful.

4. Deep brain stimulation for addiction is an expensive form of treatment for addictive disorders where access to existing treatment remains poor. Inability to pay for treatment and stigmatization often discourage addicted persons from seeking treatment.

III. DISCUSSION

As of today, there are no published randomized controlled trials on the effect of DBS in alcohol- or drug-dependent patients. The available clinical evidence is restricted to 11 case reports or case series. In these studies, two target areas have been used: the NAc and the STN Five reports described the NAc as target area for DBS—three reported on the remission of addiction as a non-intended side effect of DBS during the treatment another psychiatric disorder[9]. .In two studies the indication for DBS was addiction.[11] We found six reports that described the effects of STN DBS on addiction; in all these studies the indication for DBS was Parkinson's disease. Here, we provide a summary of these case studies.

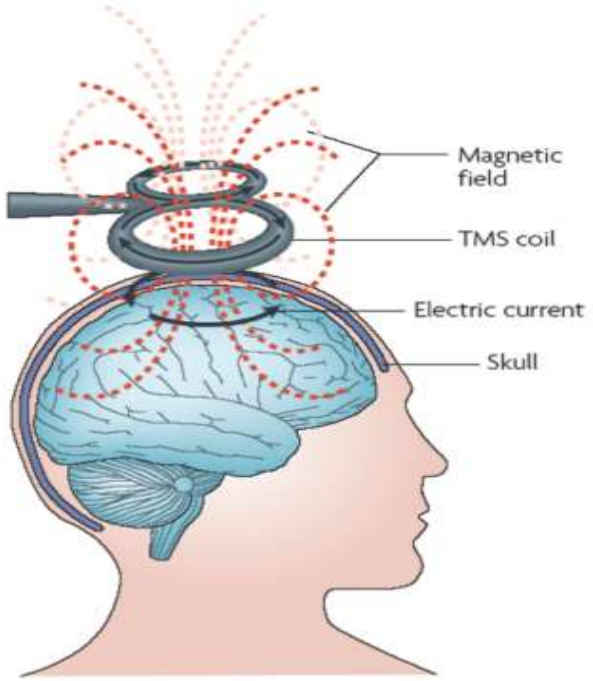
NAc

The first study that examined the effects of NAc DBS on addiction was a retrospective case series by Kuhn et al.[2, 3] They found that 3 out of 10 patients treated with high-frequency NAc DBS (five bilateral and five unilateral) for different disorders (for example, depression, OCD) stopped smoking; a much higher quit rate than unaided smoking cessation in the general population. Successful quitters were less addicted, more motivated to quit and were stimulated at higher mean voltages than non-attempters. DBS had a negligible effect on the anxiety symptoms, but rapidly and drastically reduced alcohol consumption without any particular motivation. The patient claimed to have lost the desire to drink and felt no longer a pressing need to consume alcohol. Finally, Zhou et al.[15] described a patient addicted to heroin who refrained from drug use after bilateral, high-frequency NAc DBS during follow-up period of 6 years in total. The patient was 24 years old, had been using 1–1.5 g of heroine for over 5 years and did not respond to any previous interventions. Additionally, he decreased the number of cigarettes he smoked from 40 a day before surgery to 10 a day after surgery[8]. The NAc is the **most frequently** used target area for addiction, and has consistently shown promising results across human case studies and animal research. Therefore, concluded that NAc DBS is currently the most promising candidate target for therapy-refractory addiction[16].

STN

Finally, there are several reports in which high-frequency STN DBS in patients with Parkinson's disease either induced or reduced addictive behaviors. Some Parkinson patients treated with dopamine replacement therapy develop an addictive pattern of medication use called

'dopamine dysregulation syndrome', which in turn is associated with the onset of impulse control disorders. Parkinson patients with dopamine dysregulation syndrome or impulse control disorders were followed after STN DBS treatment (18 bilateral and 1 unilateral).[3] In a study, 19 Parkinson patients with dopamine dysregulation syndrome or impulse control disorders were followed after STN DBS treatment (18 bilateral and 1 unilateral).[3] The study showed mixed results: in a small proportion of these patients the addictive behavior improved, whereas in the majority of the patients the addictive behavior did not improve or even worsened.[3] Side effects of STN DBS reported in these case studies were mild apathy (two patients[7], emotional instability and vivid dreaming (one patient)[2]. From these studies it is difficult to deduce how STN DBS influences addictive behaviors and what role adaptation of dopaminergic medication has in it. However, we like to emphasize that no firm conclusions can be drawn from uncontrolled case reports and case series. On the basis of these cases, the NAc appears to be the most promising and safe target for the use of DBS in patients with addictive behaviors.



