Sci Eng Ethics
DOI 10.1007/s11948-017-9934-y

ORIGINAL PAPER

Should DBS for Psychiatric Disorders be Considered a Form of Psychosurgery? Ethical and Legal Considerations

Devan Stahl[1] · **Laura Cabrera**[2] · **Tyler Gibb**[3]

Received: 24 February 2017 / Accepted: 17 June 2017

Abstract Deep brain stimulation (DBS), a surgical procedure involving the implantation of electrodes in the brain, has rekindled the medical community's interest in psychosurgery. Whereas many researchers argue DBS is substantially different from psychosurgery, we argue psychiatric DBS—though a much more precise and refined treatment than its predecessors—is nevertheless a form of psychosurgery, which raises both old and new ethical and legal concerns that have not been given proper attention. Learning from the ethical and regulatory failures of older forms of psychosurgery can help shed light on how to address the regulatory gaps that exist currently in DBS research. To show why it is important to address the current regulatory gaps within psychiatric DBS, we draw on the motivations underlying the regulation of earlier forms of psychosurgery in the US. We begin by providing a brief history of psychosurgery and electrical brain stimulation in the US. Against this backdrop, we introduce psychiatric DBS, exploring current research and ongoing clinical trials. We then draw out the ethical and regulatory similarities between earlier forms of psychosurgery and psychiatric DBS. As we will show, the factors that motivated strict regulation of earlier psychosurgical procedures mirror concerns with psychiatric DBS today. We offer three recommendations for psychiatric DBS regulation, which echo earlier motivations for regulating

Devan Stahl and Laura Cabrera have contributed equally to this work.

✉ Devan Stahl
stahldev@msu.edu

[1] Michigan State Univeristy, College of Human Medicine, East Fee Hall, 965 Fee Rd, RmC213, East Lansing, MI 48824, USA

[2] Michigan State University, College of Human Medicine, East Fee Hall, 965 Fee Rd, RmC211, East Lansing, MI 48824, USA

[3] Western Michigan University Homer Stryker M.D. School of Medicine, 1000 Oakland Drive, Kalamazoo, MI 49008, USA

Published online: 26 June 2017

psychosurgery, along with new considerations that reflect the novel technologies used in DBS.

Keywords Deep brain stimulation · Neuroethics · Psychosurgery · Psychiatric disorders · Legal regulations

Psychosurgery, brain surgery intended to address psychiatric conditions, has had a long and infamous history in the United States (Valenstein 1986; El-Hai 2005; Pressman 1998). In spite of its controversial past, psychosurgery has never completely vanished from the medical landscape, and today it is more commonly described as neurosurgery for psychiatric disorders. Recently, deep brain stimulation (DBS), a surgical procedure involving the implantation of electrodes in the brain, has rekindled the medical community's interest in psychosurgery. When DBS is used for psychiatric purposes, it raises similar ethical concerns as earlier forms of psychosurgery. The overuse, and in some cases abuse, of earlier psychosurgical procedures led to a number of state and federal efforts to regulate psychosurgery and protect patients. These regulatory efforts were inconsistently enforced, however, which considerably reduced their overall impact. Whereas many researchers argue DBS is substantially different from psychosurgery, we argue psychiatric DBS—though a much more precise and refined treatment than its predecessors—is nevertheless a form of psychosurgery, which raises both old and new ethical and legal concerns that have not been given proper attention. Learning from the ethical and regulatory failures of older forms of psychosurgery can help shed light on how to address the regulatory gaps that exist currently in DBS research.

To show why it is important to address the current regulatory gaps within psychiatric DBS, we draw on the motivations underlying the regulation of earlier forms of psychosurgery in the US. We begin by providing a brief history of psychosurgery and electrical brain stimulation in the US. Against this backdrop, we introduce psychiatric DBS, exploring current research and ongoing clinical trials. We then draw out the ethical and regulatory similarities between earlier forms of psychosurgery and psychiatric DBS. As we will show, the factors that motivated strict regulation of earlier psychosurgical procedures mirror concerns with psychiatric DBS today. We offer three recommendations for psychiatric DBS regulation, which echo earlier motivations for regulating psychosurgery, along with new considerations that reflect the novel technologies used in DBS.

Early Psychosurgical Procedures

The early pioneers of psychosurgery believed their interventions were effective and socially beneficial. With little regulation and a great number of institutionalized patients, however, psychosurgical procedures were abused. The widespread adoption of psychosurgery is generally attributed to the Portuguese neuropsychiatrist, Egaz Moniz, who was awarded the Nobel Prize in Medicine in 1949 for his contributions to psychosurgery. The spread of psychosurgery in America was due largely to the neurologist Walter Freeman and his neurosurgeon colleague James

Watts, who transformed Moniz's technique into what is now known as the "standard lobotomy" (Getz 2009).

In early twentieth century America, the lobotomy was seen as a potential saving grace not only because there were virtually no medications approved for use in psychiatric patients at the time, but also because there were hundreds of thousands of mentally-ill patients institutionalized throughout the country (Pressman 1998). Given the dire situation, Freeman saw the need for a novel intervention that would enable patients in state mental hospitals—where budgets, operating rooms, and the number of surgeons was limited—to receive quick and easy to perform lobotomies. This led to the introduction of the "transorbital lobotomy," a technique that involved inserting an ice pick-like orbitoclast into the patient's eye socket (Getz 2009). Freeman eventually waged a campaign to promote transorbital lobotomies, believing they ought to be the starting point of effective therapy, rather than a "last resort" treatment (El-Hai 2005). Freeman's suggestion that lobotomies could be performed in psychiatric facilities without operating rooms or surgical equipment outraged many members of the neurosurgical profession, including his partner Watts. Critics worried most psychiatrists lacked the necessary expertise to perform these procedures and would not know how to properly sterilize instruments, respond to hemorrhages, or react to other unexpected complications (El-Hai 2005). Despite protest by many physicians, a lack of alternative treatments, the need to ease the overcrowding of asylums, and the positive reports in the media created an environment in which lobotomies became widespread, over-used, and in some cases abused. Historians now believe that over 60,000 psychosurgical procedures occurred between 1936 and 1956 (Valenstein 1997).

As the number of cases of lobotomy grew and complications of the procedure became more obvious, respected members of the psychiatric and neurosurgical communities began to voice their disapproval of the procedure publically (Feldman and Goodrich 2001). Still, the legal community was reticent to interfere or to regulate the procedures. A 1949 article in the Stanford Law Review concluded, "The greater good will be achieved by avoiding legislative fetters and relying for protection on the high standards of the medical profession and the individuals who compose it" (p. 474). It was not until the 1960s and 1970s that state legislatures began to question the ability of physicians to police their own practices appropriately.

Ultimately, lobotomy (and other forms of psychosurgery) fell out of favor after the rise of antipsychotic drugs in the 1950s. Pharmaceuticals to treat psychiatric patients became more popular, not because they were scientifically proven effective, but because of the ease and low risks associated with their administration when compared to neurosurgical alternatives (Feldman and Goodrich 2001). Although psychosurgeries did not completely stop after the success of these drugs, their frequency drastically declined.

Electrical Brain Stimulation

Psychosurgery is generally regarded as the historical precedent of deep brain stimulation (DBS), yet therapeutic electrical stimulation also has a long history, dating back to the Roman Empire (Wagner et al. 2007). The use of electrical brain

stimulation to treat psychiatry and behavioral issues began around the same time more drastic treatments, such as psychosurgeries, were widely administered and generally accepted by both physicians and the lay public (Baumeister 2000). Jose Delgado, a professor of physiology, was one of the first to publish research about the use of long-term implantation of electrodes in humans between 1950 and 1970 (Delgado et al. 1952). Delgado believed electrical stimulation methods would be "far more conservative" than surgery to treat mental illness but equally effective (Delgado 1969).

Around the same time, the Tulane University School of Medicine program began researching the use of electrical brain stimulation for psychiatric conditions. The Tulane Electrical Brain Stimulation Program, operating between 1950 and 1980, involved approximately 100 patients. Initially, electrical brain stimulation was used to treat schizophrenia, but later it was applied to a variety of other conditions, including pain and psychomotor epilepsy (Baumeister 2000). The program spanned three decades without any significant breakthroughs until 1970, when brain electrodes were implanted in a 24-year-old male patient in an attempt to treat his homosexuality (Heath 1972). This experiment drew considerable public attention and sharp criticism. From a research ethics perspective, the lack of a "sound theoretic or empirical rationale" to support the experiments as a potential treatment for mental disorders meant the chance for real benefit to human subjects was small and the corresponding likelihood of harm was disproportionately high (Baumeister 2000, p. 274). Researchers attempted to justify their experiments, just as lobotomists had once done, by claiming their patients were hopelessly ill and the experiments were a last resort intervention (Heath 1954; Valenstein 1986). Just as in the case of earlier psychosurgeries, many reports of the successes of electrical brain stimulation were anecdotal in nature, lacked systematic controls, and were widely exaggerated in popular media.

