



From psychosurgery to neuromodulation and palliation: history's lessons for the ethical conduct and regulation of neuropsychiatric research

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We are certain that these experiments shall stir up keen discussions in the medical, psychiatric, psychological, philosophical, social and other fields. We expect that, but hope at the same time that this discussion shall promote the progress of science and above all the benefit of mental patients [1].
Egas Moniz, 1936

...We, the doctors, are so fallible, ever beset with the common and fatal facility of reaching conclusions from superficial observations, and constantly misled by the ease with which our minds fall into the rut of one or two experiences [2].
William Osler, 1903

Optimism tempered by history

As we contemplate the emerging era of neuro-modulation and imagine the utility of deep brain stimulation for disease entities in neurology and psychiatry, our enthusiasm is immediately tempered by history. Just a generation ago, other confident investigators were heralding invasive somatic therapies like prefrontal lobotomy to treat psychiatric illness. That era of psychosurgery ended with widespread condemnation, congressional calls for a ban [3], and a vow that history should never repeat itself. Now, just 30 years later, neurologists, neurosurgeons, and psychiatrists are implanting deep brain stimulators for the treat-

ment of Parkinson's disease and contemplating their use for severe psychiatric illnesses, such as obsessive-compulsive disorder (OCD) [4,5] and the modulation of consciousness in traumatic brain injury [6–8].

Any student of medical history would have to ask if these developments are ethically appropriate and whether the promise of neuromodulation will be able to transcend the potential peril associated with the manipulation of motor, psychiatric, or cognitive function. Can today's investigators avoid the moral blindness of their predecessors? Will society tolerate this new foray into somatic therapy and seek to regulate it as legitimate science, or will a lingering memory of psychosurgery be so overwhelming as to make this impossible?

Lay journalists covering the most exciting developments associated with deep brain stimulation often ask these questions [9]. A recent editorial in *The Economist*, for example, asserted that these new developments in neurobiology pose a "greater threat to human dignity" than the debate over cloning [10]. Editorialists like William Safire have raised questions about the world of "neuroethics" [11], and *The Washington Post Magazine* featured a story on the lobotomist Walter Freeman in response to the excitement over deep brain stimulators [12]. In the lay press, the link between psychosurgery and present efforts in neuromodulation is clear, and the message has been cautionary [13].

Historical analogies are important, but they only tell part of the story. From a scientific

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standpoint, there are critically important differences between psychosurgery and neuromodulation. Although both are somatic therapies, deep brain stimulation seeks to modulate brain function through the insertion of electrodes. In contrast, psychosurgery destroyed vital brain tissue through lesioning. These lesions were also permanent, whereas the presently known effects of neuromodulation are reversible. In addition, the permanent cognitive impairment seen with psychosurgical ablation does not occur with deep brain stimulation.

There are also important differences between Freeman's prefrontal lobotomy and psychosurgical procedures performed today. Psychosurgical operations of the past were crude and their rationale was based on a mix of anecdotal experience and supposition [14,15]. Current psychosurgical procedures utilize modern neuroimaging techniques and are more precise and procedurally diverse. They have a more benign side effect profile and demonstrate evidence of efficacy for some refractory neuropsychiatric conditions [16].

Modern neuromodulation's knowledge base, although still a nascent area of investigation, far exceeds what was known to psychosurgeons at midcentury [17]. Today, clinical investigators are supported by an extensive platform of structural and functional neuroimaging and detailed anatomic and electrophysiologic studies that allow for more precise hypotheses concerning neural systems underlying disease states.

These improvements have led to greater procedural precision and better diagnostic capacity to identify mechanisms of action, efficacy, and lack of therapeutic response. In the treatment of Parkinson's disease, these advances have coalesced so that neuromodulation is now a mature and established therapy for refractory disease [18,19]. Deep brain stimulation procedures for movement disorders are covered in the United States by Medicare and have become the standard of care for refractory disease.

Although these scientific differences are significant, a more salient distinction is the respective historical and cultural contexts of psychosurgery and neuromodulation. Historically, psychosurgery developed before the rise of modern bioethics. Neuromodulation, today, is emerging both against the historical backdrop of psychosurgery and within an ethical and regulatory context that should be far more attentive to human subject protections.

By reviewing the history of the psychosurgery movement, I will demonstrate that this work continued in an unregulated and ethically disproportionate fashion despite well-articulated and early criticism. I will maintain that this was possible because there was no mechanism to regulate the conduct of these practices until the advent of modern bioethics in the late 1960s and early 1970s as a scholarly discipline able to influence clinical practice and public policy.

Earlier critiques, although often cogent and well informed, were unable to influence clinical or research practice because they were made in a practice environment that had yet to overcome the prerogative of the physician to direct care without additional oversight. As we shall see, individuals who criticized their colleagues' practice of psychosurgery in the literature or at national meetings were powerless to ensure that their concerns were heard at the psychosurgeon's home institution. There was no mechanism to collect these arguments and regulate these activities. It would take broader societal changes, such as the decline of physician paternalism and the emergence of civil and patient rights [20] reflected in the establishment of bioethics think-tanks like the Hastings Center and the regulatory efforts of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, before broader regulations governing clinical research were put into place.

Sadly, much of this history has already been forgotten or deemed irrelevant. In an oddly analogous way, the debate over lobotomy and psychosurgery has gone the way of a Tommy Dorsey long-playing record or a Led Zeppelin eight-track tape. As we shall see, many of the regulatory recommendations made by the National Commission, such as the proposed National Psychosurgery Advisory Board or recommendations on research involving the institutionalized mentally infirmed, never went into law. This lacuna in the law necessitated the Clinton era 1998 National Bioethics Advisory Commission's "Report on Research Involving Persons With Mental Disorders That May Affect Decisionmaking Capacity" [21]. Ironically, this is yet another set of recommendations that have yet to be ensconced in Federal regulations.

The emergence of neuromodulation as credible science with real and potential clinical applications, however, makes it essential that we revisit these earlier ethical and clinical debates so that the hard-won wisdom and scholarship of earlier eras

can help to navigate what will be demonstrated as recurrent ethical challenges. Many familiar questions about consent, coercion, and personhood are now resurfacing in the debate over applying neuromodulation techniques, *née* psychosurgery, to OCD, the first of many psychiatric entities to which this modality may be applied.

