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Deep brain stimulation between 1947 and 1987: the untold story

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Deep brain stimulation (DBS) is the most rapidly expanding field in neurosurgery. Movement disorders are well-established indications for DBS, and a number of other neurological and psychiatric indications are currently being investigated.

Numerous contemporary opinions, reviews, and viewpoints on DBS fail to provide a comprehensive account of how this method came into being. Misconceptions in the narrative history of DBS conveyed by the wealth of literature published over the last 2 decades can be summarized as follows: Deep brain stimulation was invented in 1987. The utility of high-frequency stimulation was also discovered in 1987. Lesional surgery preceded DBS. Deep brain stimulation was first used in the treatment of movement disorders and was subsequently used in the treatment of psychiatric and behavioral disorders. Reports of nonmotor effects of subthalamic nucleus DBS prompted its use in psychiatric illness. Early surgical interventions for psychiatric illness failed to adopt a multidisciplinary approach; neurosurgeons often worked "in isolation" from other medical specialists. The involvement of neuro-ethicists and multidisciplinary teams are novel standards introduced in the modern practice of DBS for mental illness that are essential in avoiding the unethical behavior of bygone eras.

In this paper, the authors examined each of these messages in the light of literature published since 1947 and formed the following conclusions. Chronic stimulation of subcortical structures was first used in the early 1950s, very soon after the introduction of human stereotaxy. Studies and debate on the stimulation frequency most likely to achieve desirable results and avoid side effects date back to the early days of DBS; several authors advocated the use of "high" frequency, although the exact frequency was not always specified. Ablative surgery and electrical stimulation developed in parallel, practically since the introduction of human stereotactic surgery. The first applications of both ablative surgery and chronic subcortical stimulation were in psychiatry, not in movement disorders. The renaissance of DBS in surgical treatment of psychiatric illness in 1999 had little to do with nonmotor effects of subthalamic nucleus DBS but involved high-frequency stimulation of the very same brain targets previously used in ablative surgery. Pioneers in functional neurosurgery mostly worked in multidisciplinary groups, including when treating psychiatric illness; those "acting in isolation" were not neurosurgeons. Ethical concerns have indeed been addressed in the past, by neurosurgeons and others. Some of the questionable behavior in surgery for psychiatric illness, including the bygone era of DBS, was at the hands of nonneurosurgeons. These practices have been deemed as "dubious and precarious by yesterday's standards." *(DOI: 10.3171/2010.4.FOCUS10106)*

Key Words • **deep brain stimulation** • **stereotactic surgery** • **history** • **psychosurgery** • **ethics**

Treating obsessive-compulsive disorder. Options include medication, psychotherapy, surgery, and deep brain stimulation.

The Harvard Mental Health Letter, March 2009[5]

Deep brain stimulation is probably the most rapidly expanding field in neurosurgery. Parkinson disease, essential tremor, and dystonia are well-established, evidence-based indications for DBS, and a number of other neurological and psychiatric indications are currently being investigated.

Abbreviations used in this paper: DBS = deep brain stimulation; OCD = obsessive-compulsive disorder; PD = Parkinson disease; STN = subthalamic nucleus.

There is no doubt that the modern form of DBS was heralded by the neurosurgeon/neurologist team of Benabid and Pollak and their colleagues[13] in Grenoble, France, through their 1987 publication on thalamic DBS contralateral to thalamotomy in patients with tremor. Subsequently, DBS virtually replaced thalamotomy as a first-hand procedure for tremor.[12,55,62,89] The introduction of subthalamic nucleus (STN) DBS in 1993 by the same group,[77] and the documentation of the safety and efficacy of this method applied bilaterally, including its potential for reducing the dose of dopaminergic medications in patients with advanced PD,[61] eventually gave the coup de grâce to posteroventral pallidotomy,[60] which was the preferred surgical procedure for PD in the 1990s.[41] The nondestructive, that is, the nonablative feature of DBS, its adaptability and virtual reversibility, combined with its potential for conducting in vivo research on subcortical structures and basal ganglia functions, have attracted the interest of clinicians from several other specialties as well as that of neuroscientists, historians, and ethicists.

Common beliefs conveyed by contemporary literature on DBS include the following: DBS was "invented by Benabid and coworkers;"[57,87,99] the observation that high-frequency stimulation often mimics the clinical effects of lesional surgery was first made in 1987;[10,11] DBS was initially developed for movement disorders and has only recently been applied in neuropsychiatry;[56,99] it was the observation of psychiatric side effects after STN DBS in patients with PD that prompted DBS trials for psychiatric disorders;[57,87] and early proponents of surgical intervention for psychiatric illness failed to adopt a multidisciplinary approach with neurosurgeons often working "in isolation" from other specialists.[35]

The aim of the present review was to look for the seeds of what was to become one of the most rapidly expanding and most promising techniques in the field of functional stereotactic neurosurgery, and to establish if some of the contemporary claims related to the history of DBS can be substantiated.