To avoid the negative perceptions of early psychosurgery, current researchers tend to refer to newer forms of psychosurgical interventions in different terms, such as "functional neurosurgery," "psychiatric neurosurgery," or "neurosurgery for mental disorders" (Sachdev 2007; Lipsman et al. 2010). These procedures are typically performed at designated, specialized centers and require a psychiatrist referral and postoperative follow up (Kringelbach and Aziz 2009; Mashour et al. 2005), and follow stringent patient selection criteria (Sachdev and Chen 2009), including but not limited to treatment-refractory patients.

Psychiatric Deep Brain Stimulation

Deep brain stimulation is one of the newer forms of psychosurgical interventions to emerge from the continuing examination of biological origins of mental disease. DBS evolved from early electrical brain stimulation interventions and advances in functional stereotactic neurosurgery techniques (Sironi 2011). DBS involves the surgical implantation of at least one electrode in the brain, and the implantation of a pulse generator (sometimes called a "brain pacemaker") under the patient's clavicle or in the abdomen, which controls the settings of the brain implant (e.g. voltage and

frequency) (Lipsman and Lozana 2012). The pulse generator is carefully programmed for each patient to deliver electrical impulses to specific targets in their brain.

DBS is considered more precise than its earlier forms of psychosurgery, because neuroimaging and the use of a stereotactic frame help guide the implantation of the electrodes within a millimeter of their target. Unlike other lesioning methods, where a part of the brain is destroyed or removed, DBS is a neuromodulation approach. In DBS, electrical pulses modulate brain activity in targeted areas. The possibility of brain lesioning, while unintended and less severe than in other procedures, is still present as the mere insertion of the electrodes can cause irreparable tissue damage to the patient's brain (Foley 2014). DBS is considered reversible because the electrical stimulation can easily be turned off; however, given the possibility of unintended lesioning, one should be careful with how to interpret the reversibility claim.

Deep brain stimulation surgery is typically performed in two stages. During the first stage, a neurosurgeon makes a precise roadmap of the patient's brain with images obtained through an MRI or CT scan. Using a stereotactic frame, which provides a three-dimensional guidance system to localized areas deep inside the brain, the surgeon implants the electrodes. During the surgical procedure, patients remain awake to allow the neurosurgeon to monitor electrical activity in the brain during the procedure and to make sure the wires are in the right place. Patients usually stay in the hospital for 1–2 days after this surgery. Ten to fourteen days after the first surgery, a neurosurgeon implants the battery pack and connecting wires in the chest. Patients are usually awake under general anesthesia and can go home the same day. The generator that controls the electrical impulses is turned on 2 weeks after the implantation.

Various features make modern psychiatric DBS distinct from early versions of psychosurgery. For example, advances in neurosurgery, stereotactic and imaging techniques have brought more accuracy in localization of lesions with lower complication rates (Feldman et al. 2001; Synofzik 2013; Schlaepfer et al. 2010). Common side effects of early lobotomies, including "seizures, apathy, confusion, poor attention, inability to maintain socially appropriate behavior, and death," (Feldman and Goodrich 2001, p. 653) are much rarer in psychiatric DBS procedures (Saleh and Fontaine 2015). Several authors cite the adjustability and reversibility of current psychiatric neurosurgery procedures as the two primary improvements over earlier forms of psychosurgery (Muller et al. 2015; Mashour et al. 2005; Kringelbach and Aziz 2009; Juckel et al. 2009). Despite these perceived advantages, the superiority of DBS over lesioning procedures has not been unrefuttably established (Muller et al. 2015; Chodakiewitz et al. 2015; Eljamel 2015). In some cases, stereotactic ablative procedures can be an important alternative for some patient groups (Nuttin et al. 2014).

Another important difference between early psychosurgeries and psychiatric DBS is that early psychosurgeries were performed without strong scientific justification or data. Psychiatric DBS, currently viewed as investigational, is generally only used in the context of on-going clinical trials. Results from the first trials of DBS in obsessive–compulsive disorder (OCD) in 1999, suggested DBS could have a role in the treatment of patient with intractable OCD (Nuttin et al. 1999). Since then, studies have been conducted to assess the safety and efficacy of

DBS in treatment refractory patients for various psychiatric disorders, including mood disorders (Mayberg et al. 2005), addiction (Kuhn et al. 2007), and anorexia nervosa (Lipsman et al. 2013). Several clinical trials of DBS are currently underway for a variety of psychiatric disorders (Fig. 1) (clinicaltrials.gov).[1]

The attention paid to DBS by researchers and the popular media has also grown tremendously. A search in PubMed, for example, shows that between 2002 and 2005 only 21 articles were written about DBS for psychiatry disorders. Between 2010 and 2016, however, the number of publications jumps to 411.[2] There are various reasons for this increased attention, including evidence that many patients do not respond to drug therapies, the legacy of ablative procedures (Sachdev and Chen 2009), and the widely reported success of DBS in mitigating motor symptoms such as tremor, rigidity, slowed movement and stiffness, essential tremor (Flora et al. 2010), and Parkinson's disease (Fox et al. 2011). To date, DBS is considered an effective therapeutic option to treat these movement disorders and has received FDA approval. Yet, over the last decades, the progress of DBS in psychiatry has been slower than in movement disorders, because of the heterogenic symptomatology and complex neuroanatomy of psychiatric disorder. For that reason, DBS in psychiatry is a last-resort treatment for severely ill patients who are unresponsive to treatment with psychotherapy or pharmacotherapy.

State of the Research and Potential Benefits

Several studies reveal the potential benefit of DBS in the treatment of psychiatric disorders. The strongest evidence for the benefit of DBS has been on obsessive–compulsive disorder (OCD).[3] The first study using DBS for OCD reported benefits in three out of the four patients (Nuttin et al. 1999). Multiple groups continue the investigation of DBS for OCD using a modified target, the ventral capsule/ventral striatum (VC/VS).[4] The pooled data from those groups led to the first approval of DBS for a psychiatric disorder (Greenberg et al. 2010) by the Food and Drug Administration (FDA) under a humanitarian device exemption.[5] A number of scholars, however, have questioned the validity of the approval and its effect on

[1] www.clinicaltrials.gov, last visited Feb 15, 2017. Search covering deep brain stimulation and narrowed down to cases for psychiatric disorders in the USA.

[2] Search terms included: Deep brain stimulation AND (psychiatry OR Major depressive disorder OR obsessive compulsive disorder) only. Search was conducted on November 24, 2015 at http://www.ncbi.nlm.nih.gov/pubmed.

[3] According to a recent meta-analysis, 116 patients within 31 studies have received DBS for OCD (Alonso et al. 2015).

[4] In addition to the VC/VS, other target areas have been investigated including the nucleus accumbens (NAc), the subthalamic nucleus (STN), the anterior limb of the internal capsule (ALIC), and the inferior thalamic peduncle (ITP).

[5] A Humanitarian Use Device (HUD) is a "medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4000 individuals in the United States per year." A Humanitarian Device Exemption (HDE) is an application that is similar to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of the Food, Drug, and Cosmetic Act. FDA approval of an HDE authorizes an applicant to market a HUD subject to certain profit and use restrictions. HUDs cannot be sold for profit, except in narrow circumstances.

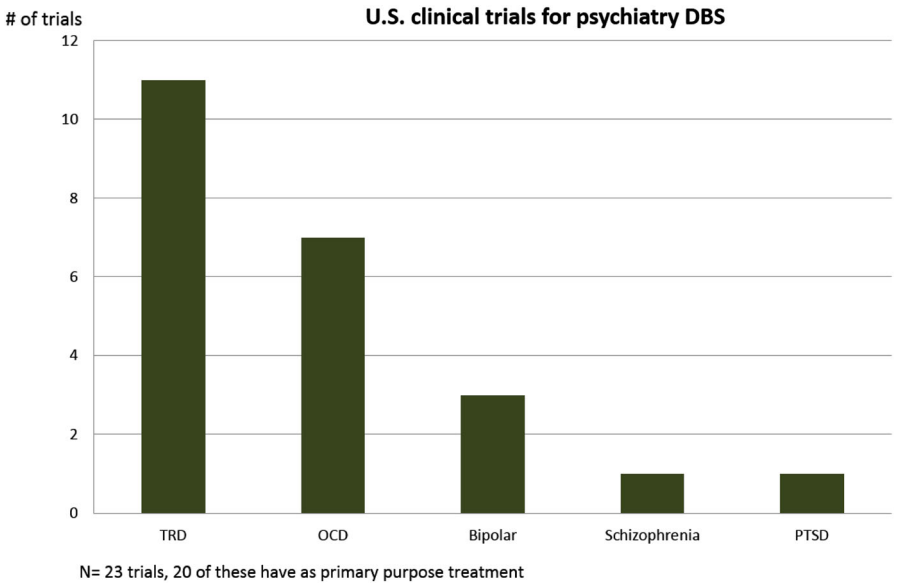

Fig. 1 Psychiatric DBS trials

expanding the use of DBS for other psychiatric conditions (Fins et al. 2011; Erickson-Davis 2012).