It is my hope that a reconsideration of this rich history in light of these promising scientific developments will deepen the insight of a new generation of psychiatrists, neurologists, and neurosurgeons who are destined to face challenges that their forbears could only have imagined.

When psychosurgery was therapy

It is one of those strange paradoxes in history that 2 years after the articulation of the Nuremberg Code and the development of the stereotactic technique, Egas Moniz won the Nobel Prize for the development of the prefrontal leukotomy [22,23]. He began his work in 1935 [24], just 3 years after the initiation of the Tuskegee Syphilis Study [25]. Both the Tuskegee Syphilis Study and psychosurgery would be criticized decades later as an abrogation of patient rights invoking the same ethical principles articulated in the Nuremberg Code. In 1949, however, the Nobel Prize celebrated Moniz's work in medicine and physiology.

Although some have maintained that the Nobel Prize was really meant for Moniz's more enduring discovery of cerebral angiography [26], the citation on his medal read simply, "For his discovery of the therapeutic value of prefrontal leukotomy in certain psychoses" [27]. The understatement in this inscription fails to capture the lack of effective therapy for severe mental illness and the desperation of patients and the frustration of their families and caregivers. When Moniz was given the prize, his work was hailed as being at the vanguard of therapeutics for severe mental illness [28]. In the era before the introduction of antipsychotics, prefrontal lobotomy offered a potential therapy for the severely and persistently mentally ill who otherwise would require institutionalization. It was viewed as a therapy of last resort and positively portrayed in the American media, at least in the early years after its introduction [29].

All was not sanguine in professional circles, however. As early as 1938, Oskar Diethelm, a contemporary of Freeman and Watts in the United States, poignantly warned about the emerging somatic therapies in psychiatry [30]. In an address at the Annual Meeting of the American

Psychiatric Association in San Francisco, the New York psychiatrist urged professional humility. He cautioned investigators to have some humility in their speculations and an awareness of the investment that they have in their own theoretic speculations. To mitigate against these excesses, he urged investigators to assume as "an inflexible duty" to gain knowledge of the mechanism of any proposed therapy [30]. Specifically, he observed:

In any scientific treatment which is not fully understood there is the serious danger of not being able to predict possible damage. It should be an inflexible duty to become thoroughly familiar with the drug or procedure to be employed. This implies a thorough understanding of the physiological and psychobiological functions which may have a bearing on the proposed treatment. No one has the right to invent theories to suit his desires without having given full consideration to what has been established or found plausible [30].

In the same address, Diethelm implicitly commented on issues that would later inform the literature on informed consent. He warned of the vulnerability of lay people to the latest scientific trend and the powerlessness of patients, "who are forced to follow":

...it is important in medicine to recognize fully the responsibility with regard to those who follow voluntarily that is the physicians; to those who follow blindly, that is lay people; and to those who are forced to follow, that is the patients. The pleasure of being an inventor and pathfinder is alluring but leads to all the dangers of adventure [30].

In these comments, Diethelm anticipates the Nuremberg Code with its emphasis on the scientific basis of human experimentation and the centrality of informed consent and voluntariness [31].

A young psychiatrist attending the same meeting tells us that, as yet, there was no mention of Moniz's work at the conference and that Diethelm did not mention lobotomy specifically in his address [32]. His comments were more generic and directed toward the growing place of somatic therapy in psychiatry, a subdiscipline of the field of which psychosurgery would become a part.

Diethelm's warnings would be applicable to the leading proponents of psychosurgery as illustrated by the hubris of both Freeman and Moniz.

Moniz himself was smug and overly optimistic about his work and methods. In an early summary article originally published in the *American Journal of Psychiatry* in 1937, he summarily dismissed any discussion of the risks and benefits of his prefrontal leukotomy. He simply concluded by asserting:

Following this exposition I do not wish to make any comment since the facts speak for themselves. These were hospital patients who were well studied and well followed. The recoveries have been maintained. I cannot believe that the recoveries can be explained upon simple coincidence. Prefrontal leucotomy is a simple operation, always safe, which may prove to be an effective surgical treatment in certain cases of mental disorder [33].

Freeman, too, was overly confident. Just months before the American Psychiatric Association meeting, he demonstrated the traits that Diethelm believed were so dangerous in a clinical investigator. Lawrence M. Weinberger recalls that as a young physician, he met Freeman in the spring of 1938. Weinberger was a second-year fellow in neurologic surgery at the University of Pennsylvania and had traveled to the Delaware State Hospital to meet Freeman and to learn how to perform the novel procedure. Freeman's method of patient selection and his "purely observational" technique of determining who might be a suitable candidate for surgery mortified Weinberger. He asked Freeman about his selection criteria and "...was answered with a prolonged silent stare and finally one word: 'Experience!'" [34]. Weinberger reported being "squelched" and saying no more [34].

Concerns were not limited to junior trainees. Roy Grinker publicly questioned Walter Freeman at a panel discussion before the Section on Nervous and Mental Diseases at the annual session of the American Medical Association held in Cleveland in 1941 [35]. At that time, Grinker was Chief of the Division of Neuropsychiatry at Michael Reese Hospital in Chicago. He would later become a training analyst and Editor-in-Chief of the *Archives of General Psychiatry* [36].

Grinker sought to moderate attitudes toward lobotomy, about which he acknowledged "...a great deal of preconception and emotional bias." He acknowledged that there was controversy between those who believed that the psychoses had an organic basis and might be amenable to "physical therapy in psychiatry" and those

opposed to a "...mutilating operation that destroys brain tissue."

Ultimately, Grinker questioned Freeman's methodology because "...once one cuts, there is no return." Given the irreversibility of the procedure, he voiced concern about how patients were selected for the procedure and the vagueness of entry criteria that required the patient to have failed "conservative measures." He was particularly aware of the vulnerability of most of the patients who came from state facilities and whose preoperative assessment was suspect:

...We are dealing with a large number of patients who have been chosen from state hospital populations. There have been some private cases, it is true, but when one thinks of what conservative treatment means, of what actual, thoroughgoing psychologic study and treatment means, it is difficult to imagine that the patients who come from state hospital populations are getting the benefit of that type of treatment [35].