Methods

We examined available publications on chronic stimulation of subcortical structures published between the dawn of human stereotactic functional neurosurgery in 1947[98] and the seminal paper of Benabid et al.[13] in 1987. Relevant papers were obtained through a PubMed search as well as by retrieving pertinent references quoted in consulted papers, and references published in books and in proceedings of meetings.

Results

Origins of DBS

In 1947, at Temple University in Philadelphia, neurologist Spiegel and neurosurgeon Wycis described a stereotactic apparatus and its use in humans to perform ablative procedures.[98] This collaborative paper heralded the era of human functional stereotaxy, initially labeled "stereoencephalotomy" by its authors.[97] Their efforts were explicitly aimed at avoiding the side effects of the all-too-crude and commonly performed frontal lobotomy. In the last paragraph of their pioneering paper, the authors wrote, "This apparatus is being used for psychosurgery … Lesions have been placed in the region of the medial nucleus of the thalamus (medial thalamotomy) …."[98] According to Gildenberg,[37,38] who was a fellow of Spiegel and Wycis in the 1950s, intraoperative electrical stimulation was used from the very beginning as a mean of exploring the brain target prior to lesioning. Thus, from its very beginning, functional stereotactic neurosurgery was multidisciplinary, was directed at the treatment of psychiatric illness, and used electrical stimulation as a physiological means of assessing and corroborating the subcortical anatomical brain target. Spiegel and Wycis soon shifted their focus to the treatment of movement disorders, starting with Huntington chorea and choreoathetosis, then PD, by performing pallidoansotomies, stereotactically ablating the same areas that had been lesioned by Meyers, Fenelon, and Guiot via an open nonstereotactic approach.[96]

In 1952, neurophysiologist and neurobehaviorist Delgado and his colleagues[23] proposed a technique of electrode implantation for chronic recording and stimulation to evaluate "its possible therapeutic value in psychotic patients." The following year, the Proceedings of the Staff Meetings of the Mayo Clinic published a symposium on "intracerebral electrography" including a paper on "Neurosurgical and neurologic applications of depth electrography" containing the following statement: "An observation that may have some practical significance was that several of our psychotic patients seem to improve and become more accessible in the course of stimulation studies lasting several days."[14] The authors speculated that a likely explanation for this effect "was that the local stimulation was having a therapeutic effect comparable to that of electroshock" and concluded, "… this aspect of localized stimulation studies requires further investigation since it may lead to a most specific, less damaging, and more therapeutically effective electrostimulation technic than can be achieved by the relatively crude extracranial stimulation methods in use at present."[14]

Meanwhile, a team at Tulane University in New Orleans led by psychiatrist Heath[47] had started depth electrode studies in patients in 1950, including chronic stimulation of the septal area in psychotic patients. Also, in 1961, a book entitled "Electrical stimulation of the brain – An interdisciplinary survey of neurobehavioral integrative systems", edited by Daniel Sheer Professor of psychology at the University of Houston, was published.[94] This multi-authored book was devoted to animal and human work on subcortical recording and stimulation in epilepsy, obesity, aggressive behavior, and other neurological and behavioral conditions. Hence, from its very beginning, the technique of chronic stimulation of deep brain structures was applied in behavioral and psychiatric studies and eventually in treatment of mental disorders (see further below).

Frequency of the Electrical Current Used for Stimulation

In a review paper published in 2009, Benabid et al.[10] wrote, "In 1987, the discovery that high-frequency deep brain stimulation (DBS) was able to mimic, in a reversible and adjustable manner, the effects of ablation of functional targets has revived functional neurosurgery of movement disorders …" The Grenoble group was certainly the first to systematically study the therapeutic role of high frequency electrical current in DBS and established 130 Hz as the "ideal" frequency now commonly used worldwide in pallidal and subthalamic DBS. A review of prior stereotactic literature reveals that frequency of the applied current during intraoperative stimulation of the brain target prior to stereotactic lesioning was often a matter of debate with several authors exploring this issue. In his review on evolution of neuromodulation, Gildenberg stated,[37]

> There was considerable discussion on 'low frequency' versus 'high frequency' stimulation, but those terms were not consistently defined. Low frequency might be anywhere from 6

