

Anthropology of Deep Brain Stimulation; the 30th Anniversary of STN DBS in 2023

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Abstract: **Background:** The year 2023 marks the 30th anniversary of deep brain stimulation (DBS) of the subthalamic nucleus (STN) for Parkinson's disease (PD). This procedure prompted a universal interest in DBS for various brain disorders and resulted in a unique expansion of clinical and scientific collaboration between many disciplines, with impact on many aspects of society.

Objective: To study the anthropology of DBS, that is, its ethno-geographic origins, its evolution, its impact on clinicians and scientists, and its influence on society at large.

Material and Methods: The authors scrutinized the geo-ethnic origins of the pioneers of modern DBS, and they evaluated, based on the literature and on a long-term praxis, the development of DBS and its impact on clinicians, on healthcare, and on society.

Results: Scientists and clinicians from various geo-ethnic origins pioneered modern DBS, leading to worldwide spread of this procedure and to the establishment of large multidisciplinary teams in many centers.

Neurologists became actively involved in surgery and took on new laborious tasks of programming ever more complicated DBS systems. Publications sky-rocketed and the global spread of DBS impacted positively on several aspects of society, including healthcare, awareness of neurological diseases, interdisciplinary relations, conferences, patient organizations, unemployment, industry, etc.

Conclusions: STN DBS has boosted the field of deep brain electrotherapy for many neurological and psychiatric illnesses, and DBS has generated a global benefit on many aspects of society, well beyond its clinical benefits on symptoms of diseases. With the ever-increasing indications for DBS, more positive global impact is expected.

In the last 30 years, starting with the introduction of deep brain stimulation (DBS) of the subthalamic nucleus (STN) for Parkinson's disease (PD) by Pierre Pollak and Alim Louis Benabid¹ (Fig. 1) in 1993, in Grenoble, France, DBS as a method for both therapy and research has undergone a tremendous—and ongoing—spread not only to many countries on the planet, but also to many areas in the cerebrum and cerebellum, for treatment of several brain diseases.² According to the latest estimates more than 244,000 patients worldwide have received DBS,³ the great majority of them for treatment of PD and other movement disorders.² Within a few years of its introduction, especially after the publication by Limousin et al's⁴ paper in *The New England Journal of Medicine* in 1998, STN DBS replaced the previously widespread posteroventral pallidotomy of

Laitinen, which had inaugurated the renaissance of surgery for post-levodopa PD.⁵ Laitinen, himself, wrote in 2001: "In my opinion, DBS of the STN represents a most important step of the last decade in the surgical treatment of PD".⁶

The lead author of the present review has been clinically and academically involved in DBS almost since its beginning,⁷ and the other co-authors not long after. At the occasion of this 30th birthday anniversary of STN DBS, and keeping in mind the extraordinary resilience and versatility of clinical and experimental potentials of this procedure—considered by the late Queen Square neurologist, David Marsden, as "the best that happened to patients with Parkinson's since the advent of levodopa",⁸ one may reflect on the origins and evolution of modern DBS and on its impact on various

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FIG. 1. Professor Alim Louis Benabid, neurosurgeon, and Professor Pierre Pollak, neurologist, studying hard copies of X-ray in view of calculation of a deep brain stimulation target's coordinates.

aspects of healthcare and society, beyond its well-publicized impact on various symptoms and illnesses. Whereas anthropology is the study of human societies and cultures, their origins and their development, the anthropology of DBS will here refer to the study of the origins of DBS, and of DBS-related culture and behaviors, aside from its impact on brain dysfunctions. Hence, the aim of this paper is to explore the ethno-geographic origins of modern DBS and to highlight its impact on clinicians and scientists and its contributions to healthcare and to society at large.

Origins of the Acronym “DBS”

Former Mayo Clinic neurosurgeon Robert Coffey, who eventually went to work at Medtronic Inc, published in 2008 a comprehensive paper about the technical history of DBS devices. He wrote that DBS is “a term that eventually has been trademarked by Medtronic, Inc. (Minneapolis, MN, USA) for the first commercially marketed devices introduced in the mid-1970s.”⁹ However, a circumstantial discovery by the present authors revealed that the acronym “DBS” appeared the first time in a novel titled “The Looking Glass War” published in 1965 by John Le Carré (1931–2020).¹⁰ On page 77, a conversation takes place between Mr. Sutherland, the United Kingdom (UK) consul in Helsinki, and Mr. Avery a British spy:

–“We’ll be seeing Inspector Peersen, ‘Sutherland explained.’
 ‘He’s been a lot of help with my DBS problems.’
 –‘Your what?’
 –‘Distressed British Subjects. We get one a day in Summer. They’re a disgrace.’”

