An update on deep brain stimulation for treatment of psychiatric conditions

Konstantin Slavin, MD

Department of Neurosurgery
University of Illinois at Chicago
USA

Abstract

In 2006, the scientific world celebrated 70th anniversary of publication of the first scientific paper by Dr. Moniz on results of small series of leucotomy patients – an event that marked birth of the modern psychiatric neurosurgery. Over the last few decades, this field of functional neurosurgery witnessed widespread popularity, almost complete disappearance, and, recently, resurgence of interest supported by the progress in surgery and imaging.

In this paper, we review current literature and clinical experience in attempt to provide an overview and update on the use of deep brain stimulation in the treatment of the obsessive compulsive disorder and other medically intractable psychiatric conditions. Detailed search of current scientific literature was performed on topics of psychiatric surgery and deep brain stimulation (DBS). The information obtained was then critically reviewed.

Review indicates that there is a growing body of literature documenting successful treatment of certain psychiatric conditions with DBS. Modern physiological and metabolic imaging appears to be useful in choosing appropriate surgical targets. Based on this review, it appears that DBS is gaining popularity in the treatment of medically intractable psychiatric disorders and one may expect significant growth in further research and clinical applications of DBS for psychiatric indications.

Key words: deep brain stimulation, depression, obsessive-compulsive disorder, Tourette syndrome

Running title: DBS for psychiatric conditions

Historical background

Little more than 70 years ago, based on observation of improved aggressiveness after undercutting of frontal fiber tracts in monkeys by Dr. John Fulton [1], Portuguese neurologist Egas Moniz together with neurosurgeon Almeida Lima started similar operation in humans (the first surgery reportedly took place on November 12, 1935). The results of the first several procedures were first reported in 1936 in Paris [2]. Even though surgical operations for psychiatric conditions have been performed prior to this by many others (Gottlieb Burckhardt in Germany, William Macewen in Britain, Ludwig Puusepp in Estonia, and others) [3-6], Moniz' work became widely known and therefore 1935 and 1936 are considered birth-years of modern neurosurgery. With refinement of surgical techniques and procedural indications, the psychiatric neurosurgery gradually shifted from large-scale lobotomy and leucotomy to more focused and precise stereotactic interventions, and by the end of 20th century, four distinct procedures have remained as an option for most severe and medically intractable psychiatric conditions. These four procedures were [1] cingulotomy, targeting the cingulum and cingulate gyrus; [2] anterior capsulotomy, focusing on the anterior limb of the internal capsule; [3] subcaudate tractotomy, aiming at the white matter tracts beneath the head of caudate nucleus; and [4] limbic leucotomy that combined the targets from cingulotomy and subcaudate tractotomy. Many papers have been published to summarize the progress and current state of these destructive procedures with excellent overview of the procedural details and outcomes [7-10].

The means of cortical and white matter destruction changed over the years - the initial approach of alcohol injection was substituted with mechanical fiber cutting or direct excision / transection, and eventually replaced with radiofrequency thermal ablation, mainly due to predictability of radiofrequency lesions and lower risk of associated hemorrhagic complications. In addition to this, two distinct directions have developed in the last 60 years in the field of psychiatric neurosurgery: one was aimed to limit the damage of frontal structures by avoiding surgical penetration of the skull by means of stereotactic radiosurgery (starting with Lars Leksell in 1953) [11], and the other used deep brain stimulation (DBS) instead of destruction (started as early as 1948 by J. Lawrence Pool) [12]. In this paper, we concentrated on DBS use only and performed analysis of the literature trying to provide overview of recent developments in the application of DBS for psychiatric conditions.

Materials and Methods

We performed search of Medline and multiple abstract databases (including online and printed proceedings of major national and international meetings) for the last 10 years as well as reference lists of the published articles on topics of psychiatric neurosurgery, psychosurgery, major depression, obsessive compulsive disorder (OCD), Tourette syndrome, deep brain stimulation (DBS), and their combinations. All reports that covered the use of brain stimulation for OCD and other psychiatric indications were analyzed and summarized in order to define the current state of affairs and possible implications for future developments. Instead of repeating previously published thorough reviews, we concentrated on the newest data and relevant research and clinical studies.