> to 60 Hz. High frequency might be 50-100 Hz, but rarely above …. When I first worked with Spiegel and Wycis from 1955 to 1959, routine stimulation was 6 and 60 Hz. When I returned in 1963, a more sophisticated Grass laboratory stimulator was used, and the parameters were 5, 50 and 100 Hz. There was a general feeling that low frequency stimulation might drive or increase involuntary movements, especially tremor, and high frequency stimulation might mimic the therapeutic effect, but such observations were inconsistent.[37]

In 1961, Alberts et al.[3] studied stimulation thresholds in various parts of the internal pallidum and ventrolateral thalamus in 62 patients with PD prior to lesioning. They stimulated at 60 Hz and could elicit or disrupt tremor. Walker[110] defined the optimal parameters of intraoperative stimulation as being a current of 50–100 Hz, stating that arrest of tremor had better predictive value than facilitation or initiation of tremor. Common observations reported by several authors in the process of performing thalamotomies and subthalamotomies in awake patients were that "low-frequency" stimulation could exacerbate tremor whereas "high-frequency" stimulation resulted in an improvement of that symptom.[2,46,53,73,83,95] In 1963 in France, neurophysiologist Albe-Fessard,[2] who pioneered the technique of subcortical semimicrorecording, reported that stimulation in the region of the ventrointermediate nucleus of the thalamus at frequencies of 100–200 Hz would effectively inhibit tremor in parkinsonian patients. In the same year, psychiatrist Robert Heath from Tulane University in New Orleans published a paper, "Electrical self-stimulation of the brain in Man;"[48] electrodes were implanted in the caudate, septal area, amygdala, central medial thalamus, and various areas of the hypothalamus to study "rewarding" and "aversive" reactions at various current intensities. In all these stimulations, Heath used a fixed frequency of "100 pulse/sec." In 1969, Blaine Nashold and his colleagues[73] stimulated various subcortical structures including the ventrolateral thalamus, the subthalamic nucleus, and the zona incerta and reported that tremor suppression occurred at frequencies of 120–300 Hz. In 1973, Bechtereva et al.[7] advocated the use of "electric stimulation with high-rate pulses" of subcortical structures, however, without specifying what she meant by high-rate pulses. In 1979, Laitinen[58] studied emotional responses to subcortical electrical stimulation in 135 psychiatric patients. The targets were the rostral and middle cingulum, the anterior internal capsule, and the subcaudate region of the "substantia innominata." He noted that stimulation frequency played an important role with "high frequency (60 Hz)" being by far the most effective in producing emotional responses while "low frequency stimulation (3-6 Hz) seldom caused such responses."[58] In almost all these instances, stimulation was performed intraoperatively as a means of physiological evaluation of the brain target prior to lesioning.

Deep Brain Stimulation in Psychiatry and Behavior

As stated earlier, chronic subcortical stimulation through chronically implanted electrodes was first tested in psychiatric patients. Three key individuals, a neurophysiologist, a neurophysiologist/psychiatrist, and a psychiatrist, working independently of each other, devoted much of their career exploring this method.

José Delgado, a Spanish neurophysiologist and neurobehaviorist who moved to Yale University in 1950 and worked there with Fulton, is probably best known for a motion picture showing his experiment with a bull whose charge in the arena could be stopped through remote brain stimulation.[40,105] Delgado worked extensively with chronic subcortical stimulation in rats, goats, monkeys, and humans. In a lecture delivered in 1965 titled "Evolution of physical control of the brain," he reported, "Monkeys may learn to press a lever in order to stimulate by radio the brain of another aggressive animal and in this way to avoid his attack. Heterostimulation in monkey colonies demonstrates the possibility of instrumental control of social behavior."[25] He concluded, "Autonomic and somatic functions, individual and social behavior, emotional and mental reactions may be evoked, maintained, modified, or inhibited, both in animals and in man, by electrical stimulation of specific cerebral structures. Physical control of many brain functions is a demonstrated fact … ."[25] Delgado's enthusiasm for this new technology led to a belief that there were no limits to its potentials. In 1969 he published a book titled "Physical control of the mind: towards a psychocivilized society."[26] Despite the book's provocative title, Delgado took great pains to negate the impression that mind control could be achieved by electrodes wired into people's brain and emphasized that the technique of "Electrical Stimulation of the Brain (ESB)" was meant as a research tool to study and understand the Human mind. Delgado developed a technique of subcortical stimulation using chronically implanted electrodes connected to a subcutaneous receiver implanted in the scalp, a "Stimoceiver," that could be controlled by radio waves. This technique of "radio communication with the brain" was initially developed for use in psychiatric patients.[24,27,28] Following his return to Spain, Delgado worked with Obrador and Martin Rodriguez. They implanted chronic electrodes bilaterally in the head of the caudate and septal nuclei of a patient with postplexus avulsion pain, which was probably the first implantation of a DBS device in Europe.[40]