Indeed, in the old era of brain stimulation, when therapeutic stimulation of deep brain structures was performed,¹¹ it was not

labeled “DBS”: for example, neurophysiologist Natalia Bechtereva called her technique of chronic subcortical stimulation “TES” (therapeutic electro stimulation).¹² Neurosurgeons Sixto Obrador and José Martín-Rodríguez in Madrid labeled it “TESB” (therapeutic electro-stimulation of the brain).^{13,14} The first record of the use of the term DBS in the context of surgery for movement disorders was in a paper by neurosurgeon Irving Cooper from 1980,¹⁵ in which he wrote: “Medtronic deep brain stimulation (DBS) electrodes were inserted by the Cooper stereotactic technique...The Medtronic DBS electrode consists of platinum wires with four bare areas...”

Geo-Ethnic Origins of Modern DBS

It is acknowledged that the birth of modern era DBS was in Grenoble, France, in 1987 when Benabid and Pollak published a paper on DBS of the ventral intermediate (VIM) nucleus of the thalamus for treatment of tremor.¹⁶ Interestingly, in that paper, one cannot find the label “DBS.” Instead, the authors repeatedly labeled their technique as “VIM stimulation.” The close collaboration between Benabid and Pollak in further developing and expanding DBS, including pioneering DBS of the STN in 1993, lasted until the retirement of Benabid in 2012.

Neurosurgeon, Alim-Louis Benabid, who is also professor of Biophysics, was born in France from an Algerian father and a French mother. Neurologist Pierre Pollak has ancestral Jewish origins from Bessarabia, which is part of today’s Moldova and Ukraine. Their probing of the STN in a parkinsonian patient in 1993 was based on the discovery by Israeli neuroscientist Hagai Bergman, who worked at Johns Hopkins in the United States (US), and who demonstrated in a paper in *Science* in 1990 the major beneficial effect of lesioning the STN in a non-human primate model of Parkinson’s.¹⁷ In a similar experiment, the same results were obtained in 1991 by Bengladeshi neurosurgeon Tipu Zahed Aziz working in Manchester, United Kingdom.¹⁸ In 1993, Abdelhamid Benazzouz, a Moroccan Neurophysiologist working in Bordeaux, was the first to demonstrate the benefits of using DBS of the STN, instead of lesioning, again in a similar experimental non-human primate model of PD.¹⁹ Finally, the first to introduce DBS of the STN to North America was the Spanish-Andalusian born Canadian neurosurgeon Andres Manuel Lozano.²⁰ Hence, it can be safely and happily said that the legacy and spirit of Al-Andalus during the middle-ages in relation to discoveries in science and medicine²¹ were nicely replicated 1000 years later.

Multidisciplinarity and Team Work

During the 1990s, the posteroventral pallidotomy of Leksell-Laitinen⁵ was the dominant surgical procedure for advanced PD,

and neurologists were becoming more and more involved in this procedure, both clinically and academically.^{22,23} DBS of the posteroventral globus pallidus internus (GPI) for PD was introduced by Jean Siegfried and Bodo Lippitz in 1994,²⁴ and STN DBS for PD continued to be publicized and documented and became increasingly adopted in many centers. The year 1999 saw the publication of five seminal DBS-related papers: three on GPI DBS for dystonia,^{25–27} one on DBS for Gilles de la Tourette syndrome,²⁸ and one on DBS for obsessive compulsive disorder.²⁹ In 2001, following the publication of the large multicenter study on DBS in STN and GPI in advanced PD³⁰ these procedures were approved by the US Food and Drug Administration. Hence, the dominance of DBS over stereotactic lesional procedures was firmly established. The initial close collaboration between a neurologist and a neurosurgeon, which was the hallmark of functional stereotactic neurosurgery since its beginning in 1947,³¹ extended to include a wider collaboration and team building involving gradually several medical specialties and allied health professionals. In most centers worldwide, DBS promoted the establishment of truly multidisciplinary units comprising specialized DBS nurses, neurophysiologists, neuroradiologists, neuropsychologists, speech therapists, and psychiatrists. Basic scientists, biomedical engineers, imaging scientists, and neuroethicists (the latter when DBS entered the realm of psychiatry at the turn of the millennium), followed suit by becoming increasingly involved in DBS, clinically and academically.