Treatment resistant depression (TRD) is another psychiatric disorder for which DBS is under investigation. During the multi-group trial on VC/VS DBS for OCD it was noted that subjects' comorbid depressive symptoms improved. These findings led to an initial open label trial for the same target, but also allowed for use in TRD (Malone et al. 2009). The positive results from this open trial led to a sham-controlled trial that failed to demonstrate a significant difference in response rates between the active and control groups (Dougherty et al. 2015). Another randomized double blind clinical trial comparing active versus sham stimulation for the treatment of severe depression targeting Brodmann Area 25 was also halted for futility prior to completion of the planned study (St Jude Medical sponsored BROADEN trial). To the detriment of the scientific process and progress, there have not been publications or official industry statements as to the possible or likely causes of the failure of these trials (Fins et al. 2017). Other studies, however, have demonstrated the efficacy of DBS for Major Depressive Disorder (MDD). For example, a recent randomized trial resulted in a significant decrease of depressive symptoms in 40% of the subjects and was well tolerated (Bergfeld et al. 2016). Most studies of DBS for mood disorders, however, are predominantly small and open-label and the published sham-controlled studies have conflicting results.

A number of case-reports have documented reversal of addictive behaviors after nucleus accumbens (NAc) DBS (Kuhn et al. 2007; Mantione et al. 2010). There is some optimism in the treatment of anorexia nervosa, but only two case reports and two small case-series of have been published (Graat et al. 2017). New psychiatric indications including schizophrenia and anxiety disorder, have shown some initial

promise in case reports, but the evidence is still too limited to draw any firm conclusions yet.

Continuing Risks and Complexities

At this point, it is still not clear that DBS for psychiatric disorders is better than lesioning methods (Muller et al. 2015). In spite of this lack of data, DBS is widely perceived as a better substitute for classical lesioning, because of its perceived reversibility and adjustability. As previously mentioned, however, DBS is not fully reversible or without some tissue destruction. The procedure, just as with early psychosurgeries, comes with a host of adverse effects such as intracranial bleeding and hardware related complications like lead isolation, lead fracture, and infection, as well as a number of stimulation-induced effects such as aggression, worsening of depression, and suicide (Muller et al. 2015).

Complicating matters further, DBS has different risk profiles for each psychiatric disorder, the potential side effects as well as the target areas (e.g. the VC/VS, NAc, the subthalamic nucleus, the anterior limb of the internal capsule and the inferios thalamic peduncle) vary even for the same disorder (Alonso et al. 2015; Graat et al. 2017). For the purposes of our argument, these differences do not need to be discussed at length, but many researchers recognize there remains a lack of strong evidence regarding effectiveness and safety, as well as best targeting and stimulation parameters of the procedure for the several indications for which research is currently ongoing (Alonso et al. 2015; Morishita et al. 2014). Moreover, DBS is being researched not only for its therapeutic possibilities, but also to gain better knowledge of underlying brain circuitry, in order to design less invasive treatments (Hariz et al. 2013; Mayberg 2009), which makes the evaluation of its efficacy for treating disorders even more complex.

The lingering complexities and risks of psychiatric DBS should not deter research, but the criteria for justifying its use and the protections afforded patients should be carefully considered. Many ethical and legal issues remain unaddressed in its current practice. The recent BROADEN trial highlights some of the ethical and regulatory issues surrounding the use of DBS for psychiatric patients. In 2008, 128 patients enrolled in the BROADEN Trial, a multi-center, controlled, doubled-blind clinical research trial that investigated the efficacy of DBS for patients with depression. Since the FDA does not yet approve DBS implants for depression, the study was carried under an investigational device exemption, which allows for a device under investigation to be used in a clinical study in order to collect safety and effectiveness data.[6] (FDA 2015). After 75 patients reached 6 months postoperative follow-up, St. Jude Medical, the trial sponsor and manufacturer of the DBS implant, terminated the trial when a futility analysis showed the probability of success to be no greater than 17.2% (Morishita et al. 2014; Fins et al. 2017).

Not only did St. Jude fail to release a public statement about the trial's termination, some participants claim they were not informed the trial had ended.

[6] FDA, last visited May 19, 2017. https://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/investigationaldeviceexemptionide/.

Moreover, to date St. Jude Medical Inc. has not yet made data on this trial available to the scientific community (clinicaltrial.gov data; Schlaepfer 2015; Fins et al. 2017). An in-depth report about the trial indicated that many participants felt abandoned and were uncertain whether they would receive follow-up care (Egan 2015). A number of study participants who had received the experimental brain stimulators also claimed to have struggled to find doctors who would agree to take on their care after the trial ended because they were considered high-risk patients. Others reported disturbing side effects including sleep disorders, worsening depression, suicidal and homicidal ideation, mania, hysteria, and paranoia. If even a fraction of what these trial participants claim is accurate, the current regulations and human protection mechanisms have failed them. We agree with several scholars in that DBS might very well hold tremendous benefit from persons suffering from a range psychiatric disorders (Graat et al. 2017; Fins et al. 2017), but any advances will be undercut if the current regulatory gaps are not addressed.

Regulation and Legislative Interventions Regarding Psychosurgery

Efforts to regulate earlier forms of psychosurgery came only after reports of abuse were rampant and trust in the medical establishment was in decline. The mood of much of the Western world in the 1960s and 1970s was increasingly critical of power structures (e.g. civil rights movement, anti-Vietnam war protests) and many people feared that government-sponsored brain modification procedures could be used as a means of social control (National Commission 1977; Feldman and Goodrich 2001). Psychiatrist Peter Breggin, along with a cadre of bioethicists who had begun to establish their voices in such ethical considerations, led an outspoken campaign against the use of both psychosurgery and electrical brain stimulation (Breggin 1972a, b). As the public became more aware and more critical of these types of interventions, the stage was set for regulatory bodies, such as professional medical organizations, state and federal legislatures, and administrative entities, to exert control over psychosurgery.

Changing Concepts of Informed Consent

Around this same time, the concept of ‘informed consent’ was also being developed in the courts, which had a direct impact on laws regulating psychosurgery. Whereas the medical community had been largely responsible for policing its own practices and creating its own standards for informed consent, many were beginning to see the “community practice standard” as paternalistic and inadequate for providing the necessary information about risks to vulnerable patients. In *Canterbury v. Spence* (1972), a new heightened standard for informed consent emerged. Within the context of psychosurgery, the case of *Kaimowitz v. Department of Mental Health* (1973) is illustrative of this heightened standard of informed consent.

Louis Smith, a psychiatric patient, was offered the chance to become a subject in a research project funded by the Michigan state legislature to study the effects of

psychosurgery on aggressive tendencies.[7] Two committees were established to determine the legitimacy of the study and to review the validity of Smith's consent to participate. Just before the procedure was to be performed, however, a local legal services attorney sued on behalf of himself, individual members of the Medical Committee for Human Rights, Smith, and other similarly situated patients to prevent the proposed psychosurgery (Spoonhour 1974). In a declaratory judgment, the court determined three points: Smith likely lacked the capacity to consent to surgery with unknown dangers involved in the procedure; no medically recognized syndrome related to aggressive behavior had been connected to the brain abnormalities being treated; and, finally, that psychosurgery did not guarantee that a dangerously violent person could be restored to the community (*Kaimowitz* 1972). In its conclusion, the court conceded an involuntarily detained mental patient might be able to give valid consent to psychosurgery if the procedure had a reasonable degree of established efficacy and if the procedure was accompanied by appropriate review mechanisms. Unhelpfully, the court did not provide thresholds or tests of reasonableness and appropriateness, but left those assessments for future debate.

Given the changing standards for informed consent, the uncertain efficacy of psychosurgery, and the vulnerable population psychosurgery targeted, a movement to erect additional legal oversight of these procedures grew. In 1974, the legal scholars George Annas and Leonard Glantz wrote, "In light of the known dangers involved in psychosurgical practice, courts would be justified in imposing upon hospitals where psychosurgery is performed a duty to provide exhaustive scientific and lay review even though such procedures are not as yet customary" (p. 262). Annas and Glantz argued the proponents of psychosurgery should be required to demonstrate *beyond a reasonable doubt* that patient consent is voluntary and informed, and there is a reasonable probability that the procedure will produce the desired effect. Annas and Glantz conceded this proposal might result in a *de facto* ban on psychosurgery. Such an unprecedentedly high standard for informed consent (normally reserved for criminal prosecution) demonstrates the radical shift the legal community began to take regarding the protection of institutionalized patients over the course of just two decades.