Paucity of published information did not allow us to perform any kind of meta-analysis. The findings presented below reflect the information published and presented on the topic recently and the conclusions drawn are based on this limited experience. The purpose of this paper is not to review the indications or patient selection but rather concentrate on reported details of DBS use in treatment of psychiatric disorders.

Current indications for psychiatric neurosurgery

Although initially psychiatric interventions were used for treatment of psychotic states, mood and personality disturbances, aggressiveness and schizophrenia, the indications over the years narrowed down to primarily three specific conditions.

The two most commonly treated disorders are medically intractable (treatment-resistant) depression and OCD [7,8,13]. Another condition that is treated with neurosurgical intervention - Giles de la Tourette syndrome – combines psychiatric and neurological symptoms [14].

Due to major concerns associated with indiscriminate use of psychosurgical interventions in the 1950-s and 1960-s, a major emphasis is now placed on appropriate patient selection that includes, along with the medical intractability, ability to sign informed consent, voluntary nature of the treatment, disability associated with the disease, chronicity of the symptoms, and appropriate review of indications by independent medical practitioners and ethicists [15,16]. Multiple research projects that include all necessary safeguards have been initiated in many countries to determine the safety and efficacy of various interventions.

Recent deep brain stimulation experience in treatment of OCD

Within last several years, there were at least 20 clinical publications regarding application of DBS for the treatment of psychiatric conditions. Most of them used same targets that were clinically tested with destructive procedures in the past.

Table 1. Overview of published reports of DBS for treatment of OCD

Reference/ year	# of patients	Target	Patients followed	Length of follow up / mean (months)	Pre-op Y-BOCS	Last follow up Y-BOCS	Results	Complications	Note
Nuttin, 03 (19)	8	AC	6	21	32.3 (30-38)	19.8 (9-28)		Fatigue, weight changes	1 patient underwent capsulotomy; 1 also had thalamic DBS
Anderson, 03(21)	1	AC	1	10	34	1		none	
Abelson, 05 (20)	4	AC	4	4-23	32.7 (26-39)	23 (8-39)	Only 1 improved during double-blind stage.	1 of 2 responders committed suicide.	Marked difference on PET between responders and non-responders.
Sturm, 03 (25)	4	AC/NA	4	24-30	?	?	Nearly total recovery in 3 out of 4 patients.	1 loss of effect with battery exhaustion.	1 electrode displacement.
Rezai, 06 (22) / Greenberg, 06 (24)	10	AC / VC/VS	8	36	35	22		1 - ICH, 1 - seizure, 1 - infection.	Transient sadness, anxiety, euphoria; 1 out of 10 deceased.
Jimenez, 04 (27) / Jimenez, 05 (28)	4	ITP	4	12	35 (25-36)	23 (17-29)		Weight gain in all.	1 explanted (TB meningitis).
Aouizerate, 04 (29)	1	Ventral CN	1	15	30	16		None	Delayed onset of remission (12 mos.).
Shapira, 06 (26)	1	AC/NA	1	1	?	?		Panic and fear	

Abbreviations: **AC** - anterior limb of the internal capsule; **CN** - caudate nucleus; **DBS** - deep brain stimulation; **ICH** - intracerebral hemorrhage; **ITP** - inferior thalamic peduncle **NA** - nucleus accumbens; **VC** - ventral capsule; **VS** - ventral striatum; **Y-BOCS** - Yale-Brown obsessive compulsive scale.

Blomstedt P, Hariz MI: Are Complications Less Common in Deep Brain Stimulation than in Ablative Procedures for Movement Disorders? Stereotact Funct Neurosurg 84:72-81, 2006.

Based on extensive experience with anterior capsulotomy, capsular DBS series from Belgium (8 patients)[17-19], University of Michigan (4 patients)[20], Loyola University in Maywood, Illinois, (1 patient) [21] and a multi-center study led by Cleveland clinic (10 patients) [22-24] investigated patients with OCD. Shell of the nucleus accumbens was a target of DBS in a series of 4 patients from Cologne [25] and in a patient from Florida [26], the inferior thalamic peduncle was targeted in a series of 4 DBS patients from Mexico [27,28], and the ventral caudate nucleus was stimulated in a patient from Bordeaux [29]. Two separate reports described significant improvement of OCD symptoms in Parkinson patients treated with subthalamic nucleus DBS [30, 31]. All together, we found reports of 33 patients that underwent DBS surgeries specifically for OCD (Table 1).

