Thirty Years of Global Deep Brain Stimulation: “Plus ça change, plus c’est la même chose”?

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Abstract
Background: The advent of deep brain stimulation (DBS) of the subthalamic nucleus (STN) for Parkinson’s disease 30 years ago has ushered a global breakthrough of DBS as a universal method for therapy and research in wide areas of neurology and psychiatry. The literature of the last three decades has described numerous concepts and practices of DBS, often branded as novelties or discoveries. However, reading the contemporary publications often elicits a sense of déjà vu in relation to several methods, attributes, and practices of DBS. Here, we review various applications and techniques of the modern-era DBS and compare them with practices of the past. Summary: Compared with modern literature, publications of the old-era functional stereotactic neurosurgery, including old-era DBS, show that from the very beginning multidisciplinarity and teamwork were often prevalent and insisted upon, ethical concerns were recognized, brain circuitries and rational for brain targets were discussed, surgical indications were similar, closed-loop stimulation was attempted, evaluations of surgical results were debated, and controversies were common. Thus, it appears that virtually everything done today in the field of DBS bears resemblance to old-time practices, or has been done before, albeit with partly other tools and techniques. Movement disorders remain the main indications for modern DBS as was the case for lesional surgery and old-era DBS. The novelties today consist of the STN as the dominant target for DBS, the tremendous advances in computerized brain imaging, the sophistication and versatility of implantable DBS hardware, and the large potential for research. Key Messages: Many aspects of contemporary DBS bear strong resemblance to practices of the past. The dominant clinical indications remain movement disorders with virtually the same brain targets as in the past, with one exception: the STN. Other novel brain targets – that are so far subject to DBS trials – are the pedunculopontine nucleus for gait freezing, the anteromedial internal pallidum for Gilles de la Tourette and the fornix for Alzheimer’s disease. The major innovations and novelties compared to the past concern mainly the unmatched level of research activity, its high degree of sponsorship, and the outstanding advances in technology that have enabled multimodal brain imaging and the miniaturization, versatility, and sophistication of implantable hardware. The greatest benefit for patients

The French quotation in the title translates to: “The more things change, the more they stay the same”.

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today, compared to the past, is the higher level of precision and safety of DBS, and of all functional stereotactic neurosurgery.

“Nothing comes from nothing”
Parthenides, 5th century B.C.

Introduction

This year marks the 30th birth anniversary of deep brain stimulation (DBS) in the subthalamic nucleus (STN) for Parkinson’s disease (PD) [1]. It was this procedure that sealed the destiny of DBS as a universal technique used not only as the dominant modality in surgical treatment for PD, but also extending to surgery for other movement disorders as well as for various neurological and psychiatric conditions. During the last three decades, many concepts and practices surrounding DBS have been developed, often branded as novelties, and in the last few years several publications have dealt with further innovations and technological advances in DBS [2–9]. What is often noticeable when reading the contemporary DBS literature is a sense of “déjà vu” in relation to the old literature on functional stereotactic neurosurgery. This “déjà vu” concerns issues such as multidisciplinarity and teamwork, the ethical discourse, frame and frameless procedures, brain imaging, brain targets, surgical indications, electrode designs and frequency of stimulation, the concept of reversibility of DBS, etc. According to Philip Gildenberg who was a fellow of the pioneer of human stereotactic neurosurgery Ernst Spiegel [10], the latter “held the belief that there is nothing that appears in the literature without some precedent in an older article” [11]. The aims of the present work were thus to review various statements, attributes, applications, and techniques of the modern-era DBS and compare them with documented practices of the past.

Multidisciplinarity

Ever since the renaissance of surgery for PD with the reintroduction of Leksell’s posteroventral pallidotomy in the early 1990s [12], and especially following the spread of DBS of the STN in the late 1990s [13], the literature has consistently insisted on the necessity to have multidisciplinary teams, including at the very minimum a neurologist along with the neurosurgeon, in order to select and manage properly patients undergoing these new surgical treatments. It has been claimed that functional stereotactic practices of the past were “hampered by the lack of involvement by medical neurologists with resultant concerns of incomplete reporting, lack of long-term follow-up, and potential minimalization of morbidity” [14]. When modern DBS extended into the realm of psychiatry at the turn of the millennium, it was stated that “It is ethically untenable for this work to proceed by neurosurgeons in isolation without psychiatrists determining the diagnosis and suitability of patients for treatment... 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” [15].