Early State and Federal Regulations

In response to the rising concerns about psychosurgeries and informed consent in the general public and legal communities, two states Oregon (35 Oregon Rev. Stat. § 426.700 *et. seq.* 1973) and California (Cal. Welfare & Institutions Code § 5325 *et seq 1974*), enacted legislation to regulate the use of psychosurgical procedures. Oregon required a Psychosurgery Review Board, made up of nine members appointed by the governor from medical, psychological, neuroscientific and lay backgrounds, approve the performance of the operation on every individual patient, including but not limited to "persons confined voluntarily or involuntarily in any

[7] Smith had been institutionalized since 1955 and was committed to a state hospital under Michigan's criminal sexual psychopath law. In 1972, after having been notably free of violence or any other inappropriate aggression for many years, Smith was selected as a candidate for psychosurgery, to which both he and his parents consented.

state institutions or private hospitals" (35 Oregon Rev. Stat. § 426.700 *et. seq.*). The Review Board was asked to verify the patient's consent was voluntary and informed; patients unable to give informed consent needed a legal guardian to provide the consent. The legislation also ensured only those patients who had already attempted "all conventional therapies" as well as "all other viable alternative methods of treatment" with no satisfactory results would be considered. In 1974, California enacted a similar approach to the regulation of psychosurgery, but provided separate regulations for voluntarily and involuntarily confined patients (Cal. Welfare & Institutions Code § 5325 *et seq*). California's legislation prohibited patients without the capacity to provide informed consent to receive psychosurgery, and their guardians or proxies could not consent to psychosurgery on their behalf. California also required judicial review for all institutionalized patients to determine their capacity for voluntary informed consent.

Not long after California's law passed, it was challenged by a physician specializing in the treatment of psychiatric illnesses on behalf of patients who believed the restrictions on psychosurgery were too onerous, in *Aden v. Younger* (1976). The petitioners alleged the new legislation was an unconstitutional infringement on patients' First Amendment and privacy protections. The court recognized restricting access to certain treatments might impair a patient's freedom of thought; however, it also asserted the state had a justified interest in protecting the right to refuse treatment. The court held that the required review procedure was constitutional, as it ensured the competency and voluntariness of the vulnerable patient's consent. The court also found the state requirement for substantive review of psychosurgery to be justified, as it was designed to protect individual autonomy.

After several healthcare organizations, including the National Institute of Mental Health, the National Institute of Neurological Diseases and Stroke, the American Psychological Association's Division of Physiological and Comparative Psychology, the American Psychiatric Association, and the Society for Neurosciences created task forces and issued various position papers on psychosurgery (National Commission 1977), the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research issued a report on psychosurgeries in 1977. The Commission conducted investigations on the kinds of psychosurgical operations being performed in the US, patient demographics, and independent evaluations of the effect of psychosurgery.[8] To the surprise of many critics of psychosurgery, the Commission discredited allegations that the surgeries were being used to hamper individual rights or control minority groups. Instead, the Commission endorsed the continued, but limited, use of psychosurgical procedures. The Commission recommended several safeguards including: the surgeries should only take place at an institution with an Institutional Review Board (IRB) made up of an interdisciplinary team of experts, pre-operative and post-operative plans must be in place, informed consent is required or, if informed consent is not possible, a national psychosurgery board should review each case and a court should approve the operation. The Commission also recommended the formation of a Joint Committee

[8] The Commission also formed a Minority Conference to ensure minorities were protected from abusive psychosurgical practices.

on Psychosurgery to establish mechanisms to ensure the surgeries were voluntary and the data be reported. Unfortunately, few of the Commissions' recommendations were acted upon, enforced, or made it into federal legislation. In the following decade, however, other states enacted legislation that limited the use of psychosurgery, similar to Oregon and California.

The Current Psychosurgery State Landscape

Currently, 26 states have statutory regulations directly involving psychosurgery. However, these states fail to define what is intended to be regulated as "psychosurgery."[9] The fact that these 26 states lack a clear definition of "psychosurgery" can be seen as the result of either one of two situations. On the one hand, drafters might have mistakenly assumed psychosurgery was a term universally understood by physicians and research scientists. On the other hand, the lack of a statutory definition of "psychosurgery" may be the result of a simple oversight, or, more likely, a failure to imagine that a precise definition of psychosurgery would be important. Regardless, in more than half of the states in this country, there are rules regarding how, when, and by whom psychosurgery may be administered, without a precise definition of the procedure.

There are six states in which psychosurgery is both defined and regulated by administrative rule or state law.[10] The California law is exemplary of statutory definitions in the other states. It states:

> 'Psychosurgery' is defined as any of those operations currently referred to as lobotomy, psychiatric surgery, and behavioral surgery and all other forms of brain surgery if the surgery is performed for the purpose of any of the following:

1. Modification, alteration, or control of thoughts, feelings, actions, or behavior rather than the treatment of a known and diagnosed physical disease of the brain;
2. Modification or alteration of normal brain function, brain tissue or brain cells in order to modify, alter, or control thoughts, feelings, actions, or behavior; or
3. Treatment of abnormal brain function, brain tissue or brain cells in order to modify, alter, or control thoughts, feelings, actions, or behavior when the abnormality is not an established cause for those thoughts, feelings, actions, or behavior.

[9] Alabama, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Kansas, Kentucky, Montana, Minnesota, Nevada, New Hampshire, New Jersey, New York, North Carolina, Ohio, Pennsylvania, South Dakota, Tennessee, Texas, Utah, Virginia, Washington, Wyoming, Vermont.

[10] Arkansas (Ark. Code Ann. § 28-47-202 (2010)]; California, [Cal. Welfare & Institutions Code § 5325(g) (2016)]; Connecticut [Conn. Gen. Stat. § 17a-540 (2012)]; Missouri [Mo. Rev. Stat. § 630.005.1 (27) (2012)]; New Mexico [N.M. Stat. § 43-1-3 (2006)]; Oregon [Or. Rev. Stat. § 426.385 (2011)]. Four states had statutory definitions and regulations, but these statues have since been repealed: West Virginia; Mississippi; Maine; and Massachusetts. Interestingly, Oklahoma is the only state where a definition of 'psychosurgery' is provided through case law; see i.e., In re KKB, 609 P. 2d 747 (Okla. 1980).

Psychosurgery does not include prefrontal sonic treatment wherein there is no destruction of the brain tissue. Psychosurgery shall not include surgery for relief of pain caused by physical disease elsewhere in the body (Cal. Welfare & Institutions 2016).

Under California's definition, psychiatric DBS is a form of psychosurgery, but it is not currently regulated as such.

Current Federal, State, and International Guidelines Relevant to DBS

Federal Guidelines

Although healthcare technologies and procedures often far outpace the responsiveness of formal regulation, governmental entities often attempt to exert control and regulate medical research and clinical trials in a variety of ways. There are various levels in which healthcare technologies can be regulated, depending on which branch of the government is attempting to regulate and how the regulation is created. At the federal level, regulatory requirements for clinical studies of significant risk that employ medical devices can be created through administrative entities. DBS devices (regardless of whether they are an unapproved device for an unapproved indication or an approved device for an unapproved indication), must comply with FDA human subject protection requirements. These requirements include informed consent and human subject protection standards, institutional review board oversight, investigator financial conflict of interest disclosure, and investigational device exemptions (IDE) (FDA 2006; Pena et al. 2007). In addition, if the clinical study is receiving federal money, it is subject to additional regulations for protection of human research subjects from the Department of Health and Human Services (HHS), which attempts to ensure the rights and welfare of the subjects are maintained (2009).

Clinical trials that receive federal funding from the NIH also must register and post results to clinicatrials.gov, a federally run database. Federal law mandates publishing of results (2007), but until recently there has not been enforcement of public reporting of study results. Many of the different psychiatric DBS trials registered in the clinicatrials.gov database are listed as inactive status, and others that are listed as "complete" do not show more than the initial registration information. At present, these databases represent the bare minimum for reporting data and provide very little useful information. A lack of public reporting can potentially endanger future human subjects. As Dorenberg and Wendler explain, sharing research results "helps to justify exposing participants to the risks of clinical trials and shows respect for those who assume these risks (2016, pp. 1149–1150)." Moreover, as was shown in the BROADEN trial, without full transparency and heightened regulatory oversight, human subjects can be abandoned and abused. Once again, enforcing the regulations already in place for these trials would go a long way in ensuring that psychiatric DBS procedures are performed ethically and transparently.

State Regulations

Statutory rules are another regulatory mechanism for medical research. Currently, there is no explicit definition or regulation of psychiatric DBS in any state or federal statutes. Clearly, under some (if not most) state definitions of psychosurgery, psychiatric DBS is psychosurgery. Although psychiatric DBS does not purposively aim to destroy brain tissue, the *intent* of the procedure is the same, namely to modify or control thoughts, feelings, actions or behavior. In its definition of psychosurgery, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research included the implantation of electrodes, destruction or direct stimulation of brain tissue by any means and the direct application of substances to the brain, when the primary purpose of such intervention is to change or control behavior or emotions (National Commission 1977). Under such a definition, DBS for Parkinson's disease or epilepsy would not count as psychosurgery; however, DBS for any other psychiatric condition would be a form of psychosurgery because of the intent of the surgery.[11] Under the current regulations scheme there does not seem to be a distinction between DBS that is used for movement disorders and those whose intent is modification of behavior. Given legitimate historical concerns around psychosurgery, current regulations should make a distinction between the different purposes for which DBS is used, to provide needed safeguards for interventions aimed at modifying behavior. Moreover, considering the motivations leading to stricter regulation of psychosurgery, psychiatric DBS should be regulated under a similar rationale, with additional stipulations to address the use of a medical device in addition to the neurosurgical procedure.

