TITLE: Deep Brain Stimulation for Parkinson’s disease and Neurological Movement Disorders: Clinical Effectiveness, Cost-Effectiveness, and Guidelines

DATE: 31 August 2011

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of deep brain stimulation versus standard of care for patients with Parkinson’s disease or neurological movement disorders?

2. What is the cost-effectiveness of deep brain stimulation versus standard of care for patients with Parkinson’s disease or neurological movement disorders?

3. What are the evidence-based guidelines for the use of deep brain stimulation for patients with Parkinson’s disease or neurological movement disorders?

KEY MESSAGE

Evidence suggests that deep brain stimulation versus standard of care may be an effective means to treat patients with Parkinson’s disease or neurological movement disorders; however, such invasive surgery places patients at increased risk of adverse events. Limited evidence regarding the cost-effectiveness of deep brain stimulation versus standard of care for patients with Parkinson’s disease or neurological movement disorders was identified. The evidence identified was inconsistent; therefore, no clear conclusions can be made.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2010, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, economic studies and guidelines. The search was also limited to English language documents published between January 1, 2009 and August 19, 2011. Internet links were provided, where available.
RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

The literature search identified one health technology assessment, two systematic reviews, two randomized controlled trials, four non-randomized studies, two economic evaluations, and two evidence-based guidelines. Additional literature of interest is located in the appendix

Health Technology Assessments


Background: Subthalamic nucleus deep brain stimulation (DBS) is currently the most widely used surgical treatment for medically-resistant Parkinson’s disease (PD). A health technology assessment (HTA) published by the Ontario Ministry of Health in 2005 concluded that DBS was associated with short-term improvement in motor function and a reduction in medical therapy. However, questions regarding the long-term performance of the treatment, particularly its impact on quality of life, cognitive function, safety and cost-effectiveness remain. Since 2005, a number of studies addressing these issues (including 3 randomized controlled trials (RCTs) and 3 cohort studies with a longer follow-up time) have been published. DBS has been performed at the MUHC for 22 years. Currently, insufficient funding has resulted in the procedure being halted for 3 months each year, resulting in the wait time for this procedure increasing to 6-12 months.

Objective: To systematically review the literature on effectiveness and safety of DBS since 2005, as well as estimate the budget required to meet the shortfall at the MUHC.

Methodology: The 2005 Ontario HTA was reviewed, and a literature search was performed to identify relevant articles published after this report. We consulted with staff at the MNH to obtain estimates of the number of patients who receive this treatment annually at the MUHC, the cost of the device and the estimated shortfall. Health Outcomes: Improvement in motor function and L-dopa use. Three RCTs comparing efficacy and safety of DBS to medical therapy, were identified. All three studies showed that patients treated by DBS improved and maintained their improvement in motor functions and activities of daily living in the “medication-off, stimulation-on” state for up to 6 months following surgery. Furthermore, it was possible to decrease L-dopa dosage by roughly 50% with DBS. Observational study results indicated maintenance of significant motor function improvement by DBS up to five years. Quality of life. Patient quality of life (QoL) as measured by the 39-Item Parkinson’s Disease Questionnaire (PDQ-39) improved by roughly 20% in DBS patients, while patients who were on medication only did not show improvements or had diminished QoL at 6 months. Adverse events. DBS was associated with a 2.6-4% risk of permanent adverse events, such as cerebral hematoma, and a 40-50% risk of temporary adverse events. In a number of studies DBS was associated with deterioration in verbal fluency. One small study of
Deep Brain Stimulation for Parkinson’s Disease and Neurological Movement Disorders