Carl-Wilhelm Sem-Jacobsen was a Norwegian neurophysiologist and psychiatrist. He pursued a fellowship in physiology at the Mayo Clinic where his main interests were "depth electrography and depth stimulation and their application in psychiatric patients."[14] In 1963, he published an article about depth-electrographic observations in psychotic patients.[90] He stated, "electrical stimulation in some regions of the ventro-medial part of the frontal lobe resulted in a temporary improvement to complete freedom from symptoms." The specific aim of his studies was "to use chronic implanted electrodes in the target area in an attempt to improve the leucotomy operation."[93] In 1972 he reported that since 1952 in Rochester, and later in Oslo, 213 patients had been treated with his "depth-electrographic stereotactic neurosurgical technique;" of these, 123 patients were suffering from mental disorders.[93] Sem-Jacobsen's technique using chronically implanted electrodes aimed merely to study brain activity and perform intermittent chronic stimulation of various brain targets prior to subsequent lesioning. His concept of chronic stimulation was that it was not the final goal of the treatment but a means to evaluate the target area and its response to stimulation before the chronic electrodes were used to produce incremental therapeutic permanent lesions. Sem-Jacobsen eventually shifted his interest to the surgical treatment of Parkinson disease using this same technique and concept (see further below).

Robert Heath was a psychiatrist at Tulane University, New Orleans. He implanted a multitude of electrodes in several subcortical nuclei and pathways to study the effect of stimulation on behavior and probably pioneered the concept of electrical "self-stimulation."[48] Heath started a program of DBS to treat schizophrenia as well as pain and epilepsy in the early 1950s.[6] Benefits of stimulation in schizophrenic patients turned out to be scarce, but Heath made the interesting observation that some patients described the experience of self-stimulation as "pleasant," "jovial," or "euphoric." In these patients the electrodes were located in the septal area.[6,105] This pleasurable response obtained from the "septal area" came to dominate Heath's further research on DBS applications. He reported relief from physical pain by stimulation of "this pleasure-yielding area of the brain" and extended studies of this brain area during sexual arousal and orgasm.[6,50,105] In 1972 Moan and Heath[70] described the use of septal stimulation to induce heterosexual behavior in a homosexual man. The individual was shown a pornographic video, then a female prostitute was introduced to him in the laboratory and following stimulation to his septal area, the individual and the woman had a sexual intercourse culminating in the subject's orgasm and description of the experience as "pleasurable." The authors wrote that during these sessions the individual "stimulated himself to a point that he was experiencing an almost overwhelming euphoria and elation, and had to be disconnected, despite his vigorous protests."[70] Two electrodes, each with 6 contacts, had been implanted in this individual and the paper contains 2 figures from the Atlas of Schaltenbrand and Bailey[85] depicting their location: one electrode lay in the "septal area" (close to the nucleus accumbens) and the other in the region of the centromedian nucleus of the thalamus.[70] Heath pursued similar and other experiments through the 1970s. One of his last publications from that decade was "Modulation of emotion with a brain pacemaker. Treatment for intractable psychiatric illness"[49] featuring an illustration showing the commonly used DBS system at the time consisting of a pulse sender with an antenna placed above the skin of the pectoral area where the receiver was implanted (the Xtrel Medtronic system). "Modulation of emotion" by DBS, an issue widely criticized in the 1970s,[105] reemerged 30 years later from the pen of another psychiatrist, Luc Mallet from Salpêtrière hospital in Paris who published a paper titled: "La stimulation cérébrale profonde: un outil pour la modulation thérapeutique du comportement et des emotions" (Deep brain stimulation: a tool for therapeutic modulation of behavior and emotions).[63]

Heath's experiments were analyzed in depth by psychologist Baumeister[6] in the paper "The Tulane Electrical Brain Stimulation Program a historical case study in medical ethics," published in Journal of the History of the Neurosciences in 2000. Baumeister reviewed 3 decades of DBS work performed at Tulane university and concluded, "… the Tulane electrical brain stimulation experiments had neither a scientific nor a clinical justification … . The conclusion is that these experiments were dubious and precarious by yesterday's standards."[6]