Currently, regulation of psychiatric DBS is only at the federal level. Although this is a good start, as discussed above, the actual enforcement of existing federal regulations is inconsistent and poses significant challenges. The patchwork nature of state and federal regulatory mechanisms make it unlikely that a single entity would feel obligated and empowered to effectively enforce the existing rules, leaving patients vulnerable to misconduct, as the ramifications of BROADEN trial clearly demonstrate. Expanding existing statutory definitions of psychosurgery to clearly cover psychiatric DBS, and creating regulation in states where psychosurgery is currently unregulated, is a necessary first step in making sure that vulnerable human subjects are truly protected and their rights respected.

International Guidelines

In addition to government-based protections, consensus guidelines should be actually enforced, rather than simply viewed as recommendations. In 2014, the World Society for Stereotactic and Functional Neurosurgery (WSSFN), outlined standards for the appropriate therapeutic uses of psychiatric DBS, as well as how subjects should be selected, enrolled, consented, and followed (Nuttin et al. 2014). The WSSFN guidelines bear a striking resemblance the guidelines for

[11] Sachdev and Chen (2009) argue that because the placement of a pacemaker is not considered 'cardiac surgery,' DBS should not be considered psychosurgery.

psychosurgery provided by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Now, just as in the 1970s, there is concern that human subjects be properly protected and that procedures not be used for social control.

Both the National Commission Report on Psychosurgery and WSSFN recommend their strict guidelines be upheld until the safety and efficacy of the procedures in question have been established. Both organizations call for strict oversight by IRBs, which make use of experts in the field who have special knowledge of the procedures. The National Commission recommended a subcommittee of the IRB be formed to evaluate surgical candidates including a neurosurgeon, psychiatrist, neurologist, and psychologist (1977). The WSSFN similarly recommends a team including a trained stereotactic and functional neurosurgeon, psychiatrist, neurologist, and neuropsychologist be formed to approve the patient selection, preoperative evaluations, and the neurosurgical therapy under investigation (Nuttin et al. 2014). Both organizations outline the need for informed consent with special attention to the decisional capacity of the subjects, including how to enroll subjects who do not have decision-making capacity as well as pre-operative and post-operative evaluation for all subjects. Finally, both recommend that an independent organization compile information on all clinical trials. The National Commission recommends information should be gathered on all psychosurgical procedures including indications for the procedures and the populations receiving them, which is evaluated and summarized for Congress annually. The WSSFN similarly recommends a de-identified independent registry should be formed for "all individuals undergoing neurosurgery for psychiatric disorders" (Nuttin et al. 2003, p. 1005). Of course, few of the National Commission's recommendations were never carried out. A "national psychosurgery advisory board," which was tasked with overseeing psychosurgeries was never established and, therefore, could not give independent oversight of ongoing psychosurgical procedures and the National Commission never was able to compile information on all psychosurgical procedures for review.

Just as earlier recommendations around psychosurgery remain largely unenforced, the recommendations of the WSSFN are inconsistently followed, unless compliance is already required under federal or state law. Thus, reasonable, ethically sound, and expert crafted recommendations are not consistently used to protect vulnerable psychosurgery patients. We propose these recommendations, and an effective enforcement mechanism, be incorporated into federal and state requirements for all future psychiatric DBS trials and treatments (see Recommendation 1).

Ethical Challenges Raised by DBS for Psychiatric Conditions

Comparing DBS to earlier forms of psychosurgery and electrical brain stimulation reveals some common ethical challenges. Given the sordid legacy of these earlier therapies, it is not surprising that many DBS researchers wish to avoid such comparisons. Neuropsychiatrists Sachdev and Chen argue, "[a]lthough this may be

a trivial distinction, it is important so as not to tar DBS with the lobotomy brush" (2009). The neurologist Matthis Synofzik, contends DBS differs from early psychosurgery "in almost all important ethical variables" (2013, p. 192), including medical indication, surgical method, damage to brain tissue, and decision-making processes. Researchers are quick to point out surgical techniques and understandings of the brain have advanced considerably since the early twentieth century. Synofzik and Schlaepfer claim in early psychosurgery, the indications were "vague," the surgical methods were "imprecise," the selection of brain targeted areas was "crude," and the primary goal was "altering wholesale personality structures" (2008, p. 1513). They also claim DBS is now only used for "patients with reduced health-related quality of life," surgical methods are now "precisely planned," the selected brain targets are "hypothesis-driven," and the primary goal is now "improving specific aspects of respective psychiatric disorder (p. 1513)."

Not everyone is so quick to dismiss the parallels between psychosurgery and contemporary DBS, however. The Presidential Commission for the Study of Bioethical Issues explicitly refers to DBS as a form of psychosurgery. In its report *Gray Matters* (2014), the Presidential Commission notes, "…contemporary advances in psychosurgery, such as DBS, must contend with the widespread cultural salience of a controversial past (p. 9)." The report cautions researchers that viewing DBS as a "ray of hope in an otherwise bleak situation for mentally ill patients," mirrors the early promises of lobotomy. (p. 10) It is noteworthy that although our understanding of psychiatric conditions and our research techniques have improved in recent decades, early lobotomists, such as Freeman, were considered the preeminent scientists of their day (Braslow 1999). There are many ethically salient similarities between earlier psychosurgeries and brain stimulation techniques and psychiatric DBS. For example, modern psychiatric also DBS is given as a 'last resort' intervention, its mechanism of effectiveness is unclear, the exact targets of the brain responsible for illness are unknown, and the goal is to modify particular undesirable behaviors or psychiatric symptoms.

In particular, there are two key ethical concerns regarding psychiatric DBS that are clearly similar to concerns in early forms of psychosurgery (including electrical brain stimulation): confirmation biases and undue influences in result interpretation and the vulnerability of the patient population used in DBS trials. These concerns, which were foundational critiques of early forms of psychosurgery, reinforce our argument for heightened regulation of DBS research. By highlighting these important similarities between psychiatric DBS and earlier practices, we argue the same justifications that supported heightened regulation decades ago could similarly justify an updated regulatory environment for medical devices and surgical procedures related to psychiatric DBS.

Bias and External Influence

Medical practitioners may be put in the difficult position of establishing realistic expectations for a DBS procedure, while acknowledging instances in which substantial improvements have been found. DBS trial sponsors have been criticized for substandard reporting methods. One meta-analysis of DBS for psychiatric

disorders (Nangunoori et al. 2013) pools results from different DBS targets, as stimulation coordinates vary substantially among patients, which significantly influenced clinical outcomes (Figee et al. 2015). Neurologist Erwin Montgomery has discussed many flaws in DBS research including confirmation bias and "the fallacy of confirming the consequence" (Montgomery 2012), which results in selecting a predicted observation that already presupposes the hypothesis. The concern that only positive results will be published at the expense of negative data is known as publication bias. Schlaepfer and Fins (2010, p. 775–776) argue publication bias is not unique to psychiatric DBS, but "this area is particularly vulnerable to bias because of an excessive reliance on single-patient case reports." These biases are particularly powerful when procedures involve advanced technology and unknown brain mechanisms—both powerfully enticing areas of medicine and research.

External influences are also ethical concerns in DBS research. In particular, financial conflicts of interest among key investigators involved in trials for psychiatric DBS. Many researchers involved in the trials hold patents and licensing rights for DBS technologies or act as consultants for DBS manufacturing companies. It is imperative to ensure conflicts of interest do not blur the ethical judgment of clinicians involved in these procedures. Additionally, the current oligopoly of DBS devices companies is an ethical concern. At this time there are only two main companies Medtronic (which has been in the pacemaker market for several years) and St. Jude Inc. Medical.

Media excitement over new medical breakthroughs is also concerning. Paralleling America's early enthrallment with psychosurgery, contemporary media coverage tends to exaggerate miracle-like outcomes and over-emphasize best-case scenarios for future cures (Bell et al. 2010). In a seminal study, Racine et al. reviewed articles published on neural stimulation techniques in the US and UK. They found 51% of the articles reviewed gave optimistic depictions of the procedures, while only 4% emphasized the risks involved (2007). A recent media article covering the BROADEN Trial is one of the few instances where media reports explore the issues with a more critical eye (Egan 2015). One commentator, who was initially enamored by the data on the use of DBS for depression, reflects, "But if the history of such treatments [mental illness] teaches us anything, it is that we must view claims of dramatic progress with skepticism, or we will fall prey to false hopes (Horgan 2014)." Clearly, we must be careful not to let our desire to cure mental illness obscure the very real ethical concerns embedded in these types of clinical trials. To ensure the scientific and media hype over DBS does not obscure the challenges and potential harms of these clinical trials, the federal government must ensure and enforce transparency (see Recommendation 2). As described above, current databases, such as clinicaltrials.gov, lack the transparency necessary for external monitoring.