In the light of the above statement from 2006, it is interesting to read what the father of Japanese stereotactic surgery, Hirotaro Narabayashi, who pioneered pallidotomy for PD in the early 1950s wrote in 1975: “Narabayashi considered important and insisted convincingly even then was the absolute necessity of working in a team with other affiliated clinical and basic specialists. From the clinical field, a neurologist, psychiatrist and psychologist should be important in the team with the stereotactic neurosurgeon, for evaluation of the results and for determining indications for surgery” [16]. Spanish neurosurgeon Sixto Obrador, the once president of the International Society for Psychiatric Surgery, wrote already in 1977: “From the clinical point of view, the tendency towards close team work between psychiatrists and psychologists, so as to study patients carefully and select suitable candidates for operation after medical treatment has failed, is most important. This collaboration is also necessary in the short and long-term follow-up to obtain proper evaluation of results...[the] New ‘centro Ramón Y Cajal’ opened this year in Madrid. Here a group of neuroscientists, medical and surgical neurologists, psychiatrists, clinical neurophysiologists and psychologists will collaborate in a multidisciplinary approach in the fascinating field of so-called functional neurosurgery for behavioral disturbances” [17]. Malcolm Parhad, neurosurgeon working in Baghdad, wrote already in 1953 that “team work” and “group practice” are essential in modern therapy [18].

The fact is that the very birth of functional stereotaxis was the fruit of a close and lifelong collaboration between a neurologist, Ernst Spiegel, and a neurosurgeon, Henry Wycis [19]. Other pioneer functional neurosurgeons did also recognize the need for multidisciplinarity and worked closely with neurologists and psychiatrists, including collaborating with psychologists, speech...
Thirty Years of Modern DBS: What’s New?

Therapists, pathologists, etc.: Talairach and neurologist Bancaud, and Guiot and physiologist Albe-Fessard in France; Penfield and neurologist-neuropsychologist Jasper and Bertrand and the same Jasper in Canada; Leksell and neurologist Svennilson, and psychiatrist Herner in Sweden; Laitinen and neuropsychologist Vilikki in Finland; van Hoytema and neurologist van Manen in The Netherlands, Riechert and neuroanatomist Hassler in Germany; Ballantine and Jenike in the USA, etc. Also, the modern-era DBS that started in 1987 [20] was a joint effort by neurosurgeon Alim Louis Benabid and neurologist Pierre Pollak, before the team expanded gradually to include more neurologists as well as neurophysiologists, neuropsychologists, and several other healthcare professionals.

**Ethics**

In the last two decades, ethical issues surrounding DBS have sprung to the forefront. Interestingly, this happened only when modern DBS entered the realm of psychiatry. If one browses the PubMed using the search word combinations “deep brain stimulation” and “ethics,” one finds 555 papers between 1980 and today (July 10, 2023). Interestingly, the very first paper on PubMed, published in 1980, that is, 7 years before the start of modern-era DBS, was authored by three neurosurgeons and titled “Indications and ethical considerations of deep brain stimulation” [21]. In addition, during the old, mainly lesional era, ethical issues were indeed discussed at meetings and conferences as evidenced by published proceedings: The proceedings of the Fourth World Congress of Psychiatric Surgery held in Madrid in 1975 listed five papers on ethics [22]. One of these, titled “Ethical aspects of psychiatric surgery,” was authored by neurosurgeon Lauri Laitinen [23]. He wrote “Model of a controlled trial: the basic problem of psychosurgery is psychiatric. Therefore, the initiative in considering surgical treatment must be taken by the psychiatrist. As soon as he is sure that conservative treatment by every available method cannot cure the patient, he should consult the neurosurgeon. Psychosurgery will remain experimental for years. Therefore, its use should be concentrated and restricted to psychosurgical research units having strong and intimate affiliation with scientists from many disciplines” [23]. In that same paper, Laitinen proposed a “prospective randomized study to compare stereotactic surgery versus psychiatric management,” and he outlined in detail a project for a multidisciplinary prospective controlled randomized trial by which eligible patient would be allocated to either stereotactic psychosurgery (e.g., cingulotomy, anterior capsulotomy) or continued conservative therapy with prolonged follow-up examinations by psychiatrists, psychologists, and scientists.