In 1977, Finnish neurosurgeon Laitinen[59] had already commented on the questionable ethic of one of Heath's papers,[50] concluding that: "There is no doubt that in this study all standards of ethics had been ignored. The ethical responsibility of the editors who accept reports of this kind for publication should also be discussed."[59] Laitinen was not against the use of DBS as a therapeutic tool in psychosurgery; in that same paper he wrote, "After implantation of chronic electrodes, long-term depth recordings and repeated electrical stimulations enable the psychosurgeon to accumulate knowledge about the pathophysiology of the brain and to improve the treatment of the patient in question. It may even be possible to treat the patient with repeated electrical stimulation without macroscopic destruction of brain tissue."[59] Laitinen proposed a "model of controlled trial," whereby eligible patients are randomized to either receive best available conservative therapy or stereotactic surgery and stated, "Psychosurgery will remain an experimental therapy for years. Therefore its use should be concentrated and restricted to psychosurgical research units having strong and intimate affiliation with scientists from many disciplines."[59]

Meanwhile, the 1970s saw few clinical applications of DBS in the treatment of psychiatric symptoms. In 1972, Escobedo et al.[33] implanted quadripolar electrodes bilaterally in the head of the caudate nucleus in 2 patients with epilepsy, mental retardation, and destructive aggressive behavior and described vegetative, motor, and behavioral responses to stimulation. In 1979, Dieckman[31] performed unilateral stimulation of the nondominant thalamus using a quadripolar Medtronic "deep brain stimulation electrode" to treat a woman with phobia. The electrode contacts extended over 12 mm and were located in the parafascicular and rostral intralaminar areas. Stimulation was intermittent at a low frequency (5 Hz) and resulted in disappearance of the phobias, while attempts at stimulation with 50 Hz "was experienced as being very disagreeable."[31]

Deep Brain Stimulation in Pain and Epilepsy

As stated above, early attempts were made in the 1950s to treat chronic pain with DBS. Heath, Delgado, Bechtereva, and others performed chronic stimulation of various brain targets including the septal area, the caudate, the cingulum and the sensory thalamus. Deep brain stimulation for pain was not as "sensational" as DBS for psychiatry and behavior, or indeed in later years, as DBS for movement disorders. There was a surge in the use of DBS for pain in the 1970s initiated by 2 teams independently of each other (Mazars et al. in France[66–68] and Hosobuchi et al.[52] in the US). The authors targeted the sensory thalamus to treat various conditions of deafferentation pain. Subsequently, Adams et al.[1] reported on internal capsule DBS for pain, but this target never gained popularity. Another target, the periventricular and periaqueductal gray matter was introduced in 1977 by Richardson et al.[80,81] Hosobuchi et al.[51] demonstrated that pain relief of periventricular and periaqueductal gray matter DBS could be reversed by the opioid antagonist Naloxone. Deep brain stimulation for chronic pain, both in thalamic targets and central gray targets, became such a popular procedure that Medtronic trademarked the term "DBS" with respect to chronic subcortical stimulation for pain in the mid-1970s.[18] Despite this, DBS for pain was never approved by the US Food and Drug Administration, probably due to lack of controlled trials to prove its efficacy.[18] Deep brain stimulation for chronic pain along with occasional stereotactic ablative surgery continued to be used in Europe,[43] and interest has resurged in recent years, riding on the wave of success of DBS in movement disorders.[16]

Epilepsy was another indication that caught the early interest of the DBS pioneers listed above. The exploration and identification of epileptic foci rapidly adopted the technique of stereotactic chronic electrode implantation for recording and intermittent stimulation.[94] Indeed, one of the first human stereotactic apparatuses, designed by Jean Talairach in 1947, was fitted with a double grid system to allow precise implantation of chronic electrodes in medial temporal structures for recording and stimulation in patients with epilepsy.[69,101,102] Therapeutic chronic stimulation as treatment for epilepsy was subsequently introduced, in cerebellar as well as in thalamic and other brain structures. One of the early DBS targets was the anterior nucleus of the thalamus,[22,82,104] the very same target that has reemerged recently and shown benefit in a multicenter blinded randomized controlled trial of DBS for epilepsy.[36] According to Rosenow et al.,[82] Cooper had implanted DBS electrodes in the anterior nucleus of the thalamus in patients with refractory complex partial seizures as early as 1979. Of the 6 initial patients, 5 showed a more than 60% reduction of seizure frequency with stimulation at 3.5 V and 60–70 Hz.[82] Velasco et al.[108] published in 1987 their results of DBS for epilepsy targeting the center median thalamic nucleus. These documented historical facts challenge contemporary statements about DBS being "a new approach" to the treatment of epilepsy.[88]