The Vulnerability of Patients

When considering who would be an ideal candidate for psychiatric DBS, some ethical and legal dilemmas are likely to arise concerning decisional capacity and

informed consent. There are at least three reasons why psychiatric DBS candidates may currently have difficulty giving informed consent to the procedure. First, DBS for psychiatry is an investigational procedure and is only reserved for the most refractory cases. Thus, there might be sufficient grounds to question the decisional capacity of these patients due to their medical condition. Of course, psychiatric disorders do not necessarily preclude patients from making informed decisions about medical treatment; however, patients who have severely debilitating psychiatric disorders (such as those with treatment refractory conditions) may lack the capacity to make decisions about treatments like DBS. For instance, OCD candidates considered for DBS often spend an inordinate amount of time each day (up to 8 h) grappling with obsessive and compulsive thoughts. As Walter Glannon attests, "experiencing compulsions 8 h each day would appear to undermine the cognitive functions necessary for consent" (2010). At present, it appears unlikely that such patients would be able to give fully informed consent for psychiatric DBS procedures by virtue of the pathology their mental illness.

Second, because DBS procedures are often considered a "last resort" options, patients are likely to be desperate for relief from their symptoms, regardless of how theoretical or experimental such treatment may be. Desperation can undermine the informed consent process because the hope for a cure of refractory symptoms might be unreasonable, and, thus, leave the patient unable to rationally interpret the provided information, appreciate the various treatment options and alternatives, or falsely believe they will personally benefit from the study. Empirical studies exploring decisional capacity and therapeutic misconception in DBS research participants suggest that therapeutic misconception is pervasive (Fisher et al. 2012). The enthusiastic reaction by the scientific and popular media may add to a patient's potentially unreasonable expectations of positive results.

Desperation of the patient population, however, is a double-edged sword because it leaves subjects vulnerable, but also in great need. Ethicists Emanuel, Wendler, and Grady argue clinical trials may be ethical if there is a lack of alternative options as long as the clinical research studies follow 7 requirements, including scientific validity, have a favorable risk–benefit ratio, and research subjects have given informed consent (2000). Although these requirements might enable more ethically sound clinical research, in practice there are systemic failures (as was seen in the BROADEN trial) that may still fail to protect people who are vulnerable because of their disease. These same people might be left more vulnerable if they are not offered proper follow-up care or misunderstand what can be expected from participating in such a trial. In this regard, the available empirical evidence suggests, contrary to what Dunn and colleagues argue (2011), a revision of current safeguards specific to psychiatric DBS and enforcement of those safeguards is needed. For this reason, in addition to more transparency in clinical trials, we recommend all IRBs enlist members or consultants who are familiar with the particular medical and ethical challenges in psychiatric DBS research (see Recommendation 3).

Finally, issues of informed consent can become much more difficult when surrogate decision makers are involved in the decision-making process. In some states, such as California, persons who cannot give informed consent are prohibited from receiving psychosurgery, even if consented to by a surrogate. In other states,

such as Arkansas and Connecticut, a court must review every case of psychosurgery when the patient is incapacitated (Arkansas Statute § 28-65-302 2011; Connecticut Statute § 17a-543 2011). Such onerous third-party review would likely preclude or at least delay psychiatric DBS for most patients who are unable to give direct informed consent. Moreover, if psychiatric DBS becomes a more common therapy, states like Kentucky, which prohibits even the court to consent to psychosurgery for minors, may need to reconsider their statutes (Kentucky Statute §645.170 1996). Parents who care for particularly unruly or difficult children, or adult children who are primary caregivers of their older parents experiencing psychotic or violent behaviors, may see DBS as an enticing option for personal convenience or social harmony, and not because it is in the patient's best interest. Much like patients who may be desperate for a cure, surrogate decisions makers (who also function as the patient's primary care giver) may be tempted to see DBS as *their* only hope for relief. Though bioethicists are divided on whether surrogate decision-makers should consider their own care-taking interests when making proxy medical decisions, most agree the interests of caretakers should be subordinated to the best interests of the patient (Brock 1996). The history of early psychosurgery and brain stimulation programs ought to encourage humility and promote a critical eye, particularly when the nature of the disorder at stake already makes psychiatric patients more vulnerable and susceptible to harm by failures in the systems that are supposed to protect them.

Recommendations

The continuing ethical challenges raised by psychiatric DBS call into question whether it should be regulated differently from other psychosurgical procedures. Many DBS researchers believe psychiatric DBS falls outside of the definition of psychosurgery, and, therefore, should not be regulated as such. We argue, however, these assumptions are misguided, leave vulnerable patients susceptible to abuse, and should carefully be reexamined. The parallels between earlier psychosurgical procedures and DBS warrant a reexamination of current laws and guidelines regulating psychiatric DBS procedures. In light of these parallels, we have three recommendations for psychiatric DBS research going forward: regulate psychiatric DBS procedures as if they were psychosurgeries under state law, establish a national database for psychiatric DBS trials, and require IRBs to ensure clinical trials provide proper follow-up care by a trained physician before accepting any protocol.

Recommendation 1: First, current state laws that regulate psychosurgical procedures ought to include psychiatric DBS procedures. As noted above, federal regulations alone, without binding regulations from states, would be insufficient to protect DBS patients adequately. Regulating DBS through state mechanisms, in addition to the current federal approaches, will close potential loopholes created by the patchwork of regulating entities and overlapping jurisdictions. Although there is not currently a single definition of psychosurgery held in common across states and not all states have psychosurgery laws, those that do should include psychiatric DBS

as a kind of psychosurgery. Additionally, we recommend that the 24 states that currently lack psychosurgery legislation adopt regulations similar to that of California. As shown, there do not seem to be compelling reasons, either historical, scientific, or ethical to regulate psychiatric DBS wholly differently than other human subjects research that involve vulnerable subjects or the current laws regarding psychosurgery. Patients with refractory psychiatric disorders are just as vulnerable as candidates for psychosurgeries or brain stimulators were decades ago. The justifications for regulating those procedures in 1970s, such as the vulnerability of subjects, and issues of informed consent, still apply today to psychiatric DBS.

Recommendation 2: Second, the Federal Government should require all psychiatric DBS trials be registered in a transparent and easily accessible database and a committee should be formed to oversee and audit these trials. As described previously, current federal and professional regulations are essentially unenforceable. Researchers who receive federal funding must follow human subjects research protocols, but, as described, the process could be much more transparent to both the public and bioethicists. Due to the ethical concerns expressed in the previous section, the efficacy of psychiatric DBS treatments, the potential for research and media bias, and the vulnerability of patients, more transparency in the clinical trial process is needed. Moreover, as shown with the BROADEN trial, medical device regulations and guidelines for neurosurgery are insufficient to protect all research subjects, and a more transparent system might enable research subjects to understand their own participation in research and the progress of the research more fully. No trial participant, much less one with refractory mental illness and an implanted brain stimulator, should ever have to find out their clinical trial has been canceled through internet forums.

Recommendation 3: Finally, all trial protocols must ensure the use of an IRB with the knowledge necessary to appropriately oversee the ethical implementation of trials involving psychiatric DBS. Protocols should also ensure participants have a physician outside the trial who will agree to take on the patient's care after the trial is over, as is common practice in stereotactic trials and is recommended by the WSSFN. Because IRBs are regulated at the institutional level, they are one of the most influential forms of regulation and oversight for psychiatric DBS; therefore, equipping IRBs with members who have specialized knowledge of innovative surgical procedures is essential. The complexity, novelty, and potential side effects of these devices should not be underestimated. At present, most DBS trials are conducted at large hospitals with many resources, but there is no guarantee IRBs are familiar with psychiatric DBS. Moreover, there is no guarantee such trials will ensure patients have access to the resources they need for follow-up. The BROADEN trial showed there is potential for subject abandonment, which can have devastating consequences for persons with refractory psychiatric illness and novel, difficult to manage technologies implanted in their brains. As discussed in the previous section, the vulnerability of these research subjects is high and demands special consideration once trials have ended but implanted devices remain.

Conclusion

Certainly, medicine has come a long way since the early psychosurgeries, but history ought to remind us of the risky nature of procedures aimed at modifying behavior. Psychosurgery and electrical brain stimulation programs ought to be told as a cautionary tale of procedures that were generally approved of by the medical community, backed by the popular press, and performed by doctors who truly believed they were helping desperate people. Eventually, however, such procedures became abused. The new frontiers of psychosurgery are subject to similar abuses and will need to be overseen by clinicians, ethicists, and the courts. "Legislative fetters" can indeed hamper medical progress, but they can also provide a much-needed safeguard for innumerable desperate patients suffering from psychiatric issues. We can and must better protect these vulnerable patients.

References

A.C.A § 28-65-302. (2011).

Aden v. Younger, 57 Cal. App. 3d 662. (1976).

Alonso, P., Cuadras, D., Gabriëls, L., Denys, D., Goodman, W., Greenberg, B. D., Fiacro, J. P., Kuhn, J., Lenartz, D., Mallet, L., Nuttin, B., Real, E., Segalas, C., Schuurman, R., du Montcel, S. T, & Menchon, J. M. (2015). Deep brain stimulation for obsessive–compulsive disorder: A meta-Analysis of treatment outcome and predictors of response. *PLoS ONE.* doi:10.1371/journal.pone.0133591.