He expressed his "surprise" that patients were lobotomized after only a few months of mental illness before a spontaneous remission might occur and in young patients in their 30s. He also questioned the application of the procedure to a wide range of diagnoses and was concerned about the postoperative defects and the means to assess their impact on intelligence.

Addressing the risks of the procedure, he suggested that more attention needed to be paid to cognitive impairment and the late effects of scarring, which might lead to the development of seizure disorders. He also noted the vague way in which cognitive defects were described noting, "There must be developed a technique of measuring very carefully both the existing function and the defect in the individuals before and after the operation" [35]. Grinker also observed that a technologic solution to psychic problems was not always in order, although the alternatives were often more time-consuming and taxing:

It is obvious that if the anxiety and suffering, the things which one wants to relieve, are based on conflict, the rational basis of treatment is a psychological therapy. This can not always be done. It is sometimes very tedious and very costly, but if it were more possible we would not hesitate to ask for more psychologic work in state hospitals rather than more operating rooms [35].

Building on a therapeutic approach that was broader than the merely surgical, Grinker also outlined the professional responsibilities of the surgeon and his obligation to ensure that adequate assessment occurred before any procedure was performed. Without equivocation, he asserted that:

I do not believe that the surgeon can assume the responsibility of being the operator at the behest of his neurologic and psychiatric friends and say “I did it because they told me to.” He must assume the responsibility of insisting that before such operations are done all conservative means—and by “conservative means” I mean thorough going psychological treatment—have been employed [35].

Grinker’s criticisms are all the more credible because he did not categorically condemn the procedure. Instead, he saw it not as a therapy but “still an experiment.” Amid proponents and critics of psychosurgery, he confessed that his point of view, “...perhaps might disappoint some, as I am not iconoclastic about the operation.” He believed that the operation had a “usefulness” but that “the delimitations of its usefulness have not been clarified.” Until those limitations became better understood, he cautioned that “...I do not think this is the time to disseminate it widely to the profession or to the public...”

Unfortunately, Grinker’s pointed-and balanced-criticism of the lobotomy in 1941 had little impact. Although he urged restraint and viewed lobotomy as experimental, the procedure was widely disseminated as therapy over the next 10 years. It is estimated that by 1951, 19,000 to 20,000 Americans were lobotomized, with many of those subjected to the procedure being returning veterans [37]. In spite of growing professional uncertainty about the effectiveness of the procedure and its safety, public sentiment was positive enough to compel the Veterans Administration and state hospitals to introduce the procedure after the war [38]. It is estimated that nearly 3000 returning veterans underwent psychosurgery [39].

Although Grinker’s early criticism did little to stem the tide of lobotomy, his well-considered concerns about methodology, patient selection, outcome data, and the morbidity associated with the procedure would be revisited by the First Research Conference on Psychosurgery convened by the National Institute of Mental Health in 1949

[40]. During this meeting, although lobotomy was being used as a therapy in the community, the editor observed that, “although we seem well warranted to continue the procedure, it is not even clear that psychosurgery, as performed now, is more beneficial than harmful” [40]. Experts were unable to reach a consensus except to conclude that “...an enormous amount of further research is an imperative need in nearly every aspect of the field” [40].

Among these needs was greater clarity about whom the procedure was being performed on and how patients fared. Eleven years after Weinberger personally questioned Freeman about his method of selecting patients and evaluating outcomes, methodologic issues remained a concern. One thoughtful commentator on that era has maintained that the patient’s diagnosis was less relevant than the severity of the patient’s symptoms in determining whether or not he or she would be a surgical candidate [41]. It was against this imprecision that experts agreed that there was a need for a comprehensive means of engaging in outcome measures to discern whether the procedure was efficacious and on which subjects. Efforts to introduce quantitative analysis were complicated, however, because markers of improvement, such as hospital discharge, could be a result of the patient’s family situation [42]. Indeed, if any consensus was achieved at the First Research Conference on Psychosurgery, it was that a majority of assembled experts urged the adoption of a “...universally accepted rating scale, with patients individualized by diagnosis or other category...[to] provide an effective method for both case-selection and evaluation of operative results” [40].

In the second edition of his comprehensive textbook on psychiatric treatment, Diethelm noted that the operative procedures under consideration had “undergone considerable modification” [43]. He viewed these modifications as evidence of what he described as “therapeutic insecurity which should exert a strong critical hesitancy on the part of the clinician who is considering surgical procedure” [43].

Despite growing controversy about the safety and efficacy of psychosurgery at subsequent national conferences [40,44] and concerns about the side effects of the procedure [45], these concerns did not decrease the incidence or popularity of the procedure. Although articulated at conferences or in journals, these criticisms had little impact on the incidence of psychosurgery in the

United States. Between 1936 and 1946, some 6000 patients were operated on in the United States alone [46]. By the late 1950s, 40,000 to 50,000 procedures had been performed in the United States, with some 4000 estimated by Freeman to have been done or directed by him in 30 hospitals in 15 states nationwide [47]. Rosemary Kennedy, the sister of President Kennedy, was among those operated on.

The popularity of the procedure needs to be contextualized against the dismal condition of state mental hospitals and the absolute lack of effective treatment for the persistently and chronically mentally ill. One representative report from a state hospital during that era describes lobotomy as a “fruitful method in the treatment of chronic mental illness,” with 37.4% of patients being able to be discharged from hospital after the procedure [48]. The authors of this study, which mostly involved patients with schizophrenia, maintained that:

...While there are many limitations and failures with this treatment, they are overshadowed by the generally satisfactory and not infrequently brilliant results. It is still difficult to assess the extent to which technical difficulties or inherent resistance of the disease process contribute to operative failures. However, it is truly gratifying to observe a patient who was previously a tremendous problem in management—secluded, untidy, aggressive, destructive, and combative to the point of requiring half a dozen attendants to carry out the basic necessities of personal care—become a quiet cooperative individual, taking pride in her personal appearance, assisting with various ward tasks, and finally returning to her own home. Possibly only those who have served in a state hospital can appreciate fully these problems. The comments we have heard occasionally to the effect that postlobotomy patients lack judgment, and cannot, for example, plan a meal or play a good game of bridge seem to lack satisfactory perspective when one regards the level from which these individuals were plucked...Lobotomy is not a cure-all but it can well be regarded as an encouraging therapeutic weapon for a very malignant disease [48].