**Frameless Stereotaxy**

With the advances in computerized imaging and the development of neuro-navigation, tools were introduced allowing the performance of functional stereotactic procedures, mainly DBS, without the use of a stereotactic frame. These techniques were promoted as innovative solutions avoiding the use of the allegedly cumbersome and heavy traditional stereotactic frames. These frameless solutions started with Medtronic’s “Nexframe” [24, 25], and eventually a more modern modification called “Clearpoint” was developed, requiring surgery to be performed into the bore of the MRI machine [26]. Frameless aiming devices, anchored at the burrhole, and orienting the probe toward the brain target based on stereotactic radiography and ventriculography were not uncommon in the old stereotactic, mainly lesional, era [27, 28]. These systems used a combination of angles and probe depth measurements defining a specific trajectory to a specific target point. Most of these frames consisted of a ball and socket. The socket was fixed usually into the burrhole on the skull [29]. Austin and Lee in 1958 [30], Mc Cau in 1959 [31], Sem Jacobsen in 1966 [32], Ray in 1967 [33], and others developed variations of such systems.

**Deep Brain Stimulation**

According to Robert J. Coffey, DBS is “a term that eventually has been trademarked by Medtronic, Inc. (Minneapolis, MN, USA) for the first commercially marketed devices in the mid-1970s” [34]. However, long before, there have been attempts to use therapeutic chronic stimulation of deep brain structures instead of ablative lesions. Similar to functional stereotactic ablative procedures that were devised for, and applied in, psychosurgery [35], so was the case for the first chronic stimulation procedures: Columbia Neurosurgeon Lawrence Pool is credited to be the first who performed in 1948 chronic stimulation of the head of the caudate nucleus in a patient with depression and stimulation of the cingulum in a psychotic patient [36]. Yale neurophysiologist José Delgado developed further the method of subcortical brain stimulation also for use in psychiatric...
patients [37]. Subsequent applications of old-era DBS extended to treatment of epilepsy, pain, and eventually movement disorders [38, 39]. The subsequent evolution of old-era DBS mirrors the evolution of lesonal surgery in that the main clinical applications of both techniques shifted from the domain of psychiatry to neurology, in particular the surgical treatment of PD and other movement disorders. Hence, the backlash against all psychosurgery, often conflated with lobotomy, that started in the 1960s and culminated in the 1970s affected the clinical orientation of both stereotactic lesioning and old-era DBS to steer away from psychiatry and focus on movement disorders. This still holds today.

**Brain Targets and Indications**

In the current modern era of DBS, it is interesting to note that, with very few exceptions, all brain targets that are subject to DBS today have been subject in the past to ablative lesions, or occasionally chronic stimulation. The exceptions are the STN, the lesioning of which was on purpose avoided in the past, and the pedunculopontine nucleus as well as the fornix that were never subject to stimulation during the old-era DBS, and the lesioning of which did not make any clinical sense. Another exception is the anteromedial GPi as DBS target for Gilles de la Tourette syndrome. We are aware that modern-era DBS as an investigational therapy method is being tried on many targets and for many indications and is in fact a work in progress [40]. However, we considered as “new” brain targets for DBS only the four listed above (STN, PPN, fornix, and anteromedial limbic GPi) because they are either widely used or were/are subject to multicenter multi-country trials. Virtually, all other subcortical structures targeted in the old era for lesioning or occasional stimulation are used or trialed in today’s DBS [40]: various thalamic nuclei, subthalamic area including forel’s fields and caudal zona incerta, posteroverentral pallidum, anterior capsule, dorsal cingulum, subgenual cingulum, head of caudate, nucleus basalis of Meynert, posteromedial hypothalamus, bed nucleus of stria terminalis, etc. The indications for surgery – with few exceptions – are also virtually the same today as in the past: PD, essential tremor, dystonia, other movement disorders, chronic pain, epilepsy, OCD, depression, aggressivity, eating disorders, etc. The notable exceptions are sexual deviations [41, 42] and homosexuality [43] that were occasionally subject to stereotactic interventions in the past but are not considered indications for surgery in the present era.