Annas, G. J., & Glantz, L. H. (1974). Psychosurgery: The law's response. *Boston University Law Review, 54*(2), 249–267.

Baumeister, A. A. (2000). The Tulane Electrical Brain Stimulation Program a historical case study in medical ethics. *Journal of History of the Neurosciences, 9*(3), 262–278.

Bell, E., Maxwell, B., McAndrews, M. P., Sadikot, A., & Racine, E. (2010). Hope and patients' expectations in deep brain stimulation: Healthcare providers' perspectives and approaches. *Journal of Clinical Ethics, 21*(2), 112–124.

Bergfeld, I. O., Mantione, M., Hoogendoorn, M. L. C., Ruhe, H. G., Notten, P., van Laarhoven, J., & Denys, D. (2016). Deep brain stimulation of the ventral anterior limb of the internal capsule for treatment-resistant depression. A randomized clinical trial. *JAMA Psychiatry, 73,* 456–464.

Braslow, J. T. (1999). History and evidence-based medicine: Lessons from the history of somatic treatments from the 1900s to the 1950s. *Mental Health Services Research, 1*(4), 231–240.

Breggin, P. (1972a). Lobotomies are still bad medicine. *Medical Opinion, 8,* 32–36.

Breggin, P. (1972b). The return of lobotomy and psychosurgery. *Congressional Record, 118,* 5567–5577.

Brock, D. W. (1996). What is the moral authority of family members to act as surrogates for incompetent patients? *The Milbank Quarterly, 74*(4), 599–618.

Cal. Welfare & Institutions Code § 5325(g). (2016).

Canterbury v. Spence, 464 F.2d 772. (D.C. Cir. 1972).

Chodakiewitz, Y., Williams, J., Chodakiewitz, J., & Cosgrove, G. R. (2015). Ablative surgery for neuropsychiatric disorders: Past, present, future. In B. Sun & A. D. Salles (Eds.), *Neurosurgical treatments for psychiatric disorders* (pp. 51–66). Dordrecht: Springer.

Conn. Gen. Stat. § 17a-543. (2011).

Delgado, J. M. (1969). *Physical control of the mind: Toward a psychocivilized society*. New York, NY: Harper and Row.

Delgado, J. M., Hamlin, H., & Chapman, W. P. (1952). Technique of intracranial electrode implacement for recording and stimulation and its possible therapeutic value in psychotic patients. *Confinia Neurologica, 12*(5–6), 315–319.

Doernberg, S. N., & Wendler, D. (2016). Ensuring respect for human research participants institutional review boards and sharing results from research. *Jama-Journal of the American Medical Association, 316*(11), 1149–1150.

Dougherty, D. D., Rezai, A. R., Carpenter, L. L., Howland, R. H., Bhati, M. T., O'Reardon, J. P., Malone, D. A. (2015). A randomized sham-controlled trial of deep brain stimulation of the ventral capsule/ventral striatum for chronic treatment-resistant depression. *Biological Psychiatry, 78,* 240–248.

Dunn, L., Holtzheimer, P., Hoop, J., Mayberg, H., Roberts, L. W., & Appelbaum, P. (2011). Ethical issues in deep brain stimulation research for treatment-resistant depression: Focus on risk and consent. *AJOB Neuroscience, 2*(1), 29–36.

Egan, D. (2015). Adverse effects: The perils of deep brain stimulation for depression. *Mad in America*, https://www.madinamerica.com/2015/09/adverse-effects-perils-deep-brain-stimulation-depression/. Accessed 20 February 2017.

El-Hai, J. (2005). *The lobotomist: A maverick medical genius and his tragic quest to rid the world of mental illness*. Hoboken, NJ: Wiley.

Eljamel, S. (2015). Ablative surgery for depression. In B. Sun & A. D. Salles (Eds.), *Neurosurgical treatments for psychiatric disorders*. Dordrecht: Springer.

Emanuel, E. J., Wendler, D., & Grady, C. (2000). What makes clinical research ethical? *JAMA, 238*(20), 2701–2711.

Erickson-Davis, C. (2012). Ethical concerns regarding commercialization of deep brain stimulation for obsessive compulsive disorder. *Bioethics, 26*(8), 440–446.

Feldman, R. P., Alterman, R. L., & Goodrich, J. T. (2001). Contemporary psychosurgery and a look to the future. *Journal of Neurosurgy, 95*(6), 944–956.

Feldman, R. P., & Goodrich, J. T. (2001). Psychosurgery: A historical overview. *Neurosurgery, 48*(3), 647–659.

Figee, M., Schuurman, R., & Denys, D. (2015). Challenges with meta-analysis in deep brain stimulation. *Stereotactic and Functional Neurosurgy, 93*(2), 147.

Fins, J. J., Kubu, C. S., Mayberg, H. S., Merkel, R., Nuttin, B., & Schlaepfer, T. E. (2017). Being open minded about neuromodulation trials: Finding success in our "failures". *Brain Stimulation, 10*(2), 1–6.

Fins, J. J., Mayberg, H. S., Nuttin, B., Kubu, C. S., Galert, T., Sturm, V., Stoppenbrink, K., Merkel, R., & Schlaepfer, T. E. (2011). Misuse of the FDA's humanitarian device exemption in deep brain stimulation for obsessive–compulsive disorder. *Health Affairs, 30*(2), 302–311.

Fisher, C. E., Dunn, L. B., Christopher, P. P., Holtzheimer, P. E., Leykin, Y., Mayberg, H. S., Lisanby, S. H., & Appelbaum, P. S. (2012). The ethics of research on deep brain stimulation for depression: decisional capacity and therapeutic misconception. *Annals of the New York Academy of the Sciencse, 1265,* 69–79.

Flora, E. D., Perera, C. L., Cameron, A. L., & Maddern, G. J. (2010). Deep brain stimulation for essential tremor: A systematic review. *Movement Disorders, 25*(11), 1550–1559.

Fox, S. H., Katzenschlager R., Lim, S., Ravina B., Seppi, K., Coelho, M., Poewe, W., Rascol, O., Goetz, C. G., & Sampaio, C.(2011). The movement disorder society evidence-based medicine review update: Treatments for the motorsymptoms of Parkinson's disease. *Movement Disorders, 26*(S3), S2–S41.

Foley, P. (2014). Deep brain stimulation for Parkinson's disease: Historical and neuroethical aspects. In J. Clausen & N. Levy (Eds.), *Handbook of neuroethics*. Amsterdam: Springer.

Food and Drug Administration. (2006). *Information sheet guidance for IRBs, clinical investigators, and sponsors*. Resource document. Office of Good Clinical Practice. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067. Accessed 20 February 2017.

Getz, M. J. (2009). The ice pick of oblivion: Moniz, Freeman and the development of psychosurgery. *Trames, 13*(2), 129–152.

Glannon, W. (2010). Consent to deep brain stimulation for neurological and psychiatric disorders. *Journal of Clinical Ethics, 21*(2), 104–111.

Graat, I., Martijn, F., & Denys, D. (2017). The application of deep brain stimulation in the treatment of psychiatric disorders. *International Review of Psychiatry, 29*(2), 178–190.

Greenberg, B. D., Gabriels, L. A., Malone, D. A., Jr., Rezai, A. R., Friehs, G. M., Okun, M. S., Shapira, N. A., Foote, K. D., Cosyns, P. R., Kubu, C. S., Malloy, P. F., Salloway, S. P., Giftakis, J. E., Rise, M. T., Machado, A. G., Baker, K. B., Stypulkowski, P. H., Goodman, W. K., Rasmussen, S. A., & Nuttin, B. J. (2010). Deep brain stimulation of the ventral internal capsule/ventral striatum for obsessive–compulsive disorder: Worldwide experience. *Molecular Psychiatry, 15*(1), 64–79.

Hariz, M., Blomstedt, P., & Zrinzo, L. (2013). Future of brain stimulation: New targets, new indications, new technology. *Movement Disorders, 28*(13), 1784–1792.

Health and Human Services. (2009). *Code of federal regulations*. 45 CFR 46. https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/. Accessed 20 February 2017.

Heath, R. G. (1954). The theoretical framework for a multidisciplinary approach to human behavior. In R. G. Heath (Ed.), *Studies in schizophrenia. A multidisciplinary approach to mind–brain relationships*. Cambridge, MA: Harvard University Press.

Heath, R. G. (1972). Pleasure and brain activity in man. *American Journal of Psychiatry, 120,* 571–577.

Horgan, J. (2014). Much hyped brain-implant treatment for depression suffers setback. *Scientific American*. https://blogs.scientificamerican.com/cross-check/much-hyped-brain-implant-treatment-for-depression-suffers-setback/. Accessed 23 May 2017.

Juckel, G., Uhl, I., Padberg, F., Brune, M., & Winter, C. (2009). Psychosurgery and deep brain stimulation as ultima ratio treatment for refractory depression. *European Archives of Psychiatry and Clinical Neuroscience, 259*(1), 1–7.