DBS for other psychiatric conditions

In regard to the treatment of intractable major depression, another multi-center study evaluated DBS of the anterior limb of the internal capsule (6 patients) [32] while another study with similar methodology is currently underway. Inferior thalamic peduncle was used as a target of stimulation in a case from Mexico City reported few years ago [27,33-35], and the stimulation of the ventral caudate nucleus improved depressive symptoms as well [29]. With a different rationale, based on results of functional imaging, subcallosal cingulate gyrus (Brodman area 25) was chosen as a target for DBS in a series of 6 patients in University of Toronto with excellent results [36]. Interestingly enough, the same subgenual cingulate area showed decrease in metabolism in response to anterior capsular DBS in OCD patients [37]. A theoretical rationale was subsequently proposed for another cingulate region (Brodman area 24a) as a target for DBS in treatment of depression [38].

As for the surgery for Tourette syndrome, a study from Netherlands included 3 patients with DBS of medial thalamic nuclei [39-41]; similar target was used in a patient from Case University in Cleveland [42] and another one in Chicago [43]. Anterior internal capsule was target of DBS in Tourette's patient operated on in Massachusetts General Hospital [44]; internal segment of the globus pallidus (GPi) was stimulated by a group from Luxembourg [45]; and in Paris, the patient with Tourette experienced improvement from both bilateral thalamic and bilateral GPi stimulation [46]. Another study is on the way evaluating effects of bilateral external pallidal (GPe) DBS in Tourette patients in Brazil [47].

Also, the use of DBS has been described in a patient with «refractory drug addiction;» the target for stimulation was the nucleus accumbens, similar to the lesioning target presented in the same clinical series [48].

Deep brain stimulation benefits and limitations

Even though there are multiple limitations related to the DBS approach, this is so far the only non-destructive surgical alternative to both open and radiofrequency lesioning, as well as to SRS that has been used in few centers worldwide. Among its other major benefits are adjustability, reversibility (at least theoretical) of action, and testability of the effect prior to permanent implantation.

The pitfalls of the DBS are related to its price, invasive nature of the electrode insertion, need in general anesthesia for permanent implantation, risks of infection and hemorrhage, and relatively high incidence of re-operations (related to device malfunction, leads placed in suboptimal location, wire and connector breakage) [49-54]. In addition to that, so far, most clinical series reported relatively high voltage requirements in DBS [19,20,40] which in turn translates into fast exhaustion of generator batteries that requires frequent device replacement that is done through yet another surgical intervention with its risks and additional expenses. A separate set of problems arises with unexpected battery exhaustion as the patients may experience acute return of their psychiatric symptoms.

On a positive side, however, is the current possibility of appropriate research associated with DBS in psychiatric conditions. It is possible that this research will yield information that will predict success of certain intervention or would allow individualizing treatment based on the patient's metabolic and physiological profile.