**Brain Circuitries and Targeting**

Today, the colorful imaging of various brain circuitries with MRI has become mainstream, owing to the development of techniques for diffusion-weighted imaging generating various methods of tractography, also called structural connectivity imaging. Sometimes, the published tractography figures or their legends may conflict with known anatomy [44–46]. So-called circuitry-based interventions have become popular [47, 48], and a new label for functional stereotactic neurosurgery has been proposed: “network surgery”: a symposium at the New York meeting of the WSSFN in 2019 was titled – “Paradigm changes in psychiatric indications – From nodes to networks.” But is it really a paradigm shift? Fact is that from the very start of human functional neurosurgery, pioneers in our field were well aware of various networks thanks to their profound knowledge of anatomy based on histological tracing studies and on studies of Wallerian degeneration at autopsy. This is what Ernst Spiegel wrote explaining the motivation to embark together with Wycis on performing the very first stereotactic operation in 1947, a dorsomedial nucleus thalamotomy: “I watched a prefrontal lobotomy being performed and I was appalled by the resulting extensive brain damage and by the severe personality changes. It occurred to me that a reduction of the emotional and behavioral disturbances attempted by lobotomy could be obtained also by small lesions of the thalamic dorso-medial nucleus that forms a circuit with the frontal lobe. Such a lesion would avoid severance of the association fibers caused by lobotomy. H.T. Wycis, a neurosurgeon participating in research in my department, enthusiastically accepted my proposal of such thalamotomies” [49]. In the same year, Freeman and Watts had published their study on “retrograde degeneration of the thalamus following prefrontal lobotomy” [50] showing that the degeneration affected mainly the dorsomedial nucleus of the thalamus. Also in that same year, a paper appeared in Brain describing the same retrograde degeneration in eight hemispheres following prefrontal leucotomy [51]. In 1949, Jean Talairach in France designed his psychosurgical procedure of electrocoagulation of thalamo-frontal fibers [52] that was later labeled anterior capsuleotomy by Leksell [53], based on the same concept of network between the frontal lobe and the thalamus. The further extension of stereotactic psychosurgical procedures targeted various “nodes” along the circuitry of emotion described by Papez in 1937 [54]. Old-era stereotactic surgery for PD and movement disorders was no different: again, cerebellothalamic circuit for tremor was well known as well as striato-
pallidothalamic circuitry for PD and other movement disorders. Pioneers in the field, starting with Spiegel and Wyse and onward, placed their lesions at various strategic nodes along these networks: pallido-anstomoy, campotomy (campus forelli), subthalamotomy (avoiding the STN), ventrolateral thalamotomy (including Vim, Vop, Voa). John Gillingham wrote about stereotactic surgery on “the basal ganglia, and the tracts and nuclei of the brain stem” describing “the destruction of cell stations or interruption of fiber connections,” and illustrated beautifully this circuitry in his publication from 1966 [55], as well as in his paper introducing the beautiful this circuitry in his publication from 1966 May 1968, with a drawing outlining “a pathway within the basal ganglia and capsule, the adequate interruption of which at any site relieves tremor and rigidity and some of the other symptoms of Parkinsonism” [56].

Recently, a paper on “personalizing” DBS stated as a rational for using advanced imaging that there is “a growing appreciation for interindividual anatomical variability” [57]. Fact is that this “growing appreciation for interindividual anatomical variability” has been growing ever since the dawn of human stereotaxis and has been the issue par excellence that has almost haunted functional stereotactic neurosurgeons since the very beginning. Numerous ways have been devised to overcome the variability, from adopting internal landmarks in brain atlases (instead of bony landmarks) to refinement of stereotactic ventriculography minimizing distortion and parallax, to macrostimulation, semi-microelectrode recording and microelectrode recording, microstimulation, etc. With the introduction of new imaging tools, CT then MRI, efforts have been continuous to provide better structural imaging quality, to minimize distortion, and to develop various imaging sequences enabling visualization in the individual patient of brain structures in view of lesion or DBS (globus pallidus internus, STN, bed nucleus of stria terminalis, anterior capsule, nucleus accumbens, pedunculopontine nucleus, etc.).