Although studies like this one failed to take into account a potential placebo effect or the possibility of spontaneous remission, criticism of lobotomy hinged on the question of side effects

and not on the important issue of efficacy. The question was not whether lobotomy altered the status of the patient's symptoms but whether the cognitive side effects were justified [49]. Nolan Lewis, Director of the New York Psychiatric Institute, asked whether “the quieting of a patient” was indeed a “cure” and worried about the number of “zombies” and “mental invalids” produced as a consequence of the procedure [50].

The decline of psychosurgery was not prompted by ethical concerns but rather by the advent of modern psychopharmacology and effective therapy for psychoses with the major tranquilizers, such as chlorpromazine in 1954. Indeed, two commentators have opined that even with the growing backlash against psychosurgery in the early 1950s, the lack of an effective alternative would have been sufficient to keep the procedure in “common use” [51].

Psychosurgery and the body politic

Not even chlorpromazine was enough of an advance to remove psychosurgery entirely from therapeutic consideration in the 1960s and early 1970s. Some physicians, such as the Harvard neurosurgeon H. Thomas Ballantine, Jr., maintained that psychosurgical procedures like cingulotomy retained a role in conjunction with standard psychiatric care for refractory patients. He articulated guidelines to regulate the judicious use of the procedure for the relief of the patient's suffering and improvement of functioning in society. Procedures were to be reserved for patients who failed all other methods of treatment. Decisions to operate were to be made in conjunction with a psychiatrist, who would also make psychiatric follow-up available, and patients and family were to be informed of potential risks and benefits. Most critically, he condemned the use of psychosurgery for political or social purposes, articulating instead a solely patient-centered rationale for the procedure [52].

It was the social uses of psychosurgery for what was called behavior control that, which Ballantine and others condemned, that caused a furor during that era. As distinct from its earlier iteration as a means to address a patient's depression or schizophrenia, this more modern dimension of psychosurgery sought to modify behavior. Amid the social turmoil of that era, sociobiologists began to suggest that psychosurgery might have a role in addressing problems like violence or civil unrest. It is perhaps hard to

imagine today that there could be serious concerns about such futuristic attempts at social control, but they were quite real. One news report in the Medical News column in the *Journal of the American Medical Association* sought to reassure the wary reader that “Logistically, psychosurgery for social control is highly unlikely, simply because there are not enough neurosurgeons” [53].

This second period in the history of psychosurgery could be said to have begun through the work of Jose M.R. Delgado. Coupling psychosurgery with burgeoning efforts in computer technology and solid state electronics, Delgado advanced the idea of “psychocivilizing society” using an implantable brain implant that could be operated by remote control [54]. Delgado came to international attention in 1965 when he returned to his native Spain for a now famous publicity stunt in which he demonstrated the potential of his work by stopping a charging bull in Cordoba’s bullring using a “stimociever” he had developed [55].

Delgado’s work raised concerns about the possibilities of mind control, and his legacy remains a lingering question for the current era of neuromodulation. Recent reports in the lay press describing a remotely controlled “cyborg” rat with a brain implant [56] alluded to Delgado’s work [57,58], thus resurfacing the question of mind control, which had explosive political consequences when first introduced.

A physician and physiologist working in the Department of Psychiatry at Yale University, Delgado studied aggression in primates and then manipulated their response through the use of implantable electrodes, arguing that “a better understanding of the neurophysiological mechanisms responsible for aggressive and destructive reactions may provide man with greater capacity to educate and direct his own behavior” [59]. Delgado, some of whose work was funded by the United States Public Health Service, the Office of Naval Research, and the Department of the Air Force [60,61], argued that society was on the cusp of a new era in which the human mind could influence its own evolution through the use of technology. Using notions of self-dominion, he envisioned an escape from the blind chance of normal evolution to one where man and technology would alter human history, ultimately leading to a “...future man with greater personal freedom and originality, a member of a psychocivilized society, happier, less destructive, and better balanced than present man” [54].

Delgado analogized cerebral pacemaking to the growing role of cardiac pacemakers as a means to suggest the utility of brain pacemaking in the future. He acknowledged concerns about the ethical implications of his work and urged “intelligent collaboration of the best minds” to address the field’s “fundamental medical, social, and even philosophical implications.” Nonetheless, he urged continued scientific progress, noting that “We are certainly facing ethical, philosophic, and practical problems not exempt from risks, but we should also expect important medical application of the new methods to epilepsy, intractable pain, involuntary movements, and mental disorders” [62]. His position might be best summed up by his observation that “Fears have been expressed that this new technology brings with it the threat of possible unwanted and ethical remote control of the cerebral activities of man by other men, but this danger is quite improbable and is outweighed by the expected clinical and scientific usefulness of the method” [63].

Leading proponents of psychosurgery for the control of violence were Frank R. Ervin, a psychiatrist at the Neuropsychiatric Institute at the University of California at Los Angeles, and Vernon H. Mark, a Harvard neurosurgeon, who together coauthored *Violence and the Brain* [64]. Much of their work hinged on seeking to demonstrate the relation between organic brain disorders, such as temporal lobe epilepsy (TLE), and violent or aggressive behavior. In one early case, they were able to demonstrate a left temporal horn lesion by means of a pneumoencephalogram in a young woman with TLE in whom violent outbursts were inducible using implantable electrodes and telemetric equipment supplied “through the courtesy and assistance of Dr Delgado” [65].

Echoing Delgado’s notion of “greater personal freedom,” Mark maintained that “I believe the correction of that organic condition gives the patient more rather than less, control over his own behavior. It enhances, and does not diminish, his dignity. It adds to, and does not detract from, his human qualities” [66]. Although many of Mark’s aspirations for psychosurgery seem overly optimistic, he did foreshadow developments in psychiatry, moving that field from being dominated by psychoanalysis and “political psychiatrists” toward those having an interest in the organic basis of disease [67].

He wrote about the “absurd split” and the:

...historical dichotomy between 'purely organic' and 'purely social' abnormalities. Specifically, physicians tend to categorize a few abnormal behaviors, such as paralysis, blindness and dementia as neurological problems. At the same time, certain other abnormalities, such as depression and aggression, have found a hard niche within the domain of the psychiatrists, sociologists and criminologists. Many of them view these behaviors as nothing but the reflections of particular environments. They tend to believe that brain function or dysfunction is not an important determinant of abnormal behavior [68].