Deep Brain Stimulation in Movement Disorders

Chronologically, DBS for PD and other movement disorders was the last indication of the older era of chronic subcortical stimulation. Initially, chronic stimulation of thalamic and other basal ganglia targets was used intermittently for days or weeks to ensure satisfactory results prior to lesioning via the chronically implanted electrodes. The first detailed account of this technique was provided by the aforementioned Norwegian neurophysiologist Sem-Jacobsen[91,92] in 1965 and 1966. Multiple electrodes were implanted in the thalamus around a point "midway between the foramen of Monro and the corpus pineale."[91] Chronic stimulation allowed identification of the optimal lesioning site. Sem-Jacobsen wrote, "The electrodes could be kept in for several months without any undesirable irritation around the electrode leads .… It is possible for the patient to go home for a week, on vacation, with electrodes in his head."[91] The electrode(s) yielding the best stimulation results could then be used to make incremental lesions. This recently rediscovered technique[30,79] was not uncommonly used in the past.[73,106]

The idea of using chronic subcortical stimulation as a "permanent" therapy for movement disorders was first presented in the early 1970s by Bechtereva,[7–9] who was a neurophysiologist at the Institute of Experimental Medicine in Leningrad, Union of Soviet Socialist Republics. Electrodes were implanted into the ventrolateral and the centromedian thalamus allowing intermittent sessions of "electric stimulation with high-rate pulses of suprathreshold current."[7] Bechtereva[8] coined the term "therapeutic electrostimulation" to describe this technique. Since the Union of Soviet Socialist Republics did not have access to implantable neurostimulators at that time, the last steps of the treatment were ultimately small lesions performed through the electrodes yielding the best stimulation responses[7] (Nathalia Bechtereva [July 7, 1925–June 22, 2008], personal communication to Patric Blomstedt, April 6, 2008).

In 1977, Mundinger[71] reported his experience in DBS for cervical dystonia. Electrodes were implanted unilaterally in the ventral oral anterior and ventral oral internal nuclei of the thalamus as well as the zona incerta allowing intermittent stimulation with frequencies of up to 390 Hz. In 1982 he wrote: "Stereotactic implantation of stimulation systems for autostimulation in subcortical deep brain structures (deep brain stimulation, DBS) for control of chronic pain and motor diseases is a functional and a reversible treatment which is characterized by the lack of complications involved. The advantages over dissection coagulation with irreparable destruction of nerves, nuclei or neuronal structures are obvious."[72]

Cooper[21,22] performed chronic stimulation in the thalamus and the internal capsule for various movement disorders. It is interesting that his paper from 1980 was titled "Reversibility of chronic neurologic deficits. Some effects of electrical stimulation of the thalamus and internal capsule in man."[22] "Reversibility", a hallmark of modern DBS, was an acknowledged value since the technique's inception. Cooper was probably the first to use the term "Medtronic deep brain stimulation (DBS) electrodes" in the context of surgery for movement disorders. Cooper described stimulation in the internal capsule in a patient with torticollis and illustrated the improvement of the position of the patient's head and neck after the operation.[22]

Brice and McLellan[17] from Southampton, United Kingdom, published in 1980 a paper on "deep brain stimulation" of the subthalamic area in 3 patients with intention tremor due to multiple sclerosis. In 2 of these patients stimulation continued to provide benefit at 6-month follow-up using stimulation frequencies between 75 and 150 Hz. McLellan had previously worked with Cooper with whom he published a paper in 1977 related to safety and efficacy of chronic stimulation in the brain.[20]

In 1983, Andy[4] published a paper on DBS in 9 patients with movement disorders, 5 of whom had parkinsonian tremor. Andy targeted the ventral intermediate nucleus and other areas of the thalamus and subthalamus. He reported effective stimulation frequencies ranging from 50 to 200 Hz and wrote that DBS "… in contrast to thalamic lesion … is preferred for the treatment of intractable motor disorders in high-risk elderly patients and patients with diffuse lesions secondary to trauma … the beneficial effects are reversible even after several months of applied therapeutic stimulation …. Lesion studies indicate that optimum sites for alleviating Parkinson tremor and other movement disorders are the Vim and other thalamic and subthalamic areas. Optimum sites for stimulation electrode implants tend to parallel those findings."[4]

Deep Brain Stimulation in Minimally Conscious States

In August 2007, a paper was published in *Nature* by Schiff et al.[86] describing how bilateral central thalamic DBS improved conscience levels in a patient who had been in a minimally conscious state for 6 years following traumatic brain injury. The printed issue of this groundbreaking paper, much publicized in the lay press at the time, quoted 23 references, none of which referred to any of the several previous studies on DBS for decreased consciousness, published by various workers between 1969 and 1993 in Germany,[45,100] in France,[19,29] and in Japan.[54,103,111]