**Functional Imaging**

PET, SPECT, and functional MRI are other modern techniques that can be used in conjunction with functional stereotactic neurosurgery allowing mapping the regional changes in metabolism, evaluation of dopamine-related ligands, and local blood oxygen levels in brain areas remote from the specific location of the stereotactic lesion or of the DBS electrode. These imaging modalities have been applied in surgery for movement disorders [58–61] and for psychiatric illnesses [62, 63]. Boecker et al. [61] showed in a PET study that following left-side thalamotomy, there was a decrease of activation of left-sided sensorimotor lateral premotor cortices on hand movement. Nuttin et al. [62] and Sueven et al. [63] showed that DBS in anterior internal capsule in OCD patients resulted in important reduction of metabolism in prefrontal and orbitofrontal cortices, and even more reduction of metabolism in patients who had undergone anterior capsulotomy.

Already in the old era of functional stereotactic neurosurgery, there have been attempts to perform “functional” brain imaging: Gunvor Kullberg, a psychiatrist turned neurosurgeon from Lund, Sweden [64], used inhalation of radioactive xenon 133 to measure regional cerebral blood flow following ablative interventions. She showed that after thalamotomy there was a flow reduction in the operated hemisphere that persisted in further measurements performed a year after surgery, indicating a diminished level of activity in the hemisphere subjected to thalamotomy [65]. In 1978, she showed, in patients who had cingulotomy or capsulotomy, that there was a frontal flow reduction postoperatively, most striking following capsulotomy [66].

**Frequency of Stimulation**

After more than three decades of modern-era DBS, it is established that in most brain targets and for most indications, stimulation with high frequency is needed for good clinical results. Indeed, this has been one of the major contributions of the pioneer Grenoble group, establishing 130 Hz as the benchmark of high-frequency DBS and equating this to a reversible and adjustable “lesion” [67]. In the old-era DBS, including during stimulation of various brain targets prior to lesioning, the frequency of the electric current was debated in terms of low and high, often without specifying or defining what is low and what is high [68]. An examination of the old literature on the subject shows, however, that in surgery for tremor (mainly thalamotomy and subthalamotomy) the application of a higher frequency during intraoperative stimulation could be used as a prediction of good clinical effect of a subsequently performed lesioning [69–74]. Walker [75] advised that stimulation at 50–100 Hz that could arrest tremor had better predictive value than stimulation at lower frequency that facilitated or desynchronized the patient’s tremor. Denise Albe-Fessard, the neurophysiologist who is considered the mother of semi-microelectrode recording, worked with the French neurosurgeon Gérard Guiot and stated that...
intraoperative stimulation of the Vim at frequency of 100–200 Hz would effectively inhibit tremor [69]. Nas-hold and Slaughter [72] tested intraoperative stimulation of the ventrolateral thalamus, the zona incerta, and even the STN, at 120–300 Hz, and reported suppression of tremor. Tóth and Tomka stimulated the thalamus and pallidum with 100–300 Hz [76]. In almost all the examples above, the stimulation was performed intraoperatively prior to performing a lesioning.

Also in the old era of therapeutic DBS, chronic stimulation at high frequency was favored: in 1977, Mundinger treated spasmodic torticollis with intermittent stimulation in the thalamus and subthalamic area at a frequency of 390 Hz [77]. In 1980, Brice and McLellan used a frequency of 75–150 Hz to stimulate patients with MS tremor with electrodes implanted in the subthalamic area [78]. Orlando Andy used a frequency of 50–200 Hz for DBS of ventrolateral thalamus and subthalamic area in patients with tremor [79].

The frequency of the current was also evaluated in subcortical stimulation in psychiatry. In 1963, the team at Tulane University implanted electrodes in the caudate nucleus, the septal area, the amygdala, the central thalamus, and the hypothalamus and used a fixed frequency of 100 Hz to study “rewarding” and “aversive” responses at various current intensities [80]. In 1979, Laitinen [81] stimulated the rostral and middle cingulum, the anterior internal capsule, and the subcaudate region of the substantia innominate and noted that “high frequency” at 60 Hz was more effective in producing emotional responses compared to “low-frequency” stimulation at 3–6 Hz.

### Reversibility of DBS

Ever since the dawn of modern-era DBS, pioneered in 1987 by Benabid et al. [20], reversibility has been consistently a main argument in favor of DBS as opposed to ablative lesional surgery that was considered irreversible. Even if these categories may be discussed today in hindsight, the concept of reversibility was also highlighted during the old era of DBS as well, by Irving Cooper in 1980 [82], Fritz Mundinger in 1982 [83], Orlando Andy in 1983 [79], and others.