As much as his work in psychosurgery, these views seemed to have engendered a backlash from the more purely socially oriented practitioners who saw psychiatry in political or sociologic terms [69]. This schism made Mark the target of what he described as an "anti-psychiatry campaign" [70]. Reacting to a brief letter he wrote with colleagues to the *Journal of the American Medical Association* in 1967 on the potential relation between brain disease and urban riots [71], Mark was accused of racism by proponents of social psychiatry [72].

This assault on psychosurgery was led by Peter Roger Breggin, a Washington social psychiatrist. A self-described political conservative and civil libertarian [73], Breggin sought to characterize psychotherapy and on a continuum of a totalitarian-libertarian axis in which a "high degree of autonomy and personal freedom characterizes more libertarian therapies" [74]. In this context, public psychiatric hospitals and psychosurgery were seen as vectors of social control and described as "custodial concentration camps" and "powerful totalitarian technologies," respectively.

In Congressional hearings before the Subcommittee on Health of the Senate Committee on Labor and Public Welfare, Breggin charged that psychosurgeons were unethical because of how they obtained consent for the procedures they performed. He was deeply suspicious of how psychosurgeons sought to regulate their activities through review committees that relied on "professional ethics and medical control" to maintain physician control of the situation. Ultimately, Breggin said, "It creates for themselves an elitist power over the human mind and spirit. If America ever falls to totalitarianism, the dictator will be a behavioral scientist and the secret police will be armed with lobotomy and psychosurgery. And by the way, lobotomy is still with us...Lobotomy

and psychosurgery is an ethical, political and spiritual crime. It should be made illegal" [75].

Breggin's accusations seem more suited to the clinical work of Freeman than to the positions taken by Mark, who was opposed to any social application of his work. In a talk delivered at the Hastings Center's Institute of Society, Ethics and Life Science's Working Group on Behavior Control, he sought to refute the charge of racism lodged against the neurosurgical treatment of violent epileptics [76]. He asked, "Does the theory that some violence is caused by brain disease lead us to expect it is a characteristic mainly of black people? Certainly not. On the other hand the theory that personal violence is caused exclusively by social conditions might very well lead us to look at the black ghettos. The environmental cues to personal violence may very well cluster around racially differentiated areas" [76]. Citing the prevalence of domestic violence across all demographics, both rich and poor as well as black and white, he asserted that "From this perspective, claret is the predominant color [of violence], not black or white" [76]. He would consistently maintain that violence was colorblind in both domestic and international contexts [77].

Indeed, he was one of the first to advocate an "integrated approach" to psychosurgical care. At Boston City Hospital, where he was Director of Neurosurgery, he sought to overcome the dichotomous practices of his neurologic and psychiatric colleagues and to develop a "holistic" therapy in which "...treatment of a patient should involve not only his brain but his family, living conditions, job and role in society. It is very important, therefore, to imbed a neurological diagnosis of problems of violence into a larger integrated approach to human behavior." Along these lines of comprehensive care, he also advocated a "committee of some sort" that would oversee consent while not accepting patients who do not want therapy.

In retrospect, Mark's attempt to address organic illness with due attention to the patient's voluntary consent comes across as moderate during immoderate times prone to hyperbole, overreaction, and suspicion. There was a prevailing sense of alarm that psychosurgery was being broadly applied in law enforcement. Contemporary accounts of that era observed that one of the "appeals" of psychosurgery was viewed as the willingness of law enforcement agencies to embrace this technology for the purpose of addressing seemingly intractable problems. One international

perspective from a New Zealander behavioral scientist observed that:

Still another cultural aspect which adds to the appeal of psychosurgery is the readiness of the American government to seek solutions to its domestic problems which hide the causes of the problems. Psychosurgery can be one such solution if used to “cure” the nation’s social problems. The Justice Department and several state departments of correction (notably California’s) have shown great interest both in establishing that black rioters and aggressive inmates are suffering from brain dysfunction and in curing them through psychosurgery. Three leading proponents of psychosurgery have advanced the view that many of those involved in ghetto rebellions acted violently because of brain dysfunction. The accumulated results of racism and poverty were discounted as causal factors since *not everyone rioted* [78].

Although this citation would suggest widespread use of psychosurgery for social control, the data suggest that it was otherwise. A 1974 study conducted by the Behavioral Control Research Group of the Hastings Institute surveyed the Commissioners of Corrections for all 50 states to ascertain the prevalence of behavior control in the nation’s prisons [79]. Forty-seven states and the District of Columbia responded. If behavior modification was done at all, the least coercive treatments, such as group therapy or token economy systems, were employed. None of the respondents used psychosurgery as a treatment procedure, although one added, “not at this time.” Although these data would suggest that things were better than feared, the author of the report cautioned the reader to be wary of the results. Perhaps reflecting the distrust prevalent during the end of the Nixon administration and the Watergate scandal, she notes that “In dealing with prisons, however, the publicly announced programs may be only a small percentage of what is actually occurring” [79].

This prevalence data concerning psychosurgery for nonmedical purposes was corroborated by a study conducted by the American Psychiatric Association Task Force on Psychosurgery and by the work of the National Commission. As the American Psychiatric Association report put it, “Both reports concluded that there is no reliable evidence that psychosurgery has been used for political purposes, social control or as an instru-

ment for racist repression” [80]. The National Commission report would later confirm this finding. In a review of 600 psychosurgery procedures performed in 1974, only six Hispanics and one black patient were identified. The Commission noted that “The fact that so few patients from minority groups have undergone psychosurgery...is due not to discrimination on the part of surgeons but to the economic realities and public policy” [81].

Furthermore, although minority communities were indeed fearful of these procedures, not all were in opposition. Two black neurosurgeons speaking at the 1976 National Minority Conference on Human Experimentation in Reston, Virginia, urged limited use of psychosurgery with appropriate oversight and review boards [82]. Dr Jesse Barber, Chief of Neurosurgery at Howard University, observed, “I personally feel guilty about not developing a program (of psychosurgery) at Howard University.” He added that “When it was considered we were reluctant to face the opposition and destroy our image in the black community.”