Kaimowitz v. Department of Mental Health for the State of Michigan. (1973). 2 Prison L. Rptr 433.

Kringelbach, M. L., & Aziz, T. Z. (2009). Deep brain stimulation: avoiding the errors of psychosurgery. *JAMA, 301*(16), 1705–1707.

Kuhn, J., Lenartz, D., Huff, W., Lee, S., Koulousakis, A., Klosterkoetter, J., & Sturm, V. (2007). Remission of alcohol dependency following deep brain stimulation of the nucleus accumbens: Valuable therapeutic implications? *Journal of Neurology, Neurosurgery and Psychiatry, 78,* 1152–1153.

KY Rev Stat §645.170. (1996 through Reg. Sess.).

Lipsman, N., Bernstein, M., & Lozano, A. M. (2010). Criteria for the ethical conduct of psychiatric neurosurgery clinical trials. *Neurosurgical Focus, 29*(2), E9. doi:10.3171/2010.4.FOCUS09327.

Lipsman, N., & Lozana, A. M. (2012). Neurosurgery and deep brain stimulation for psychiatric disease: Historical context and future prospects. *AJOB Neuroscience, 3*(1), 9–12.

Lipsman, N., Woodside, D. B., Giacobbe, P., Hamani, C., Carter, J. C., Norwood, S. J., Sutandar, K., Staab, R., Elias, G., Lyman, C. H., Smith, G. S., & Lozano, A. M. (2013). Subcallosal cingulate deep brain stimulation for treatment-refractory anorexia nervosa: A phase 1 pilot trial. *The Lancet, 381*(9875), 1361–1370.

Malone, D. A., Jr., Dougherty, D. D., Rezai, A. R., Carpenter, L. L., Friehs, G. M., Eskandar, E. N., Rauch, S. L., Rasmussen, S. A., Machado, A. G., & Kubu, C. S. (2009). Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. *Biological Psychiatry, 6*(4), 267–275.

Mantione, M., Van De Brink, W., Schuurman, P. R., & Denys, D. (2010). Smoking cessation and weight loss after chronic deep brain stimulation of the nucleus accumbens: Therapeutic and research implications: Case report. *Neurosurgery, 66*(1), 1–4.

Mashour, G. A., Walker, E. E., & Martuza, R. L. (2005). Psychosurgery: Past, present, and future. *Brain Research Reviews, 48*(3), 409–419.

Mayberg, H. S. (2009). Targeted electrode-based modulation of neural circuits for depression. *The Journal of Clinical Investigation, 119*(4), 717–725.

Mayberg, H. S., Lozano, A. M., Voon, V., McNeely, H. E., Seminowicz, D., Hamani, C., Schwalb, J. M, & Kennedy, S. H. (2005). Deep brain stimulation for treatment resistant depression. *Neuron, 45,* 651–660.

Montgomery, E. B., Jr. (2012). The epistemology of deep brain stimulation and neuronal pathophysiology. *Frontiers in Integrative Neuroscience, 6,* 78.

Morishita, T., Fayad, S. M., Higuchi, M. A., Nestor, K. A., & Foote, K. D. (2014). Deep brain stimulation for treatment-resistant depression: Systematic review of clinical outcomes. *Neurotherapeutics, 11*(3), 475–484.

Muller, S., Riedmuller, R., & van Oosterhout, A. (2015). Rivaling paradigms in psychiatric neurosurgery: Adjustability versus quick fix versus minimal-invasiveness. *Frontiers of Integrative Neuroscience, 9,* 27.

Nangunoori, R., Tomycz, N. D., Quigley, M., Oh, M. Y., & Whiting, D. M. (2013). Deep brain stimulation for psychiatric diseases: A pooled analysis of published studies employing disease-specific standardized outcome scales. *Stereotactic and Functional Neurosurgy, 91*(6), 345–354.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1977). *Report and recommendations: Psychosurgeries*. Washington D.C.: DHEW Publication No. (OS)77-0001. https://videocast.nih.gov/pdf/ohrp_psychosurgery.pdf. Accessed 23 May 2017.

Nuttin, B., Cosyns, P., Demeulemeester, H., Gybels, J., & Meyerson, B. (1999). Electrical stimulation in anterior limbs of internal capsules in patients with obsessive–compulsive disorder. *The Lancet, 354*(9189), 1526.

Nuttin, B. J., Gabriëls, L. A., Cosyns, P. R., Meyerson, B. A., Andréewitch, S., Sunaert, S. G., Maes, A. F., Dupont, P. J., Gybels, J. M., Gielen, F., & Demeulemeester, H. G. (2003). Long-term electrical capsular stimulation in patients with obsessive–compulsive disorder. *Neurosurgery, 52*(6), 1263–1272.

Nuttin, B., Wu, H., Mayberg, H., Hariz, M., Gabriëls, L., Galert, T., Merkel, R., Kubu, C., Vilela-Filho, O., Matthews, K., Taira, T., Lozano A. M., Schechtmann, G., Doshi, P., Broggi, G., Reǵis, J., Alkhani, A., Sun, B., Eljamel, S., Schulder, M., Kaplitt, M., Eskandar, E., Rezai, A., Krauss, J. K., Hilven, P., Schuurman, R., Ruiz, P., Chang, J. W., Cosyns, P., Lipsman, N., Voges, J., Cosgrove, R., Li, Y., & Schlaepfer, T. (2014). Consensus on guidelines for stereotactic neurosurgery for psychiatric disorders. *Journal of Neurology and Neurosurgical Psychiatry, 85*(9), 1003–1008.

Peña, C., Bowsher, K., Costello, A., De Luca, R., Doll, S., Li, K., Schroeder, M., & Stevens, T. (2007). An overview of FDA medical device regulation as it relates to deep brain stimulation devices. *IEEE Transactions on Neural Systems and Rehabilitation Engineering, 15*(3), 421–424.

Presidential Commission for the Study of Bioethical Issues. (2014). *Gray matters: Integrative approaches for neuroscience, ethics, and society* (Vol 1). Washington, D.C. http://www.bioethics.gov/sites/default/files/Gray%20Matters%20Vol%201.pdf. Accessed 23 May 2017.

Pressman, J. D. (1998). *Last resort: Psychosurgery and the limits of medicine (Cambridge history of medicine)*. Cambridge: Cambridge University Press.

Racine, E., Waldman, S., Palmour, N., Risse, D., & Illes, J. (2007). "Currents of hope": neurostimulation techniques in US and UK print media. *Cambridge Quartely Healthcare Ethics, 16*(3), 312–316.

Sachdev, P. (2007). Is deep brain stimulation a form of psychosurgery? *Australasian Psychiatry, 15*(2), 97–99.

Sachdev, P. S., & Chen, X. (2009). Neurosurgical treatment of mood disorders: Traditional psychosurgery and the advent of deep brain stimulation. *Current Opinion in Psychiatry, 22*(1), 25–31.

Saleh, C., & Fontaine, D. (2015). Deep brain stimulation for psychiatric diseases: What are the risks? *Current Psychiatry Reports, 17*(5), 1–14.

Schlaepfer, T. E. (2015). Deep brain stimulation for major depression—Steps on a long and winding road. *Biological Psychiatry, 78*(4), 218–219.

Schlaepfer, T. E., & Fins, J. J. (2010). Deep brain stimulation and the neuroethics of responsible publishing: When one is not enough. *JAMA, 303*(8), 775–776.

Schlaepfer, T. E., Lisanby, S. H., & Pallanti, S. (2010). Separating hope from hype: Some ethical implications of the development of deep brain stimulation in psychiatric research and treatment. *CNS Spectrums, 15*(5), 285–287.

Sironi, V. A. (2011). Origin and evolution of deep brain stimulation. *Frontiers of Integrative Neuroscince, 5,* 42.

Spoonhour, J. M. (1974). Psychosurgery and informed consent. *University of Florida Law Review, 26*(3), 432–452.

Synofzik, M. (2013). Functional neurosurgery and deep brain stimulation. In C. Anjan & M. J. Farah (Eds.), *Neuroethics in practice*. Oxford: Oxford University Press.

Synofzik, M., & Schlaepfer, T. E. (2008). Stimulating personality: Ethical criteria for deep brain stimulation in psychiatric patients and for enhancement purposes. *Biotechnology Journal, 3*(12), 1511–1520.

Valenstein, E. S. (1986). *Great and desperate cures: The rise and decline of psychosurgery and other radical treatments for mental illness*. New York: Basic Books.

Valenstein, E. S. (1997). History of psychosurgery. In S. H. Greenblatt, T. Gadi, & M. Epstein (Eds.), *A history of neurosurgery: In its scientific and professional contexts*. Rolling Meadows, IL: The American Association of Neurologica (Thieme/AANS).

Wagner, T., Valero-Cabre, A., & Pascual-Leone, A. (2007). Noninvasive human brain stimulation. *Annual Review of Biomedical Engineering, 9,* 527–565.

(1949). Lobotomy: Surgery for the insane. *Stanford Law Review, 1*(3), 463–474.