Impact of DBS on Neurology-Neurosurgery Relationships

The close, almost daily, collaboration between the two main clinicians involved in DBS, that is, the functional neurosurgeon and the movement disorders neurologist, has influenced and cross-fertilized both. Neurologists were not only involved in selection and follow-up of patients, but became also an integral part of the surgical team and were highly active in the operating room for monitoring the patient during surgery (Fig. 2) and sometimes scrubbing and assisting hands-on the surgeon in the procedure (Fig. 3). Sometimes, the neurologists contributed with innovative ideas related to the preoperative targeting procedure on magnetic resonance imaging (MRI) in view of the DBS surgery; indeed, it was a neurologist from Lebanon, Paul Bejjani,³² working at the Salpêtrière hospital in Paris who defined the target point in the STN as lying at the level of the line connecting the anterior borders of the red nuclei on axial MRI.³³ This line became known as the “Bejjani line” and is widely used by surgeons when planning the surgical STN target on MRI. Inversely, many functional neurosurgeons attending the multidisciplinary clinics could learn substantially from the neurologists about selection of patients for DBS and managing medication and stimulation. This generated a common understanding of the diseases and of their medical and surgical treatments and contributed to



FIG. 2. Professor Pierre Pollak, neurologist, assessing rigidity during a deep brain stimulation procedure.

increased collegiality and friendship. DBS is probably the only surgical procedure that systematically and efficiently brought neurologists and neurosurgeons together both physically and mentally. Additionally, outside the hospital setting, DBS has resulted in more and more neurologists attending and speaking at surgical meetings and functional neurosurgeons doing the same at neurological meetings. Hence, DBS contributed to foster a unique symbiosis and “entente cordiale” between these two specialties, a fact that has not always been evident before the modern DBS era. The main benefactors of this symbiosis have been, and are, the patients.

Impact of DBS on Neurologists

DBS has resulted in the emergence of a new brand of movement disorders neurologist, the DBS neurologist. This sub-sub- (or super-super-) specialist became well versed in detailed stereotactic surgical anatomy and neuro-electricity and learned the intricate skills of dosing the electrical energy delivered to the patient by the DBS. The DBS neurologist cares now for patients who often need more clinic time and more often attention than the regular movement disorders patient who is treated solely with medication. With the development of newer and more sophisticated DBS hardware, neurologists needed to learn more and must master the new technical innovations. In many centers, the burden has become such that movement disorders nurses have been recruited to be trained in managing DBS to assist the DBS neurologist in programming and caring for an increasing number of DBS patients. The patients in turn, have



FIG. 3. Professor Patricia Limousin, neurologist, assisting Professor Hariz during surgery.

often higher expectations from DBS and request more visits to their clinicians and nurses. DBS neurologists have had to adapt to the fact that STN DBS has not only created a new phenotype of PD,³⁴ but also transformed chronic slowly progressive diseases into acute fulminant conditions when the battery of the DBS neurostimulator suddenly runs out. Because abrupt cessation of DBS, especially STN DBS for PD or GPi DBS for dystonia, may result in rebound of symptoms and sudden emergence of potentially fatal malignant parkinsonian crisis or dystonic storm,^{35,36} the DBS neurologist needs to be ready to care in emergency for such eventualities. This resilience of neurologists and neurosurgeons in face of the new diagnosis labeled “DBS withdrawal syndrome”^{37–39} has brought them even more closely together.