References

1. Fulton JF, Jacobsen DF: The functions of the frontal lobes: A comparative study in monkeys, chimpanzees, and man. Adv Mod Biol (Moscow) 4:113-125, 1935.
2. Moniz E: Essai d'un traitement chirurgical de certaines psychoses. Bull Acad Natl Med 115:385-392, 1936.
3. Burckhardt G: Über Rindenexcisionen, als Beitrag zur operativen Therapie der Psychosen. Allegemeine Z Psychiatr 47:463-548, 1891.
4. Stone JL: Dr. Gottlieb Burckhardt—the pioneer of psychosurgery. J Hist Neurosci 10: 79-92, 2001.
5. Macmillan M: An odd kind of fame: stories of Phineas Cage. Cambridge, MA, MIT Press, 2000.
6. Puusepp L: Alcune considerazioni sugli interventi chirurgici nelle malattie mentali. G Acad Med Torino 100: 3-16, 1937.
7. Binder DK, Iskandar BJ: Modern neurosurgery for psychiatric disorders. Neurosurgery 47:9-23, 2000.
8. Feldman RP, Alterman RL, Goodrich JT: Contemporary psychosurgery and look to the future. J Neurosurg 95: 944-956, 2001.
9. Feldman RP, Goodrich JT: Psychosurgery: a historical overview. Neurosurgery 48: 647-657, 2001.
10. Slavin KV: Current status and future directions in psychiatric neurosurgery. J Neuropsychiatry Cogn Neurosci 2(2): 48-51, 2002.
11. Leksell L, Backlund EO: Stereotactic gamma capsulotomy. In: Hitchcock ER, Ballantine HT Jr, Meyerson BA (eds): Modern Concepts in Psychiatric Surgery. Amsterdam, Elsevier/North-Holland Biomedical Press, 1979, pp 213-216.
12. Pool JL: Psychosurgery in older people. J Am Geriatr Soc 2: 456-465; 1954.

23. Mashour GA, Walker EE, Martuza RL: Psychosurgery: past, present and future. Brain Res Brain Res Rev 48: 409-419, 2005.

14. Temel Y, Visser-Vandewalle V: Surgery in Tourette syndrome. Mov Disorders 91: 3-14, 2004.

15. Nuttin B, Gybels J, Cosyns P, Gabriels L, Meyerson B, Andréewitch S, Rasmussen S, Greenberg B, Friehs G, Rezai AR, Montgomery E, Malone D, Fins JJ: Deep brain stimulation for psychiatric disorders. Neurosurgery 51: 519, 2002 (letter).

16. Kopell BH, Greenberg B, Rezai AR: Deep brain stimulation for psychiatric disorders. J Clin Neurophysiol 21: 51-67, 2004.

17. Nuttin B, Cosyns P, Demeulemeester H, Gybels J, Meyerson B: Electrical stimulation in anterior limbs of internal capsules in patients with obsessive-compulsive disorder. Lancet 354:1526, 1999 (letter).

18. Gabriëls L, Cosyns P, Nuttin B, Demeulemeester H, Gybels J: Deep brain stimulation for treatment-refractory obsessive-compulsive disorder: Psychopathological and neuropsychological outcome in 3 cases. Acta Psychiatr Scand 107: 275–282, 2003.

19. Nuttin BJ, Gabriëls LA, Cosyns PR, Meyerson BA, Andréewitch S, Sunaert SG, Maes AF, Dupont PJ, Gybels JM, Gielen F, Demeulemeester HG: Long-term electrical capsular stimulation in patients with obsessive-compulsive disorder. Neurosurgery 52: 1263-1274, 2003.

20. Abelson JL, Curtis GC, Sagher O, Albucher RC, Harrigan M, Taylor SF, Martis B, Giordani B: Deep brain stimulation for refractory obsessive-compulsive disorder. Biol Psychiatry 57: 510-516, 2005.

21. Anderson D, Ahmed A: Treatment of patients with intractable obsessive-compulsive disorder with anterior capsular stimulation. Case report. J Neurosurg 98: 1004-1108, 2003.

22. Rezai AR, Friehs GM, Malone D, Rasmussen SA, Kubu CS, Machado AG, Malloy PF, Greenberg BD: Deep brain stimulation for the treatment of intractable obsessive compulsive disorder: long-term outcome from a multicenter prospective trial. J Neurosurg, 104: A640, 2006.

23. Rauch SL, Dougherty DD, Malone D, Rezai A, Friehs G, Fischman AJ, Alpert NM, Haber SN, Stypulkowski PH, Rise MT, Rasmussen SA, Greenberg BD: A functional neuroimaging investigation of deep brain stimulation in patients with obsessive-compulsive disorder. J Neurosurg 104:558-565, 2006.

24. Greenberg BD, Malone DA, Friehs GM, Rezai AR, Kubu CS, Malloy PF, Salloway SP, Okun MS, Goodman WK, Rasmussen SA: Three-year outcomes in deep brain stimulation for highly resistant obsessive-compulsive disorder. Neuropsychopharmacology, Epub ahead of print, July 19: 1-10, 2006.