### Closed-Loop DBS

There are ongoing efforts aiming to harvest biomarkers based on local field potentials to enable so-called adaptive “closed-loop” stimulation for various illnesses, mostly PD [9, 84–87] and essential tremor [87]. The general idea to record and analyze local field potentials during stereotactic procedures was suggested by Spanish-American neurophysiologist José Delgado in 1958 [88], his stated aim being to verify accurate location of the brain electrode. Later, he collaborated on “intracerebral therapy with electrical stimulation” with neurosurgeon Sixto Obrador who wrote “Recent reviews of the technical aspects of TESB (Therapeutic Electrical Stimulation of the Brain) include...”stimoeceiver-computer” designed to receive and analyse signals from the brain and send back signals to the brain. This apparatus allows the following programs: artificial links between unrelaxed cerebral areas, functional feedbacks and programs of stimulation contingent on the appearance of preselected brain waves” [17].

However, the first use in human of an on-demand DBS based on physiological closed loop was described by Southampton (UK) neurosurgeon Jason Brice and neurologist Lindsay McLelland. In their paper in Lancet in 1980, they reported on 2 patients with tremor of multiple sclerosis, in whom DBS electrodes were implanted in the subthalamic area [78]. The high-frequency stimulation (75–150 Hz) was delivered by a pulse generator controlled by a switching device triggered by electromyographic signals from the deltoid muscle of the appropriate arm. This switched on automatically as soon as the deltoid muscle was activated and switched off 5–7 s after activation ceased. In this way, stimulation was given contingently or “on demand” [78].

### Directional Electrodes

The last few years have seen an increase in the use of the newly developed directional DBS electrodes enabling to steer the electrical current perpendicular to the axis of the electrode, thereby contributing to decrease side effects of stimulation [2, 4, 7]. In 1965, neurosurgeon Nicholas Zervas from Boston was probably the first to design a rigid electrode insulated at the tip in such a manner as to steer the radiofrequency coagulation perpendicular to the axis of the probe. He called it “excentric radiofrequency lesion” [89]. Variations along the same principle of off-axis thermocoagulation probes were subsequently developed [90], consisting of a flexible electrode that could be extruded in a desired direction from the shaft of the rigid probe, and used to perform directional RF lesioning [91–94]. This technique has been used as recently as in 2022 by Savas et al. [94] from Türkiye to perform thalamotomies and campotomies in patients with dystonia.
Several Targets in One Electrode Pass

There has been a growing interest in performing DBS on several targets along the electrode trajectory, enabled either by electrodes with long interspaces between the four contacts or by the newly designed leads with eight electrode contacts along the axis of the lead [95–97]. In the past, RF lesioning has also been performed on successive targets along the path of the electrode. Probably, the first and most famous example was the experience of Guiot and Albè-Fessard using a stereotactic frame with a posterior approach. They performed semi-microelectrode recording starting from the pulvinar posteriorly, then advancing to the motor thalamus and continuing across the internal capsule to the internal pallidum [69, 98], and could perform a thalamotomy and a pallidotomy through one electrode trajectory. Also, when aiming at the ventrolateral thalamus through the usual frontal approach, it was not rare that neurosurgeons did both a thalamotomy and a sub-thalamotomy with the same electrode trajectory [99].

Multiple Electrodes in Different Targets

Some authors of the modern-era DBS have implanted multiple electrodes to stimulate different targets for the same indication [100–103] or to treat two different conditions [104–106]. In the old era, implantation of chronic electrodes in multiple targets was often used, the aim being to record and stimulate to define the best target area to be later lesioned [107–109]. Some attempted also therapeutic DBS through several electrodes implanted in different targets: at the third symposium on PD held in Edinburgh in 1968, Feinstein et al. [110] presented a patient with tremor who had four DBS leads, shown on a frontal X-ray, two in the Vim area and two in the subthalamic area. Heath in New Orleans stimulated psychiatric patients with several leads chronically implanted in various subcortical areas [111].

