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Technique

Preparing the ethical future of deep brain stimulation

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Abstract

Background: Deep brain stimulation is an approved and effective neurosurgical intervention for motor disorders such as PD and ET. Deep brain stimulation may also be effective in treating a number of psychiatric disorders, including treatment refractory depression and OCD. Although DBS is a widely accepted therapy in motor disorders, it remains an invasive and expensive procedure. The ethical and social challenges of DBS need further examination, and discussion and emerging applications of DBS in psychiatry may also complicate the ethical landscape of DBS.

Methods: To identify and characterize current and emerging issues in the use of DBS, we reviewed the neurosurgical literature on DBS as well as the interdisciplinary medical ethics and relevant psychological and sociological literatures. We also consulted the USPTO database, FDA regulations and report decisions, and the business reports of key DBS manufacturers.

Results: Important ethical and social challenges exist in the current and extending practice of DBS, notably in patient selection, informed consent, resource allocation, and in public understanding. These challenges are likely to be amplified if emerging uses of DBS in psychiatry are approved.

Conclusions: Our review of ethical and social issues related to DBS highlights that several significant challenges, although not insurmountable, need much closer attention. A combination of approaches previously used in neuroethics, such as expert consensus workshops to establish ethical guidelines and public engagement to improve public understanding, may be fruitful to explore.

Keywords: Deep brain stimulation; Parkinson disease; Psychiatry; Depression; Ethics; Patient selection; Neuroethics; Resource allocation; Informed consent; Knowledge translation

1. Introduction

Deep brain stimulation is a form of neurosurgery that is now widely used to treat PD and is emerging as a potential treatment for some neuropsychiatric disorders [4]. Deep brain stimulation involves the implantation of at least one electrode, typically in thalamic, subthalamic, or ventral pallidus regions (for PD or ET), which is connected by very small wires and electrically stimulated by an IPG in the upper portion of the chest (subclavicular region). Deep brain stimulation was approved by the US FDA in 1997 for the treatment of tremor in ET and PD and in 2002 was more widely approved for the management of refractory PD. Deep

Abbreviations: CAPSIT-PD, Core Assessment Program for Surgical Intervention Therapies in PD; DBS, deep brain stimulation; ECT, electroconvulsive therapy; ET, essential tremor; FDA, Food and Drug Administration; IPG, implanted pulse generator; IRB, institutional review board; MRI, magnetic resonance imaging; NIH, National Institutes of Health; OCD, obsessive-compulsive disorder; PD, Parkinson disease; TMS, transcranial magnetic stimulation; TS, Tourette syndrome; USPTO, United States Patent and Trademark Office; VNS, vagus nerve stimulation; WHO, World Health Organization.

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Table 1
Common contemporary neurostimulation techniques

DBS involves unilateral or bilateral implantation of electrodes in specific structures of the brain, under stereotactic techniques, including MRI guidance, physiological mapping, and computerized surgical navigation. The electrodes are usually inserted after clinical examination and then connected to a pulse generator implanted in the infraclavicular region. The clinical effects of DBS appear similar to traditional neurosurgical ablation with added benefits such as greater safety and reversibility.
VNS is a well-established and now standard procedure for the treatment of refractory epilepsy (approved in 1997 by the FDA for this use). VNS involves subcutaneous implantation of a pulse generator from which a bipolar electrode extends from the device and is wrapped around the left vagus nerve as it passes through the neck [49]. VNS, unlike DBS, results in diffuse effects on many regions of the brain. Although it rarely causes complete seizure remission, patients benefit from a significant reduction in epileptic seizure frequency [20]. Some clinical research has shown VNS to be a successful treatment in depression, and in 2005, the FDA approved, not without controversy, VNS for the treatment of severe depression.
TMS refers to an external (not implanted) device that activates or deactivates brain function through magnetic stimulation. A magnetic field, generated by an electric current, induces an electric current within the brain. Results from several studies indicate that TMS has antidepressant properties [14]. TMS is generally considered a noninvasive, reversible, and relatively safe procedure. TMS does not involve surgical procedures.