25. Sturm V, Lenartz D, Koulousakis A, Treuer H, Herholz K, Klein JC, Klosterkötter J: The nucleus accumbens: a target for deep brain stimulation in obsessive-compulsive- and anxiety-disorders. J Chem Neuroanat 26: 293-299, 2003.

26. Shapira NA, Okun MS, Wint D, Foote KD, Byars JA, Bowers D, Springer US, Lang PJ, Greenberg BD, Haber SN, Goodman WK: Panic and fear induced by deep brain stimulation. J Neurol Neurosurg Psychiatry 77: 410-412, 2006.

27. Jimenez F, Velasco F, Salin-Pascual R, Hernandez JA: Electrical stimulation of inferior thalamic peduncle in major depression and obsessive compulsive disorder. Acta Neurochir (Wien) 146: 918-919, 2004.

28. Jiménez F, Velasco F, Castro G, Velasco M, Nicolini H, Madrigal A, Velasco AL, Trejo D, Salín R: Electrical stimulation of inferior thalamic peduncle in obsessive-compulsive disorder. In: Meglio M (ed): Proceedings of 14th Meeting of the World Society for Stereotactic and Functional Neurosurgery, Medimond, Rome, 2005, pp 199-204.

29. Aouizerate B, Cuny E, Martin-Guehl C, Guehl D, Amieva H, Benazzouz A, Fabrigoule C, Allard M, Rougier A, Bioulac B, Tignol J, Burbaud P: Deep brain stimulation of the ventral caudate nucleus in the treatment of obsessive-compulsive disorder and major depression. Case report. J Neurosurg 101: 682-686, 2004.

30. Mallet L, Mesnage V, Houeto JL, Pelissolo A, Yelnik J, Behar C, Gargiulo M, Welter ML, Bonnet AM, Pillon B, Cornu P, Dormont D, Pidoux B, Allilaire JF, Agid Y: Compulsions, Parkinson's disease, and stimulation. Lancet 360: 1302–1304, 2002.

31. Fontaine D, Mattei V, Borg M, von Langsdorff D, Magnie MN, Chanalet S, Robert P, Paquis P: Effect of subthalamic nucleus stimulation on obsessive-compulsive disorder in a patient with Parkinson disease. Case report. J Neurosurg 100: 1084-1086, 2004.

32. Rezai AR, Friehs G, Malone DA, Carpenter LL, Machado AG, Tyrka AR, Price LH, Rasmussen S, Kubu CS, Greenberg BD: Deep brain stimulation for the treatment of intractable major depression: preliminary results from a multicenter prospective trial. J Neurosurg, 104: A650, 2006.

33. Jimenez F, Velasco F, Salin-Pascual R, Hernandez JA, Velasco M, Criales JL, Nicolini H: A patient with a resistant major depression disorder treated with deep brain stimulation in the inferior thalamic peduncle. Neurosurgery 57: 585-593, 2005.

34. Velasco F, Velasco M, Jimenez F, Velasco AL, Salin-Pascual R: Neurobiological background for performing surgical intervention in the inferior thalamic peduncle for treatment of major depression disorders. Neurosurgery 57: 439-48, 2005.

35. Velasco M, Velasco F, Jimenez F, Carrillo-Ruiz JD, Velasco AL, Salin-Pascual R: Electrocortical and behavioral responses elicited by acute electrical stimulation of inferior thalamic peduncle and nucleus reticularis thalami in a patient with major depression disorder. Clin Neurophysiol 117: 320-327, 2006.

36. Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, Schwalb JM, Kennedy SH: Deep brain stimulation for treatment-resistant depression. Neuron 45: 651-660, 2005.

37. Van Laere K, Nuttin B, Gabriels L, Dupont P, Rasmussen S, Greenberg BD,Cosyns P: Metabolic imaging of anterior capsular stimulation in refractory obsessive-compulsive disorder: a key role for the subgenual anterior cingulate and ventral striatum. J Nucl Med 47: 740-747, 2006.