Lesioning through Chronically Implanted Electrodes

In 2001, the Toronto group pioneered the concept of performing lesions through implanted DBS electrodes [112]. This technique has been subsequently used by several authors as a rescue therapy in cases where the implanted lead had to be removed due to infection [113–115]. In the old era, in both psychiatric indications and in treatment of movement disorders, patients could be implanted with several electrodes lasting for several weeks for recording and stimulation before finally receiving ablation through some of the implanted electrodes that were deemed to be in the right targets. [107–109], and in some instances, these electrodes were used for incremental and repeated lesioning over time [32, 116–118].

Evaluation of Results

In the current era of DBS and ablative surgery, it is certainly mandatory to use validated disease-specific evaluation scales when reporting outcome, whether related to clinical symptomatic results, or with respect to quality of life. These “modern” scales such as the Unified Parkinson’s Disease Rating Scale (UPDRS) – that was first used in a surgical context to evaluate modern pallidotomy for PD [119], the Parkinson’s Disease Questionnaire (PDQ), the Essential Tremor Rating Scale (ETRS), the Burke-Fahn-Marsden Rating Scale (BFMRS), the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and various scales measuring depression provide numerical scores that are used on an individual or group level to quantify outcome after surgery. The surgical outcomes of the old era of functional neurosurgery have often been criticized for being biased and unreliable because results were often based on a simple qualitative evaluation by the surgeon as being good, fair, or poor in comparison with baseline. These results could also differ between reports by surgeon and reports by neurologist [120]. However, there have indeed been attempts to use scales in the old-era functional stereotactic surgery: the most known scales used to evaluate PD patients were the Hoehn and Yahr scale [121] and the Schwab and England ADL scale [120], then the Northwestern University Disability Scale (NUDS), the Webster scale [122], and various other scales [123]. But even if in general results of surgery were mostly reported qualitatively, they could sometimes convey a wealth of detailed information that is not available in contemporary “modern” scale-based publications. To give few examples, the famous paper on pallidotomy by the Leksell group reported on 81 patients [124]; the results were given for each individual patient in terms of severity of tremor and rigidity graded from 1 to 3 before and after surgery, showing how many patients were considered having good results, moderate results, and failures, respectively. Also, the degree of incapacity before and after surgery was reported in detail with respect to employment and dependence on help. In today’s surgical results frequently expressed by mean ± standard
deviation of UPDRS scores for a given cohort, there is no way to know how many patients or percentage of patients had failed surgery or had less than desired outcome in terms of functional capacity. Similarly, in old reports on capsulotomy [53], individual details were given on the fate of each patient, including the degree of functional capacity after surgery, and whether the patient could return to work partially or totally.

Finally, the evaluations of results in the literature of the old-era functional stereotactic neurosurgery have been considered unreliable as compared to the contemporary era: because they were “hampered by the lack of involvement by medical neurologists with resultant concerns of incomplete reporting, lack of long-term follow-up, and potential minimalization of morbidity” [14]. In light of some publications from the modern era, these claims cannot always be taken at face value: a paper published in Neurology in 1997 described the long-term follow-up of eleven Parkinsonian patients at 1 to 4 years after unilateral pallidotomy [125]. In 1 patient, the off-medication UPDRS score was 43 preoperatively and then zero at 4 years; in another, it was 63 at baseline and then six at 4 years; in yet another, it was 39 and then scored one point at 3 years and 1 patient’s UPDRS score went from 55 preoperatively to two points at 3 years. Such results following unilateral pallidotomy may be rather difficult to believe. In 2001, the famous multicenter study on DBS in GPi and STN was published in the New England Journal of Neurology [126]. Table 5 in that paper listed the adverse events of stimulation: in the 102 patients with bilateral STN DBS, there was only one case of dysarthria, and in the 41 patients with bilateral GPi DBS, there was zero dysarthria.

Controversial Indications

The ongoing enthusiasm for DBS as a potential treatment for a variety of conditions has prompted numerous trials for a wide spectrum of neurological, psychiatric, and behavioral indications, as illustrated in the recent review by Lozano et al. [6], and been confirmed by the large list of DBS trials available on https://clinicaltrials.gov/ (613 registered trials as of July 10, 2023). Apart from these trials, there have been aspirations that DBS might be used for promoting pleasure [127], or to improve morality [128], or even as a method to enhance cognitive faculties in healthy people [129]. Some of these contemporary potential “indications” did also occur during the old-era DBS: José Delgado considered that brain stimulation may evoke more happiness and may contribute to bring about a more civilized society [130]. Vernon Heath at Tulane University in New Orleans is well known to have experimented with DBS to elicit pleasure and orgasm [132].