Discussion

There is no doubt that the tremendous worldwide spread of DBS in surgical treatment of movement disorders, especially DBS of the STN for PD, is the result of the pioneering work of Benabid, Pollak, and the Grenoble multidisciplinary group. While this technique is firmly established for PD, dystonia, and other movement disorders, its future potential and development seem to lie mainly in the realm of psychiatry. In the past 11 years since the publication of the first 2 papers of the modern era of DBS for psychiatric illness in 1999,[74,107] this field has known a great academic activity. Contemporary publications on DBS in psychiatry and behavior have discussed various brain targets and various applications of this technique including in OCD, Tourette syndrome, depression, aggressive behavior, obesity, and most recently addiction. However, the majority of publications dealing with psychiatric and behavioral DBS over the last decade contains no patient data and consists of reviews, editorials, opinions, viewpoints, ethical analyses, theoretical models of neuronal circuitry, and comments, none of which has really shed light on the use of DBS in psychiatry and behavior during the 1950s through the 1970s.

The Revision of History

It has been claimed, "… the observation of induced psychiatric side effects (e.g., changes in mood, hypomania, reduction of anxiety) gave the impulse to try DBS also for psychiatric disorders."[87] The fact is that the first applications of modern era DBS in psychiatric disorders had nothing to do with the observation of psychiatric and behavioral side effects of DBS of the STN. Vandewalle et al.[107] pioneered DBS for Tourette syndrome in February 1999, and Nuttin et al.[74] pioneered DBS for OCD in October 1999. Both authors targeted the very same brain structures that had been stereotactically lesioned in the past by Hassler and Dieckmann[44] in the case of Tourette syndrome, and by Leksell et al. in the case of OCD.[15]

While some contemporary publications on surgery for psychiatric illness fail to refer to, or acknowledge previous work, historical facts are sometimes misrepresented even in purportedly historical publications and reviews.[42] A review paper "Behavioral neurosurgery" published in 2006 in *Advances in Neurology* and authored by 2 psychiatrists stated, "One of the most notable surgeons was the American neurosurgeon Walter Freeman … Freeman began to apply his relatively untested procedure, the prefrontal lobotomy, in which he transorbitally inserted an ice pick into the frontal cortex."[64] It should be known by all those working in the field of psychosurgery and DBS that Freeman was a neuropsychiatrist, and James Watts was the neurosurgeon with whom he initially collaborated. The neurosurgeon actually abandoned Freeman following the latter's increasingly erratic attitude to lobotomy.[32] One may wonder whether Freeman's enthusiasm for, and prolific practice of, lobotomy had any influence on another psychiatrist, Ørnulf Ødegård, director of Norway's main psychiatrist hospital, who wrote in 1953 in the *Norwegian Medical Journal*, "Psychosurgery can be easily performed by the psychiatrist himself with the tool he might have in his pocket, and strangely enough it may be harmless and effective …"[76]

As detailed above, in the older era of DBS for psychiatry, the work of psychiatrist Heath in Tulane, had been criticized on ethical grounds by psychologist Baumeister[6] and by neurosurgeon Laitinen.[59] Therefore it came as a surprise to read the statements of neuroethicist Fins and coworkers[35] who wrote in *Neurosurgery* in 2006:

> It is ethically untenable for this work to proceed by neurosurgeons in isolation without psychiatrists determining the diagnosis and suitability of patients for treatment … Such errant behavior is especially inappropriate because it represents a recapitulation of the excesses associated with psychosurgery … If this generation of neuroscientists and practitioners hope to avoid the abuses of that earlier era, and avoid conflation of neuromodulation with psychosurgery, it is critical that neuromodulation be performed in an interdisciplinary and ethically sound fashion.[35]

Our present review of historical literature demonstrates that "errant behavior," "excesses," and "abuses of that early era" were not at the hands of "neurosurgeons in isolation." It was often nonneurosurgeons who worked in this field "in isolation," and some of the leading neurosurgeons of the old era were in fact skeptical to the use of psychosurgery altogether. In 1973, one of Sweden's most famous psychiatrists, Rylander,[84] recounted how he, as a junior psychiatrist, wanted to introduce Moniz's lobotomy procedure in Sweden. He wrote "… I approached Olivecrona, the neurosurgeon. He said definitely no, adding somewhat sarcastically that psychiatrists damaged the brain by electroshock treatment and that there was no reason to destroy part of it in such a doubtful way as Moniz had done."[84]

Multidisciplinary Approach, Ethics, and Contemporary DBS in Psychiatry

As stated above, ever since the birth of functional stereotactic surgery a multidisciplinary approach has been the rule, and it was seldom the neurosurgeons who took exceptions to that rule. In a publication from 2003, neuroethicist Fins[34] acknowledged neurosurgeon and psychosurgeon Ballantine for his multidisciplinary approach whereby "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."