38. Sakas DE, Panourias IG: Rostral cingulate gyrus: A putative target for deep brain stimulation in treatment-refractory depression. Med Hypotheses 66: 491-494, 2006.

39. Vandewalle V, van der Linden C, Groenewegen HJ, Caemaert J: Stereotactic treatment of Gilles de la Tourette syndrome by high frequency stimulation of thalamus. Lancet 353: 724, 1999.

40. Visser-Vandewalle V, Temel Y, Boon P, Vreeling F, Colle H, Hoogland G, Groenewegen HJ, van der Linden C: Chronic bilateral thalamic stimulation: a new therapeutic approach in intractable Tourette syndrome. Report of three cases. J Neurosurg 99: 1094-1100, 2003.

41. Visser-Vandewalle V, Ackermans L, van der Linden C, Temel Y, Tijssen MA, Schruers KR, Nederveen P, Kleijer M, Boon P, Weber W, Cath D: Deep brain stimulation in Gilles de la Tourette's syndrome. Neurosurgery 58: E590, 2006.

42. Maddux BN, Maciunas RJ, Whitney CM, Riley DE: Chronic DBS for medically intractable Tourette syndrome: Long-term follow up. In: Program of 2006 Biennial Meeting of the American Society for Stereotactic and Functional Neurosurgery, Boston, 2006, p 90.

43. Slavin KV: Thalamic deep brain stimulation in treatment of disabling Tourette syndrome. Proceedings of 2nd Ann Neurosurg Conf on Internet, 2006, p 11.

44. Flaherty AW, Williams ZM, Amirnovin R, Kasper E, Rauch SL, Cosgrove GR, Eskandar EN: Deep brain stimulation of the anterior internal capsule for the treatment of Tourette syndrome: technical case report. Neurosurgery 57 (4 Suppl): E403, 2005.

45. Diederich NJ, Kalteis K, Stamenkovic M, Pieri V, Alesch F: Efficient internal pallidal stimulation in Gilles de la Tourette syndrome: a case report. Mov Disord 20: 1496-1499, 2005

46. Houeto JL, Karachi C, Mallet L, Pillon B, Yelnik J, Mesnage V, Welter ML, Navarro S, Pelissolo A, Damier P, Pidoux B, Dormont D, Cornu P, Agid Y: Tourette's syndrome and deep brain stimulation. J Neurol Neurosurg Psychiatry 76: 992-995. 2005.

47. Vilela Filho O, Ragazzo PC, Silva DJ, Sousa JT, Ribeiro TMC, Oliveira PM: Bilateral globus pallidus externus deep brain stimulation (GPe-DBS) for the treatment of Tourette syndrome: an ongoing prospective controlled study. In: Program of 2006 Biennial Meeting of the American Society for Stereotactic and Functional Neurosurgery, Boston, 2006, p 91.

48. Sun B: Lesioning and stimulation of bilateral nucleus accumbens for drug addiction. In: Program of 14th meeting of World Society for Stereotactic and Functional Neurosurgery, Rome, 2005, p. 17.

49. Kondziolka D, Whiting D, Germanwala A, Oh M: Hardware-related complications after placement of thalamic deep brain stimulator systems. Stereotact Funct Neurosurg 79: 228-33, 2002.

50. Temel Y, Ackermans L, Celik H, Spincemaille GH, van der Linden C, Walenkamp GH, van de Kar T, Visser-Vandewalle V: Management of hardware infections following deep brain stimulation. Acta Neurochir (Wien) 146: 355-361, 2004.

51. Blomstedt P, Hariz MI: Hardware-related complications of deep brain stimulation: a ten year experience. Acta Neurochir (Wien) 147: 1061-1064, 2005.

52. Venkatraghavan L, Manninen P, Mak P, Lukitto K, Hodaie M, Lozano A: Anesthesia for functional neurosurgery: review of complications. J Neurosurg Anesthesiol 18: 64-67, 2006.

53. Voges J, Waerzeggers Y, Maarouf M, Lehrke R, Koulousakis A, Lenartz D, Sturm V: Deep-brain stimulation: long-term analysis of complications caused by hardware and surgery—experiences from a single centre. J Neurol Neurosurg Psychiatry 77: 868-872, 2006.