Compare Brain Stimulation Different Techniques And Application

Most promising is NAc

The precise mechanisms behind DBS are still a matter of investigation and we can only speculate about the mechanism of action of NAc DBS in the treatment of addiction. Here, we elaborate on two plausible mechanisms. First, NAc stimulation could normalize dysfunction in striatal areas of which the NAc is an important part. Recent studies show reduced striatal dopamine activity in individuals with drug addiction that might be responsible for decreased sensitivity to natural reinforces whereas long-lasting drug-induced increases of dopamine are likely to activate the reward circuits.4 This situation might strengthen the relative salience of drugs over natural reinforces leading to fixed motivational choices[10]. NAc DBS might activate afferent and efferent pathways leading to distant synaptic inhibitory and excitatory effects, modulating dysfunctional neuronal network activity. The first study suggested that stimulation of the NAc shell can decrease dopamine and serotonin turnover (measured as the metabolite-transmitter ratio's in post-mortem tissue) locally, whereas stimulation of the NAc core did not.

Cases where DBS trial is justified

In accordance with Carter *et al.*, [7] we would like to emphasize that DBS for addiction can only be considered when the highest medical ethical standards are applied. These include careful patient selection, responsible publishing and media reporting, and free and non-coerced choice to be treated with DBS[11]. For more detailed ethical guidelines, we refer to previous papers.[6, 7, 8;] In DBS for addiction, patient selection deserves special attention because of the serious social and physical problems that often accompany chronic alcohol or drug dependence. In the screening process, patients will have to undergo careful physical examination and laboratory testing to determine their fitness for anesthesia and surgery. Furthermore, patients should be seriously motivated and be able to keep their appointments since DBS is an intensive procedure that requires extensive follow-up and careful observations of symptoms and possible side effects. DBS should, therefore, be restricted to chronically addicted, treatment-refractory patients stable enough to comply with an intensive period of treatment and research. Lastly, patients should have (had) unrestricted and free of charge access to alternative treatments, that is, DBS has to be a free and non-coerced choice, which is important since serious concerns have been expressed about some neurosurgical lesion studies in addicted patients on these issues.[16]

For trials of deep brain stimulation to be justifiable in patients with addiction, the following requirements need to be met. First, there needs to be strong evidence that any participants in such trials suffer from a severely debilitating form of addiction that carries a high risk of morbidity or premature death and that has not responded to adequate trials of effective treatments. Second, there needs to be a reasonable expectation that the intervention will improve the patients' quality of life. This should include preclinical evidence of likely benefit, evidence on the long-term effects of deep brain stimulation on patients with other psychiatric conditions (e.g., OCD and depression), and a good theoretical basis for stimulating the targeted brain region. Accordingly, we believe that it would be premature to trial deep brain stimulation in the treatment of addiction on the basis of available animal models, the small number of selected case studies, and the evidence from uncontrolled studies of neurosurgery for heroin addiction. it has been outlined above the type of research in animals and individuals required to make a case for undertaking trials of deep brain stimulation in the future [3] We also support calls for the creation of a register of all cases treated with deep brain stimulation, as suggested recently [9], to minimize the potential of selective publication of good outcomes. However, even if these conditions are met and deep brain stimulation proves to be safe and effective in treating addiction, we suggest that the high costs involved make it a lower priority for public funding than trials of pharmacotherapy.