Although there was little evidence for the use of psychosurgery for law enforcement purposes, the issue of behavior control dominated the deliberations of advocates of all stripes whether they were physicians, philosophers, attorneys, or nascent bioethicists. In the political climate of that era, there was, it seemed, a fine line between scientific fact and science fiction [83]. In contrast to the media’s favorable—and distorted—depiction of psychosurgery in the early years of lobotomy [84], the popular culture of the 1970s heightened fears of abuse. Works like Crichton’s *The Terminal Man* depicted the “treatment” of a violent criminal with implantation of electrodes. The setting for the procedure was a fictitious neuropsychiatric institute located in Los Angeles, which, not so coincidentally, borrowed the name of Ervin’s own institution [85].

In this broader cultural context, fears of psychosurgery transcended the internecine battles of psychiatric subdisciplines, as exemplified by Breggin’s less than restrained ideologic attacks. More balanced criticism came from individuals like Edward Mearns, a professor of law at Case Western Reserve University, who observed that:

There is something promising about the notion that the effort to cure sick individuals may result in considerable social

benefit as well. But there is something disturbing about the conscious effort to use medicine and medical men institutions to cure a “sick” society. For it is one thing to use medicine as an instrument of healing and quite another to use it as an instrument for social control [86].

The philosopher Robert Neville, who directed the Hastings Center Working Group on Psychosurgery, echoed this sentiment. Neville asserted that “The ethics of good medicine isn’t easily transferred to good social control, so there is a danger of having the appearance of therapy, when the real purpose is punishment” [87]. Hal Edgar of Columbia Law School pointed out that although procedures on the brain are justifiable if they result in a cure of a physical illness like Parkinson’s disease without undue side effects, it becomes more complex when the focus of the intervention is mental illness which is “...a concept which is heavily influenced by social norms, and a label which is often imposed in a particular case because people engage in ‘strange’ behavior of one sort or another” [88]. Echoing the sentiments of the times about questioning authority, he asked, “...how does one know whether the sick are being cured or whether medicine is being used as yet another tool in society’s ever present effort to secure comfort through conformity” [88].

Much of the resistance to psychosurgery—and the broader issue of behavior control—was closely related to emerging concerns about the use of the procedure on prisoners, who might be coerced or unable to give appropriate consent to experimental procedures [89]. Some of this was related to a fear of somehow legitimizing a deeply flawed penal system through an affiliation with medicine [90], but much of it was a central concern about the ability of inmates to give voluntary and informed consent.

This issue came to national prominence in the 1973 case of *Kaimowitz v. Department of Mental Health*, in which a three-judge panel in Michigan sought to determine whether a confined prisoner could voluntarily consent to an experimental procedure that might temper his aggressive and criminal behavior [91]. The court opined that there was no scientific basis to suggest that psychosurgery would be therapeutic in the absence of a discernible disorder like epilepsy and that the risk-benefit ratio was disproportionate given the current state of knowledge and the known risks of the procedure. More critically, the

court went on to cite the entirety of the Nuremberg Code to argue that reasoned and voluntary consent in prison was so greatly impaired as to make lawful consent in that setting impossible [92,93]. Indeed, one of his attorneys, Professor Robert A. Burt, pointed out that the prisoner himself illustrated the coercive nature of incarceration when his confinement was declared unconstitutional and he had the opportunity to revisit his decision after initially consenting to psychosurgery. When these new developments allowed him to imagine being set free, he suspended his consent to reconsider surgery given his new circumstances [94].

Regulatory bioethics: the National Commission’s report on psychosurgery

Elliot S. Valenstein, commenting on this period, observed that “The coalition of civil-rights, anti-psychiatry, and minority groups opposed to psychosurgery proved to be much more effective politically than the earlier opposition to psychosurgery from within the medical profession had been” [95]. Indeed, public sentiment, catalyzed in part by an organized and growing scholarly bioethics movement, led the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to issue a report on psychosurgery in 1977 [81]. As such, the report was a political compromise in lieu of a moratorium or an outright ban as proposed, most prominently, by Senator J. Glenn Beall, a Republican from Maryland [96].

The National Commission was created by the National Research Act of 1974 [97] in the wake of revelations about the Tuskegee Syphilis Study and other research ethics abuses. The National Commission was constituted and staffed by a number of prominent bioethicists, and their work was prolific. They issued a number of reports in addition to the one on the ethics of psychosurgery, although they were specifically mandated to address this issue by Congress. Concerns about psychosurgery were prominent in testimony leading up to the passage of the act. Willard Gaylin, President of the Hastings Center, warned of the dangers of psychosurgery during 1973 Senate hearings [98].

It is somewhat ironic, given the public origins of the report, that it failed to reach the conclusion that most of the public wanted. Instead of adopting the more politically correct position, to invoke a more modern phrase, the National

Commission found sufficient evidence of efficacy of the modern procedures like cingulotomy and not the prefrontal leukotomies of Freeman's day to endorse continued experimental work in psychosurgery as long as strict regulatory guidelines and limitations were in place. As Chairman of the National Commission, J. Kenneth Ryan of Harvard Medical School told a *Science* correspondent:

We looked at the data and saw they did not support our prejudices. I, for one, did not expect to come out in favor of psychosurgery. But we saw that some very sick people had been helped by it, and that it did not destroy their intelligence or rob them of their feelings. Their marriages were intact. They were able to work. The operation shouldn't be banned [96].

The National Commission's view of psychosurgery was tempered, however, by the endorsement of stringent regulatory guidelines and procedural safeguards that would prohibit psychosurgery for anything other than a patient-centered application:

The Commission affirms that the use of psychosurgery for any purpose other than to provide treatment to individual patients would be inappropriate and should be prohibited. Accordingly, the Commission is recommending safeguards that should prevent the performance of psychosurgery for purposes of social or institutional control or other such misuse [81].

Furthermore, although the National Commission decided not to recommend a ban of psychosurgery, it was careful to note that it did not recognize psychosurgery as "accepted practice." This addressed a lingering question since the 1940s, posed most eloquently by Professor Mearns of Case Western Reserve Law School in 1975:

...Moreover, psychosurgeons do not submit research protocols to review committees for another reason. They simply do not perceive their operations to be experiments. They view them as therapy... They see the patient as ill with a condition that requires specific treatment geared to his particular illness. This need for treatment suggests speed or at least the avoidance of cumbersome review procedures... Somehow, the inconsistency of characterizing psychosurgery as therapy at the time it is performed and as experimentation at the time of publication seems to escape

them... The inconsistency results from characterizing psychosurgery at either point in time as solely therapy or solely experimentation. It is clearly both [86].