Furthermore, despite the increased clinical burden of DBS on neurologists, it seems that DBS has contributed to increase their happiness.^{40,41} Additionally, the often publicized psychiatric side effects of especially STN DBS, rather than contributing to decrease neurologists’ enthusiasm for this therapy, have, on the contrary, spurred them to publish, document, and analyze these side effects, leading them to sharpen their patient selection criteria for DBS. If one summarizes data from the literature, it appears that the truly ideal patient for STN DBS is a patient who has a definite diagnosis of PD, is rather young, with a short duration of disease, with dopa-responsive symptoms, intact speech intelligibility, normal brain MRI, no co-morbidities, no cognitive decline, no depression, no behavioral issues, and who has a readily available support, a stable and harmonious family situation, realistic expectation from surgery, and who does not live too far from the DBS center.⁴² Because such an ideal patient may be easier to find earlier in the disease process, STN DBS was offered to patients earlier than usual, so called “early stim.”⁴³ One neurologist advocated STN DBS as early as 6 months after PD diagnosis,⁴⁴ as a more or less prophylactic procedure. This rendered some critic from...a neurosurgeon.⁴⁵ Others have been carried away by the glamor of DBS and its unlimited possible

applications, as to suggest a potential use of DBS to treat antisocial behavior and abnormal morality.⁴⁶

Impact of DBS on Neurosurgeons

The enthusiasm of neurosurgeons toward DBS, especially for patients with movement disorders, was at least equal to that of the neurologists. Functional neurosurgery, that includes both non-stereotactic and stereotactic procedures, became synonymous with DBS. With the almost disappearance of stereotactic lesioning surgery, there were no longer training programs in radiofrequency (RF) thalamotomy or pallidotomy. This resulted in a whole generation of young neurosurgeons, over more than two decades, who no longer received training in RF lesioning, whereas old generation functional neurosurgeons trained in doing RF stereotactic lesions have either retired or passed away.^{47,48} As Manjul Tripathi and Tipu Aziz put it recently,⁴⁹ “The science of lesioning is dying. Even many established functional neurosurgery centers do not have neurosurgeons experienced in lesioning, or they will be retiring soon.” This has had consequences not only for patients in need of surgery and those who cannot afford or do not want DBS, but also for patients who suffered the above mentioned potentially fatal “DBS withdrawal syndrome” and whose wellbeing, and indeed life could have been saved if they had received a RF pallidotomy.⁵⁰ Although magnetic resonance (MR)-guided focused ultrasound (MRgFUS) lesioning has emerged in the last few years as a mean to perform lesions, it remains a costly procedure approved only for unilateral thalamotomy for essential or parkinsonian tremor, and it “runs the risk of making lesions unaffordable”.⁴⁹ Moreover, it seems that the side effects of MRgFUS lesioning are not negligible even at long follow up,⁵¹ and it is still not clear if its efficacy in control of symptoms surpasses that of RF procedures.

Impact of DBS on Industry

In the beginning of the modern era DBS, there was one single manufacturer of DBS hardware globally, the Medtronic company. With the success of DBS as a therapy for movement disorders and beyond, other companies started to manufacture and market DBS hardware, introducing innovations and sophistications. Currently there are four main companies (Medtronic, Abbott, Boston Scientific, and PINS), and a few other smaller industries marketing DBS hardware.⁵² This has allowed competition and diversity, although DBS remains, regardless of brand a rather expensive procedure, not affordable by the majority of patients in countries lacking free healthcare. Along with the DBS industry, there has been an expansion of companies that develop and market hardware for microelectrode recording, as well as companies specialized in computerized imaging and image manipulation software used in many centers to process MR and computed tomography (CT) images in view of calculation of a brain target coordinates. All this has had a positive impact on employment in various countries.

Impact of DBS on Research and Meetings

DBS has undoubtedly been a boost for neuroscience research, both basic and clinical. The site “clinicaltrials.gov” (accessed 12 June 2023) revealed that there are 614 registered studies under the label “deep brain stimulation.” Various learned societies, including neurological, neurosurgical, neurophysiological, and others, have incorporated program sessions dedicated to DBS in their regular meetings. In addition, the DBS industries, aside from sponsoring the Societies’ meetings, have themselves organized frequent workshops, courses, symposia, etc., inviting DBS clinicians free of charge. Industry has also been active in sponsoring various research programs and multicenter trials, as well as financing university professorships dedicated to DBS and sponsoring international fellows to travel to, and spend time at, various recognized DBS centers worldwide. Lately, a new International Society called “Society of Deep Brain Stimulation” has been launched and is holding its first congress in Grenoble this year.