DBS patients treated at the MUHC, concluded there were no clinically meaningful changes in cognitive function among patients without depression or dementia. A review of the DBS cases done at the MUHC over the last fifteen years showed no cases of permanent neurological deficit, and a 0.5% risk of intracerebral hematoma, which were not symptomatic. Cost issues: Turnover. Currently, 25 new DBS treatments are done during the first 9 months of the year (January-September) at the MUHC. During the remaining 3 months, no procedure is done due to lack of sufficient budget for the devices. If operating could be continued all year round, turnover could be increased by a further 15 patients per year. In the province of Quebec, there is an estimated need for approximately 35 additional procedures per year. Unit cost. The average cost to the MUHC of each procedure (including one year of follow-up) is approximately $27,444. (Equipment Cost $16,400) Budget shortfall. The budget required to purchase the devices for 15 additional cases would be $246,000. The total annual budget impact (due to device costs and MUHC resource use) would be approximately $411,672 for the first 5 years and $619,154 for the next 5 years. Cost effectiveness. The cost of DBS per 10-point decrease in the UPDRS score has been estimated to be $11,650 in the Ontario study. Two cost-effectiveness studies have shown that there is a significant reduction in the average cost of medication and hospital resource use per patient following DBS treatment. Conclusions: There is clear evidence that Deep Brain Stimulation improves motor function and sustains quality-of-life in patients with medically-resistant disease for a period of at least 5 years. It is important that this intervention be performed by a skilled and experienced centre such as the MNH where expertise and experience have already been accumulated. Optimal selection and follow-up of patients is necessary to minimize the risk of adverse outcomes. There is an increasing waiting list in Quebec. To increase the turnover at the MNH by 15 patients per year would require $246,000 per year for equipment, or a total of approximately $411,672 (excluding costs of treating procedure related complications) per year during the first 5 years. Through reduction in medication costs there would be a significant saving from the point of view of the provincial health authority, but this would not affect the MUHC.

CRD abstract: http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?AccessionNumber=32010000171

Systematic Reviews and Meta-analyses


INTRODUCTION: Dystonia is usually a lifelong condition with persistent pain and disability. Focal dystonia affects a single part of the body; generalised dystonia can affect most or all of the body. It is more common in women, and some types of dystonia are more common in people of European Ashkenazi Jewish descent. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of drug treatments, surgical treatments, and physical treatments for focal, and for generalised dystonia? We searched: Medline, Embase, The Cochrane Library, and other important databases up to February 2011 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 15 systematic
reviews, RCTs, or observational studies that met our inclusion criteria. We performed a
GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this
systematic review, we present information relating to the effectiveness and safety of
the following interventions: acetylcholine release inhibitors (botulinum toxin),
acupuncture, anticholinergic/antihistaminic drugs, anticonvulsants, atypical antipsychotic
drugs, benzodiazepines, biofeedback, chiropractic manipulation, deep brain stimulation
of thalamus and globus pallidus, dopaminergic agonists and antagonists, gamma-
aminobutyric acid (GABA) analogues, microvascular decompression, muscle relaxants,
myectomy, occupational therapy, osteopathy, pallidotomy, physiotherapy, selective
peripheral denervation, serotonergic agonists and antagonists, speech therapy, and
thalamotomy.

3. Clarke CE, Worth P, Grosset D, Stewart D. Systematic review of apomorphine infusion,
levodopa infusion and deep brain stimulation in advanced Parkinson's disease.

The effectiveness of oral levodopa in complex Parkinson's disease (PD) is limited by its
short half-life, and the resulting pulsatile dopaminergic stimulation leads to complex motor
fluctuations and dyskinesia. Several treatments provide more continuous/less pulsatile
dopaminergic stimulation by modifying the pharmacokinetics of levodopa or dopamine;
however, patients with advanced disease can be refractory to these treatments. In such
cases infusion therapies (apomorphine and intraduodenal levodopa) and neurosurgery
(deep brain stimulation [DBS]) may be used. The purpose of this systematic review is to
assess, as far as possible, the relative effectiveness of these therapies. There were
no randomised controlled trials comparing the three treatment modalities or any
directly comparable studies, therefore a descriptive analysis of the data was
performed. Studies identified for levodopa infusion and DBS supported a
significant benefit compared with best medical management in terms of
improvements in the proportion of the waking day in a functional "on" state,
activities of daily living and motor score. This finding was supported in
observational studies for all three therapies. Adverse events were not adequately
reported in the majority of included studies and it was therefore not possible to obtain a
reliable tolerability profile of the different treatment options. The absence of direct
comparative data means that, for the immediate future at least, treatment choices
for advanced PD will be determined by clinical judgement and patient preference.
There is an urgent need for well-designed clinical trials to generate reliable data to inform
the clinical management of this difficult-to-treat subgroup of PD patients.
CRD abstract:
http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?AccessionNumber=12010000896&Us
erID=0

Randomized Controlled Trials

stimulation plus best medical therapy versus best medical therapy alone for advanced
Parkinson's disease (PD SURG trial): a randomised, open-label trial. Lancet Neurol
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2874872
PubMed: PM20434403
BACKGROUND: Surgical intervention for advanced Parkinson's disease is an option if medical therapy fails to control symptoms adequately. We aimed to assess whether surgery and best medical therapy improved self-reported quality of life more than best medical therapy alone in patients with advanced Parkinson's disease.