The ambiguity over psychosurgery's status as experimental or therapy is also implicit in the report. Psychosurgery is generally viewed as investigational, although the National Commission does acknowledge that some patients had been helped by these interventions.

For the purposes of the report, psychosurgery was defined as surgery whose "primary object of the performance... is to control, change, or affect any behavioral or emotional disturbance..." and included both classic psychosurgeries like ablation as well as its more modern iteration of electric stimulation: "Psychosurgery includes the implantation of electrodes, destruction or direct stimulation of the brain by any means..." [81]. It is interesting to note that brain surgery for the treatment of movement disorders like Parkinson's disease or for epilepsy and pain management was excluded from this definition.

Given the investigational nature of psychosurgery, the National Commission recommended strict oversight by specially constituted institutional review boards (IRBs) with a subcommittee of Department of Health, Education, and Welfare (DHEW)-sanctioned experts or consultants in neurology, neurosurgery, psychology, and psychiatry to review the technical aspects of the surgery. IRB review was recommended until the "safety and efficacy of any psychosurgical procedure have been demonstrated." The IRB was charged with assessing the competence of the surgeon, the appropriateness of the procedure for a selected patient, and the adequacy of the patient's informed consent. In addition, harkening back to historical concerns about the evaluation of procedural efficacy, the National Commission recommended that the IRB ensure adequate pre- and postoperative evaluations.

Addressing concerns about regulatory oversight, informed consent, and the risks of coercion for the voluntarily institutionalized psychiatric inpatient, the National Commission recommended the establishment of a National Psychosurgery Advisory Board that would determine whether the "specific psychosurgical procedure has demonstrated benefit for the treatment of the psychiatric symptom or disorder of the patient." If the procedure was part of a research study, the advisory board would determine whether enrollment was in compliance with the National Commission's

recommendations on research involving the institutionalized mentally infirmed [81,99].

The report set even more stringent guidelines for prisoners and those who were involuntarily committed, had a legal guardian, or were believed to be unable to give informed consent because of impaired decision-making capacity. Attempting to balance “access to potentially beneficial therapy” against the coercion or a breach of voluntariness, the National Commission outlined a complex regulatory approach requiring, among other strictures, that the proposed National Psychosurgery Advisory Board determine whether the specified psychosurgical procedure had a demonstrable benefit for the patient’s condition and if the operation were to be performed as an element of a research protocol, whether these efforts would be in compliance with the recommendations on research involving the institutionalized mentally infirmed [81].

To engage in some rudimentary health services research, the National Commission also suggested the establishment of a national data collection registry to assess the safety and efficacy of these procedures. This fundamental issue remained an open question given the small sample of cases reviewed by National Commission consultants. In addition to this data, the National Commission recommended that this registry note the indications for procedures and the demographics of those who underwent psychosurgery.

In addition, with one abstention, the National Commission actually encouraged (their word) the Secretary of the DHEW “...to conduct and support studies to evaluate the safety of specific psychosurgical procedures and the efficacy of such procedures in relieving specific psychiatric symptoms and disorders, provided that the psychosurgery is performed in accordance with these recommendations” [81].

Finally, the National Commission recommended to Congress the imposition of strict sanctions and the threat of Federal defunding if these recommendations were violated and the exclusion of Federal agencies from psychosurgery funding “unless such agencies or components are primarily concerned with health care or the conduct of biomedical and behavioral research” [81].

Not all the National Commission’s recommendations were accepted by DHEW Secretary Joseph Califano in his determination [100]. He decided to promulgate regulations that would limit psychosurgery to those individuals who could provide informed and voluntary consent. Thus, he

determined to ban psychosurgery for prisoners, children, the involuntarily confined mentally ill, and those who were decisionally or legally incompetent and unable to provide consent. Furthermore, he endorsed the establishment of a joint committee on psychosurgery, composed of leading professional organizations, “to establish mechanisms for the voluntary regulation and reporting of psychosurgical procedures.” This was a position he later reversed.

Despite Califano’s narrowing of the National Commission’s broader recommendations regarding whom psychosurgery might be performed on, he and the report were still criticized liberally. One of the more strident columns was by William Raspberry of *The Washington Post*. In an Op-Ed written after Califano’s determination, he said that he wished the Commission had called psychosurgery “...by its right name: making holes in people’s heads and slicing their brains in a hit-or-miss attempt to make them behave themselves” [101]. He criticized Califano’s about-face on the National Psychosurgery Advisory Board and urged the “immediate cessation of butchery-in-the name of medicine.” He concluded by suggesting that someone take Califano to see “One Flew Over the Cuckoo’s Nest” [101]. Despite this response, progressive commentators like George Annas viewed the report, as submitted to the Secretary, as balanced. He observed that “Certain provisions are unlikely to please either avid promoters of psychosurgery or those favoring a complete ban; nonetheless, it is a reasonable response to a highly complex problem, and its basic approach is likely to gain general acceptance” [102].

Professor Annas was right to appreciate the complexity of these issues and the report’s balanced approach to them. He was, however, overly optimistic that the National Commission’s recommendations would eventually be accepted. Three years after the report was issued, Califano’s successor, Health and Human Services (HHS) Secretary Patricia Harris, still had failed to make a determination over proposed regulations [103]. Today, we still have failed to reach a national consensus on research on subjects whose medical, psychiatric, or neurologic conditions make it impossible for them to provide voluntary consent.

The 1998 National Bioethics Advisory Commission report on “Research Involving Persons With Mental Disorders That May Affect Decisionmaking Capacity” attempted to address aspects of this question, but it too remains in

bureaucratic limbo [21,104,105]. The proposed Psychosurgery National Advisory Board would have been empowered to adjudicate these morally complex decisions in the context of psychosurgery or neuromodulation. Because this body never came into being, we have been left without both a regulatory framework and a national locus for a debate about the ethical implications of neuro-modulation.