Discussions and Debates

It would be too tedious to quote the many opinions, debates, and controversies expressed at several meetings and in the literature of the last three decades, on various issues related to functional stereotactic surgery in general, and DBS in particular, to name but a few: DBS versus ablative surgery; DBS of STN versus DBS of GPi for PD; DBS in Vim versus DBS in zona incerta for tremor; asleep versus awake surgery; microelectrode recording versus no microelectrode recording; frame-based stereotaxis versus frameless or robotics; ablative surgery using radiofrequency coagulation versus Gamma Knife versus focused ultrasound; surgery early or late for PD, etc. In fact, virtually the same kind of controversies and debates has been constantly around ever since the dawn of our discipline 75 years ago. At the meeting of the Congress of Neurological Surgeons in Chicago in 1965, Edinburgh Neurosurgeon John Gillingham gave a lecture titled “Stereotactic surgery – past, present and future.” Speaking about the earlier days of he said, “In those earlier days, the papers, discussions, and the sometimes heated controversies that followed were centered around the best type of apparatus, the best method of creating lesions, the ideal target sites for tremor and rigidity, and the problems of overcoming the individual variation between one brain and another, in particular the variations of the basal ganglia and their relation to the adjacent internal capsule. Too many claims were made of accurate target sitting when the lesion was not only large, but when it was also impossible to be certain of its site. Conclusions were drawn, perhaps too hastily, about the ideal targets...and the anatomical disposition of pathways...” [55]. Pondering on the last sentences above about lesion size, ideal targets, and conclusions drawn too hastily, we may reflect in the DBS era of today about the best target for this or that indication, or about what exactly we are stimulating in some “targets” of the brain and what conclusion to draw, when sometimes the electric field and the resulting volume of tissue activated at a given brain target involve areas well beyond the target aimed at, encompassing several adjacent fibers and nuclei.
Conclusions

Reviewing the many aspects of contemporary DBS in relation to practices of the old era of functional stereotaxis, one may be tempted to quote the French Journalist Alphonse Karr (1808–1890): “Plus ça change plus c’est la même chose” (the more things change, the more they stay the same). Thus, it appears that virtually everything done today in the field of DBS bears resemblance to old-time practices, or has been done before, albeit with partly other tools and techniques, whether with stimulation or by lesioning. The dominant clinical indications remain today as in the past in the realm of movement disorders. The main true novelties of the modern era of functional neurosurgery, in particular DBS, are few: the STN – that was considered a no man’s land in the past – has become in fact an every-man’s land, especially in DBS for PD. Other novel brain targets – that are so far subject to stimulation trials only – are the pedunculopontine nucleus for gait freezing, the anteromedial GPi for Gilles de la Tourette, and the fornix for Alzheimer’s disease. Thus, the major innovations and novelties compared to the past concern mainly the unmatched level of research activity surrounding DBS, its high degree of sponsorship, and the outstanding advances in technology, engineering and electronics, that have enabled the advent of computerized multimodal brain imaging paving the way for connectomic surgery [133], and the miniaturization, versatility, and sophistication of implantable hardware. The greatest real benefit for patients today, compared to the past, is the higher level of precision and safety of DBS, and of all functional stereotactic neurosurgery.

Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on published literature.

Conflict of Interest Statement

Marwan Hariz has received fees and travel expenses from Boston Scientific for speaking at meetings. Laura Cif has nothing to declare. Patric Blomstedt is consultant for Medtronic, Abbott, and Boston Scientific and shareholder in Mithridaticum.

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Marwan Hariz contributed to study design, study conduct, data collection, analysis and interpretation, and first manuscript drafting, revision, and approval. Laura Cif contributed to analysis and interpretation, and revision and approval. Patric Blomstedt contributed to study design, analysis and interpretation, and revision and approval.

Data Availability Statement

This is a review paper based on the listed references below. All data generated or analyzed during this study are included in this article and its reference list. Further inquiries can be directed to the corresponding author.

References


49 Spiegel EA. This week’s citation classic, cc/ Number 33, August 15, 1983, page 325.


Thirty Years of Modern DBS: What’s New?