brain stimulation is now an established therapy for PD and ET patients whose diseases are severe and drug refractory [26]. More than 35 000 patients worldwide have received DBS for those indications [39]. The current scientific and medical knowledge surrounding the mechanisms of action of DBS is still incomplete, but a widespread hypothesis is that DBS replicates the effects of neurosurgical lesioning [4]. In comparison to ablative surgery, DBS is considered reversible and nondestructive [42]. Other forms of neurostimulation techniques and devices currently used should not be conflated with DBS. Table 1 distinguishes DBS from 2 other forms of neurostimulation: VNS, whish is commonly used for the treatment of epilepsy, and TMS, which relies on the external stimulation of the brain to temporarily activate or deactivate cortical activity.

Recent studies claim that DBS is efficacious, and although not without major risks, it is relatively safe for the long-term management of severe ET, PD, and dystonia [10,56]. Investigations of DBS in other motor and nonmotor conditions have emerged, in refractory depression, TS, OCD, chronic pain, and in multiple sclerosis [36,46,53] given the efficacy of DBS in PD and based on the undesirable irreversibility of ablative surgeries. Currently, there is an emerging literature documenting the efficacy of DBS in these disorders, and researchers have highlighted some potentially promising results [4]. In addition, case reports of DBS used to treat an anxiety disorder [40] and morbid obesity [28] have lead to unexpected results: relief of a comorbid alcohol dependence in the first case and memory enhancement in the second case (without any effects on the anxiety disorder or the obesity problem). In fact, a new clinical trial investigating DBS for memory improvement in patients with Alzheimer disease has emerged from the results of the second case study (NCT00658125, NIH clinicaltrials.gov). The number of clinical trials investigating DBS in established and emerging areas is likely to expand as trials already underway produce results over the coming years. Table 2 shows the current NIH-registered and completed clinical trials using DBS in neuropsychiatric conditions such as depression, TS, and OCD.

To realize the full potential of DBS, the ethical and social issues associated with this procedure must be addressed proactively. Some of these issues have already been acknowledged by leaders in the field of DBS neurosurgery [4] and neurosurgical ethics [16,17,19,38]. In this article, we provide what to our knowledge is a first overview and discussion of current ethical and social issues in the use of DBS for PD and motor disorders including challenges in the identification of good surgical candidates, in health care resource allocation, and in conveying an appropriate public understanding about the procedure and its outcomes. We also comment, where appropriate, on the challenges related to the emerging uses of DBS in psychiatry. Our approach is based on the belief that identifying ethical and social issues now

Table 2
Current and past NIH-registered clinical trials for neuropsychiatric disorders

Clinical trial	Condition	Open date	Status
Berlin Deep Brain Stimulation Study	MDD	September 2007	Recruiting
Deep Brain Stimulation for Treatment Resistant Depression	MDD	September 2006	Recruiting
Deep Brain Stimulation for Treatment-Refractory Major Depression	MDD	July 2005	Active, not recruiting
Deep Brain Stimulation for Depression	MDD	January 2004	Enrolled by invitation
Deep Brain Stimulation for Refractory Major Depression	MDD	June 2002	Recruiting
Effectiveness of Deep Brain Stimulation for Treating People with Treatment Resistant OCD	OCD	October 2008	Recruiting
Subthalamic Nucleus Stimulation and OCD	OCD	October 2005	Completed
Unilateral Deep Brain Stimulation of the Nucleus Accumbens in Patients with Treatment Resistant OCD	OCD	February 2004	Completed
Deep Brain Stimulation for Treatment-Resistance OCD	OCD	January 2001	Active, not recruiting
Pallidal Stimulation and Gilles de la Tourette Syndrome	TS	June 2007	Not yet recruiting
Thalamic Deep Brain Stimulation for Tourette Syndrome	TS	June 2005	Completed
Deep Brain Stimulation for Alzheimer Disease	AD	March 2007	Recruiting

Data from Clinical Trials Database http://clinicaltrials.gov/. Accessed November 28, 2008. MDD indicates major depressive disorder; AD, Alzheimer disease.