REFERENCES

[1] **Amiaz R, Levy D, Vainiger D, Grunhaus L, Zangen A (2009).** Repeated high-frequency transcranial magnetic stimulation over the dorsolateral prefrontal cortex reduces cigarette craving and consumption. Addiction 104: 653–660

[2] **Anderson SM, Famous KR, Sadri-Vakili G, Kumaresan V, Schmidt HD, Bass CE et al (2008).** CaMKII: a biochemical bridge linking accumbens dopamine and glutamate systems in cocaine seeking. Nat Neurosci 11: 344–353.

[3] **Aston-Jones G, Deisseroth K (2013).** Recent advances in optogenetics and pharmacogenetics. Brain Res1511: 1–5.

[4] **Batista EK, Klauss J, Fregni F, Nitsche MA, Nakamura-Palacios EM (2015).** A randomized placebo-controlled trial of targeted prefrontal cortex modulation with bilateral tdcs in patients with crack-cocaine dependence. Int J Neuropsychopharmacol 18: pii: pyv066.

[5] **Boggio PS, Liguori P, Sultani N, Rezende L, Fecteau S, Fregni F (2009).** Cumulative priming effects of cortical stimulation on smoking cue-induced craving. Neurosci Lett 463: 82–86.

[6] **Boggio PS, Sultani N, Fecteau S, Merabet L, Mecca T, Pascual-Leone A et al (2008).** Prefrontal cortex modulation using transcranial DC stimulation reduces alcohol craving: a double-blind, sham-controlled study. Drug Alcohol Depend 92: 55–60.

[7] **Boggio PS, Zaghi S, Villani AB, Fecteau S, Pascual-Leone A, Fregni F (2010).** Modulation of risk-taking in marijuana users by transcranial direct current stimulation (tDCS) of the dorsolateral prefrontal cortex (DLPFC). Drug Alcohol Depend 112: 220–225.

[8] **Bunse T, Wobrock T, Strube W, Padberg F, Palm U, Falkai P et al (2014).** Motor cortical excitability assessed by transcranial magnetic stimulation in psychiatric disorders: a systematic review. Brain Stimul 7: 158–169.

[9] **Camprodon JA, Martinez-Raga J, Alonso-Alonso M, Shih MC, Pascual-Leone A (2007).** One session of high frequency repetitive transcranial magnetic stimulation (rTMS) to the right prefrontal cortex transiently reduces cocaine craving. Drug Alcohol Depend 86: 91–94.

[10] **Ceccanti M, Inghilleri M, Attilia ML, Raccah R, Fiore M, Zangen A et al (2015).** Deep TMS on alcoholics: effects on cortisolemia and dopamine pathway modulation. A pilot study. Can J Physiol Pharmacol 93: 283–290.

[11] **Da Silva MC, Conti CL, Klauss J, Alves LG, do Nascimento Cavalcante HM, Fregni F et al (2013).** Behavioral effects of transcranial direct current stimulation (tDCS) induced dorsolateral prefrontal cortex plasticity in alcohol dependence. J Physiol Paris 107: 493–502.

[12] **Den Uyl TE, Gladwin TE, Wiers RW (2015).** Transcranial direct current stimulation, implicit alcohol associations and craving. Biol Psychol 105: 37–42.

[13] **Deng ZD, Lisanby SH, Peterchev AV (2014).** Coil design considerations for deep transcranial magnetic stimulation. Clin Neurophysiol 125: 1202–1212.

[14] **Di Chiara G, Imperato A (1988).** Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. Proc Natl Acad Sci USA 85: 5274–5278.

[15] **Dinur-Klein L, Dannon P, Hadar A, Rosenberg O, Roth Y, Kotler M et al (2014).** Smoking cessation induced by deep repetitive transcranial magnetic stimulation of the prefrontal and insular cortices: a prospective, randomized controlled trial. Biol Psychiatry 76: 742–749.

[16] **Eichhammer P, Johann M, Kharraz A, Binder H, Pittrow D, Wodarz N et al (2003).** High-frequency repetitive transcranial magnetic stimulation decreases cigarette smoking. J Clin Psychiatry 64: 951–953.

[17] **Everitt BJ (2014).** Neural and psychological mechanisms underlying compulsive drug seeking habits and drug memories—indications for novel treatments of addiction. Eur J Neurosci 40: 2163–2182.

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