Impact of DBS on Publications

DBS has prompted the publication of many professional books and handbooks and especially numerous scientific articles. A look on PubMed (accessed on 12 June 2023) using the search word “deep brain stimulation” yields 16,761 papers. DBS has also contributed to increase the impact factor of scientific journals. One of the authors (M.H.) was member of the Editorial Board of the Movement Disorders Journal (MDJ) and was present at

the Board meeting during the congress of the Movement Disorders Society (MDS) in Rome in 2004. At that Board meeting, one of the two Editors of the MDJ presented the impact factor according to various categories of articles from the MDJ. It appeared that the highest impact stemmed from review papers and the next highest was from surgery-related papers, that is, mostly DBS-related papers. It is also apparent from a survey of DBS-related papers on PubMed that those who publish on DBS belong to a wide range of specialties far beyond neurologists, neurophysiologists, and neurosurgeons. Lead authors or senior authors on DBS papers have included psychiatrists, anesthetists, dermatologists, psychologists, basic scientists, physiotherapists, occupational therapists, ethicists, DBS nurses, speech therapists, imaging scientists, biomedical engineers, epidemiologists, philosophers, lawyers, and others.

Additionally, DBS has been the subject of numerous novels and movies, with more or less science fiction characters. Finally, the lay press has also joined the ship both in print magazines as well as in audiovisual media. Sensational articles on DBS, sometimes criticized for too much positive bias⁵³ have been frequent, and illustrations of DBS have made the front cover of several magazines (Fig. 4).

Impact of DBS on the Public’s Awareness of Movement Disorders

The popularization of DBS at many levels of society, and the innovative, exciting and often spectacular perceptions of this treatment modality have undoubtedly contributed to an increased awareness among the public at large about the illnesses categorized as “movement disorders”, especially PD, essential tremor, and dystonia. These chronic conditions may have been considered as marginal in the public conscience, but thanks to DBS, a whole group of people living with PD and other movement disorders have been highlighted and were made more visible in the public domain, which has benefitted all persons with these conditions irrespective of them having received DBS or not. Even patients’ organizations have witnessed an increase in membership and a more prominent visibility, following the advent of DBS.

Impact of DBS on Employment and Economy

The overall global spread of DBS has, therefore, generated new industries, new societies, new journals, new research, more international meetings, and not the least, new specialties and new positions for many workers in hospital settings. This DBS-related expansion on many levels of society is probably the biggest that has happened in the context of healthcare since the advent of the new imaging tools (i.e., CT and MRI). The spin-off of DBS,



FIG. 4. Covers of various lay-press magazines in relation to deep brain stimulation.

considering the number and frequency of various international DBS-related meetings for example, has benefitted conference centers, audiovisual industry, transportation companies (air travels, trains, and taxis), hotels, restaurants, and shops and has therefore, benefitted global economy aside from facilitating regular contacts between clinicians, scientists, paramedical workers, and researchers. The basal ganglia, which have been and are the main target for DBS, have been categorized as the center of regulation of motion and emotion by Marsden and Obeso.⁵⁴ By a strange coincidence, the motto “motion and emotion” has been adopted by one car-maker company to advertise its cars.

Conclusion

Modern DBS, especially DBS of the STN—that celebrates its 30th anniversary this year—has boosted the clinical and scientific field of deep brain electrotherapy for many neurological and psychiatric illnesses. The success and spread of DBS has highlighted the public’s awareness about a whole group of patients with chronic neurological diseases. DBS has also generated a true global benefit on many aspects of the society at large, well

beyond its established clinical benefits on many symptoms of various diseases. The main drawback will remain the lack of access to STN DBS, and indeed to any DBS, because of financial reasons, for a majority of patients globally who would potentially benefit from it.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

M.H.: 1B, 1C, 2A, 2B.

Y.B.: 1B, 1C, 2B.

P.B.: 1B, 2B.

G.M.H.: 1A, 1C, 2B.

Disclosures

Ethical Compliance Statement: This is a historical review of the evolution of DBS. There are no patients described or

reported and therefore, informed patient consent is irrelevant for this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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