One cannot but totally agree with Fins when he wrote, "… it is critical that neuromodulation be performed in an interdisciplinary and ethically sound fashion."[35] Indeed, this has been, and still is, without exception the consistent practice of the neurosurgeons involved in modern DBS (and also of old era's functional neurosurgeons as shown above). The neurosurgeon who pioneered modern DBS for movements disorders,[13] as well as neurosurgeons who pioneered modern DBS for psychiatric illness,[65,74,107] have all from the beginning been part of multidisciplinary groups involving neurologists, psychiatrists, and others. Neurosurgeons have taken the initiative on seeking ethical review on the use of DBS in psychiatry. In the June 13, 2002 issue of *Nature*, Sally Goodman wrote the following: "Last October, Alim-Louis Benabid, a neurosurgeon at the Joseph Fourier University in Grenoble, asked the French commission to consider the ethics of using neurostimulation on OCD patients."[39] Neurosurgeons collaborated with psychiatrists, neurologists, ethicists, and others to promote and establish guidelines for this kind of surgery insisting on approaches that are ethically sound and multidisciplinary, and on close interaction between the various involved specialties.[75,109] Unfortunately modern history shows that multidisciplinary teams may not always be all inclusive, as shown below.

Multidisciplinary Team for Functional Neurosurgery but Without Neurosurgeons

The September 2009 issue of the *Archives of General Psychiatry* featured a paper titled "Scientific and Ethical Issues Related to Deep Brain Stimulation for Disorders of Mood, Behavior, and Thoughts."[78] This paper summarizes a 2-day conference that was convened to examine scientific and ethical issues in the application of DBS in psychiatry, to "establish consensus among participants about the design of future clinical trials of deep brain stimulation for disorders of mood, behavior, and thought" and to "develop standards for the protection of human subjects participating in such studies."[78] Among the 30 participants at the meeting, 19 of whom are authors of the paper, there was not one single neurosurgeon.

Conclusions

Based on our review of the literature we found the following: The technique of chronic stimulation of subcortical structures through permanently implanted electrodes was proposed soon after the introduction of human stereotactic surgery in 1947. Frequency of the electrical current used for stimulation of subcortical structures has always been a consideration, with "high-frequency" stimulation being advocated early on, either to confirm electrode location and expectations prior to subsequent lesioning, or as a therapeutic mean in cases of chronic stimulation. However, what was exactly meant by "high frequency" was seldom specified in the old literature. Stereotactic ablation and electrical stimulation of subcortical structures have developed in parallel. Aside from its consistent use intraoperatively prior to lesioning, electrical stimulation has been applied through chronically implanted electrodes prior to deferred incremental lesioning, or, subsequently, as a therapy in itself. Chronic subcortical stimulation was initially used as a tool to study and eventually treat psychiatric illness. The first use of DBS mirrors that of stereotactic ablative surgery: both were initially performed to treat psychiatric disease. Chronic subcortical stimulation was not originally introduced for the treatment of movement disorders. The chronological order of applications of old time DBS was first for psychiatry and behavior, then for pain, then for epilepsy, and last for movement disorders. Modern DBS for psychiatric illness was not promoted by observations of psychiatric side effects of STN DBS. Rather, DBS was applied to the same targets that were previously lesioned for the same diseases. While "It is ethically untenable for this work to proceed by neurosurgeons in isolation without psychiatrists determining the diagnosis and suitability of patients for treatment",[35] it was indeed others than neurosurgeons who were working "in isolation" during the early era of DBS. Ethical concerns have indeed been addressed in the past, by neurosurgeons and others. Some of the erratic behavior in surgery for psychiatric illness, including the bygone era of DBS, were at the hands of nonneurosurgeons. These practices have been deemed as "dubious and precarious by yesterday's standards."[6] Neurosurgeons have been pioneers in taking the first initiatives to seek ethical opinions, and to establish multidisciplinary teams, for the application of modern era DBS into psychiatry. Multidisciplinary meetings and multidisciplinary guidelines related to functional neurosurgery without including neurosurgeons are not multidisciplinary enough.

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