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Is Deep Brain Stimulation a viable treatment for substance-related addiction?

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ABSTRACT

For the ability to modulate the activity of dysregulated networks Deep Brain Stimulation (DBS) of areas involved in reward system and motivational states may have a potential application in addiction despite risks associated with its invasiveness. To date nucleus accumbens core (NAcc) appares to be the most effective target but also anteromedial portion of subthalamic nucleus (STN) and lateral hypothalamus (LH) are studied for clinical purposes. The choice of the target may vary based on the form of addiction: NAcc in alcohol and opiate addiction and STN in cocaine addict patients. Additional studies are still necessary to establish effectiveness and safety of DBS in addiction.

Keywords: DBS, addiction, nucleus accumbens, subthalamic nucleus

Deep brain stimulation (DBS) is a neurosurgical intervention first used for treatment of pain, epilepsy and behavioral modifications and afterwards for movement disorders and others neuropsychiatric conditions like OCD, depression and Tourette syndrome (1,2).

The technique uses a implantable device to deliver electrical stimulation in targeted areas of brain circuits to control the dysfunctional neurophysiological signal and improve brain function by local and distant effects. DBS device consists of a battery-powered pulse generator (IPG) implanted subcutaneously in the chest below the clavicle and a quadripolar coiled wire lead, implanted unilaterally or bilaterally with stereotactic technique in the desidered brain area using a skull burr-hole. Although the exact mechanisms of DBS are not fully understood it is a safe and well tollerate therapy with the advantage compared with the advantage compared with ablative procedures to be reversible and adjustable.

Due to application and approval for several neurological disorders, DBS is meanwhile known as a powerful tool to modulate dysregulated networks and has already been considered for substance-related addiction as well (4).

Substance-related addictions therefore constitute the most frequently occurring psychiatric disease category. In addiction to genetic, social and contextual factors underliyng drug addiction there is an alteration of the brain mechanisms that control system of reward or gratification and motivational states, that is the compulsive behaviors associated with the consumption of substances, as well as numerous other functional systems such as those involved in learning and memory (3).

Promising case reports on DBS in addiction in humans have just recently been published (13,20).

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Likewise animal studies, mimicking addiction to several psychotropic substances, point in direction of effectiveness of DBS in substance-related addiction (15,19).

The human use of DBS for the treatment of addiction started from observation in some Parkinson's Disease patients of a phenomenon known as dopamine dysregulation syndrome (DDS), due to a dysfunction of the reward system observed in some individuals taking dopaminergic medications for an extended period of time. It is characterized by self-control problems such as addiction to medication, gambling or sexual behavior. DBS of subthalamic nucleus improved DDS and associated psychiatric symptoms, possibly in relation to reduced misuses and craving for dopamine consumption (5,6,7,8).

Data concerning DBS in substance-related addiction are not only limited but they have also not been shown large impact due to the invasiveness of implanting brain leads. However, it should be noted that the few studies using DBS include very small number of patients with very refractory illness.

Some target areas are proposed for DBS in refractory addiction and the most interesting are nucleus accumbens (NAcc), subthalamic nucleus (STN) and lateral hypothalamus (LH) (9,10). All these targets lie along the circuits of reward and motivation that are involved in development of dependence. A well-documented rationale for the target choice is required in order to investigate the effectiveness, safety and feasibility of the procedure. Since one of the challenge to treat addiction is to diminish the motivation for the drug or object of addiction, without diminishing other forms of motivated behavior, it is important that the targeted structure for a treatment of addiction can dissociate various rewards.

There is considerable preclinical evidence to support a role for NAcc in mediating the motivational effects of conditioned stimuli associated with the drug leading to its anticipation. Findings that DBS of NAcc core decreases motivation for heroin taking and cue-conditioned behaviour and facilitates extinction learning are promising while DBS of NAcc shell seems to have effects only on natural reward decreasing the motivation to food intake. On the basis of this preclinical evidence DBS of NAcc has been proposed in treating behavioral component of addiction disorders and substance abuse in humans. Unfortunately few clinical studies are considering its application and clinical data about its efficacy exist in the literature in small case series, mostly concerned with alcohol and opiate addiction that is in situation where negative reinforcement plays a crucial role (11,12,13).

STN represents another potentially effective target in addiction that can decrease the desire for drugs without influencing other motivated behaviors. Within STN exists a topological specialization in such a way that motivational and emotional contents are related to anteromedial portions (limbic and associative parts) and motor control to its posterolateral portion (sensory-motor part): DBS in limbic and associative parts can have effects on substance-related dependence. However STN DBS may not be appropriate for all forms of addiction and literature data suggest that it may be usefull specially to diminish the desire for cocaine (14,15,16).

LH drive control of food motivated behavior has been extended to drug reward. Electrical stimulation of the posterolateral hypothalamus seems to have similar effects to the hypothalamotomy producing a reduction of cocaine intake but preserving the processes of motivation. Lack of effectiveness on motivation and possible severe adverse effects make posterolateral hypothalamus a target that cannot be used in addiction at the moment (17).

In conclusion, despite no published randomized controlled trial on effect of DBS in patients with addictive behaviours is available, NAcc appears to be a interesting target followed by STN and LH. but additional study are need to establish suitability for clinical purposes. Moreover it is possible that target varies depending on the addiction form the patient suffers from: STN in cocaine addict patients and NAcc in alcohol and opiate addiction.

Choosing invasive procedure for a treatment always raises ethical issues, but for extreme severe treatment-resistant cases or when there is no real efficient treatment as for certain forms of addiction, DBS can be valid therapeutic option. Invasiveness of the method should be kept in mind and clinicians should be particularly vigilant in explaining the risk of DBS to drug dependent patients, who are likely to be much younger than individuals seeking treatment for neurodegenerative diseases.

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