Recent history suggests that there remains a need for such a dialogue as well as a national body empowered to review the science behind proposed clinical trials to ensure that our ethical sensibilities are not offended. In the United States, there is no such body to provide this oversight or catalyze this discussion. The most evolved forums for such deliberations are local bodies like the Cingulotomy Committee at the Massachusetts General Hospital, which provides oversight for therapeutic interventions for patients who are able to provide consent themselves [106]. Professional groups are also evolving to articulate ethical principles for the conduct of neuromodulation research as in the case of the Obsessive-Compulsive Disorder Working Group [107].

In France, the neurosurgeon Alim Benabid voluntarily sought the approval of the French National Bioethics Commission for approval of a clinical trial of deep brain stimulation in refractory OCD, the first of many psychiatric maladies for which neuromodulation is likely to be investigated [108,109]. Benabid's actions suggests a continued need for extramural oversight of these still contentious interventions along the lines of the proposed National Psychosurgery Advisory Body.

Summary: fairness, palliation, and psychosurgery

Moving forward, we need to create regulatory mechanisms that will balance human subject protections for individuals with intractable neurologic and psychiatric disorders against scientific progress and access to potentially beneficial interventions. This fiduciary obligation of practitioners, clinical investigators, and public policy makers can be facilitated by building on the yet uncompleted efforts of the 1977 National Commission Report on Psychosurgery. This report should serve as a foundation on which additional analysis could be built.

In the spirit of this evolution, I would like to anticipate some of this analytic work in the

context of OCD. OCD has already been the object of sophisticated psychosurgical interventions, most notably the cingulotomy as currently performed by Cosgrove's group [110] and the closed radioablation techniques employing the gamma knife as studied by Greenberg et al [111].

If we begin with definitional issues, we will immediately realize that the distinction between somatic and psychiatric interventions is no longer as neatly sequestered as in the report. Increasingly, the line between mind and brain—and neurology and psychiatry—has become blurred, and it becomes increasingly problematic to treat one brain condition differently than another. For example, although the National Commission distinguished treatment of Parkinson's disease from psychosurgery, we now know that treatment of the movement disorders of Parkinson's disease with deep brain stimulation can affect the patient's emotions. As was described in the *New England Journal of Medicine*, French investigators have demonstrated that deep brain stimulation has the unrecognized potential to alter a mood state and induce a reversible but acute depression [112]. What is the boundary between modulating a movement disorder and potentially altering emotions? Is one intervention a neurologic procedure and the other psychosurgery, or are both neuromodulation?

This overlap phenomenon is especially confusing if the mechanisms of Parkinson's disease are compared with those of severe OCD. They share mechanistic similarities and are characterized by hypersynchronous activity. The pathophysiology and neural circuits of both diseases share cortico-basal gangliothalamic interactions [18] and both could be construed as tremors. In the case of Parkinson's disease, it is a motor tremor. In OCD, it is a limbic-thought tremor.

Although this analogy is not airtight, it is reminiscent of Vernon Mark's prescient anticipation of a time when the mind-brain dichotomy would be less tenable as an ethical demarcation, justifying treatment for one disorder but proscribing another. This categorization should be disconcerting to those who embrace equity in the treatment of mental and physical disease as a value, especially when the distinction is predicated on a Cartesian dualism unsubstantiated by modern neuroscience. This regard for fairness becomes even more troubling if we recall Surgeon General David Satcher's call for parity in the treatment of physical and mental illness [113].

A second analytic issue, in my view, will be to move beyond viewing psychosurgery or neuromodulation as either research or therapy and consider it instead as a form of palliative care. The ethos of pain and symptom management articulated in the palliative care community is applicable to this work. These interventions are not directed toward cure but rather at the masking of intractable symptoms [114] and the alleviation of suffering, a strategy consistent with palliative care [115].

I believe the National Commission may have anticipated the relationship between psychosurgery and neuromodulation and palliation in its willingness to endorse surrogate consent. Justification for surrogate authorization may have been linked to an implicit view of psychosurgery as palliation when it was being applied to intractable psychiatric suffering. Viewing the relief of suffering as an ethical mandate, the National Commission may have been willing to allow surrogates to provide authorization even when the intervention was yet unproven to be therapeutic. Whether notions of palliation entered into the National Commission's balancing and specification of ethical principles is a question that merits additional study. Although the recommendation regarding surrogate consent was reversed by Secretary Califano, the National Commission's thinking might suggest an alternative analytic framework than that offered by the more restrictive National Bioethics Advisory Commission report [106].

The analogy to palliative care may also be helpful in fostering a collaborative and patient-centered model of care. In this regard, I offer an analogy to patient-controlled analgesia (PCA). In PCA, the patient is given the ability to determine the frequency of dosing of pain medication to address his/her perception of pain and level of suffering within preset and safe limits. This precedent for joint patient and physician control has important implications for deep brain stimulators given the history of "behavior control." The still present fear of mind control by the modern equivalent of Delgado's stimociever makes it critical that patients have an appropriate opportunity to adjust the frequencies of their stimulators within safe and monitored parameters. This will allow for a sharing of power and help ameliorate fears of co-optation of personhood.

This is more than a hypothetical issue, because investigators have begun to recognize that subjects with OCD have affective changes depending on the setting of their stimulator. This is not

entirely unexpected because of the downstream effects of the stimulation target, the frontal lobe's cingulum gyrus, which is a site often ablated in the classic prefrontal leukotomy of Moniz and Freeman. These affective changes can range from euthymia to varying degrees of blunting or hypomania. Either extreme should be avoided, especially the blunting end of the spectrum, which is reminiscent of Nolan Lewis's concerns about the "the quieting of a patient" after the primitive lobotomy [50].

These affective changes may unsettle some observers. If the past is a prologue, we might expect new charges of mind control and a call for the prohibition of this new technology. If history's lessons are heard, however, we will appreciate that a more fruitful response is articulating an ethic of responsibility that palliates the suffering of those with intractable psychiatric illness. As Willard Gaylin told us a quarter of a century ago, "To be afraid of our technology is to be afraid of ourselves. It is only essential that we protect ourselves here, as everywhere, from arrogance and insensitivity. The answer is not to prohibit technology but to insist that it always be subservient to the transcending values of human worth and human dignity" [116].

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