METHODS: The PD SURG trial is an ongoing randomised, open-label trial. At 13 neurosurgical centres in the UK, between November, 2000, and December, 2006, patients with Parkinson's disease that was not adequately controlled by medical therapy were randomly assigned by use of a computerised minimisation procedure to immediate surgery (lesioning or deep brain stimulation at the discretion of the local clinician) and best medical therapy or to best medical therapy alone. Patients were analysed in the treatment group to which they were randomised, irrespective of whether they received their allocated treatment. The primary endpoint was patient self-reported quality of life on the 39-item Parkinson's disease questionnaire (PDQ-39). Changes between baseline and 1 year were compared by use of t tests. This trial is registered with Current Controlled Trials, number ISRCTN34111222. FINDINGS: 366 patients were randomly assigned to receive immediate surgery and best medical therapy (183) or best medical therapy alone (183). All patients who had surgery had deep brain stimulation. At 1 year, the mean improvement in PDQ-39 summary index score compared with baseline was 5.0 points in the surgery group and 0.3 points in the medical therapy group (difference 4.7, 95% CI 7.6 to 1.8; p=0.001); the difference in mean change in PDQ-39 score in the mobility domain between the surgery group and the best medical therapy group was -8.9 (95% CI -13.8 to -4.0; p=0.0004), in the activities of daily living domain was -12.4 (-17.3 to -7.5; p=0.0001), and in the bodily discomfort domain was -7.5 (-12.6 to -2.4; p=0.004). Differences between groups in all other domains of the PDQ-39 were not significant. 36 (19%) patients had serious surgery-related adverse events; there were no suicides but there was one procedure-related death. 20 patients in the surgery group and 13 in the best medical therapy group had serious adverse events related to Parkinson's disease and drug treatment. INTERPRETATION: At 1 year, surgery and best medical therapy improved patient self-reported quality of life more than best medical therapy alone in patients with advanced Parkinson’s disease. These differences are clinically meaningful, but surgery is not without risk and targeting of patients most likely to benefit might be warranted.


CONTEXT: Deep brain stimulation is an accepted treatment for advanced Parkinson disease (PD), although there are few randomized trials comparing treatments, and most studies exclude older patients. OBJECTIVE: To compare 6-month outcomes for patients with PD who received deep brain stimulation or best medical therapy. DESIGN, SETTING, AND PATIENTS: Randomized controlled trial of patients who received either deep brain stimulation or best medical therapy, stratified by study site and patient age (< 70 years vs > = 70 years) at 7 Veterans Affairs and 6 university hospitals between May 2002 and October 2005. A total of 255 patients with PD (Hoehn and Yahr stage > = 2 while not taking medications) were enrolled; 25% were aged 70 years or older. The final 6-month follow-up visit occurred in May 2006. INTERVENTION: Bilateral deep brain stimulation of the subthalamic nucleus (n = 60) or globus pallidus (n = 61).
Patients receiving best medical therapy (n = 134) were actively managed by movement disorder neurologists. MAIN OUTCOME MEASURES: The primary outcome was time spent in the "on" state (good motor control with unimpeded motor function) without troubling dyskinesia, using motor diaries. Other outcomes included motor function, quality of life, neurocognitive function, and adverse events. RESULTS: Patients who received deep brain stimulation gained a mean of 4.6 h/d of on time without troubling dyskinesia compared with 0 h/d for patients who received best medical therapy (between group mean difference, 4.5 h/d [95% CI, 3.7-5.4 h/d]; P < .001). Motor function improved significantly (P < .001) with deep brain stimulation vs best medical therapy, such that 71% of deep brain stimulation patients and 32% of best medical therapy patients experienced clinically meaningful motor function improvements (> or = 5 points). Compared with the best medical therapy group, the deep brain stimulation group experienced significant improvements in the summary measure of quality of life and on 7 of 8 PD quality-of-life scores (P < .001). Neurocognitive testing revealed small decrements in some areas of information processing for patients receiving deep brain stimulation vs best medical therapy. At least 1 serious adverse event occurred in 49 deep brain stimulation patients and 15 best medical therapy patients (P < .001), including 39 adverse events related to the surgical procedure and 1 death secondary to cerebral hemorrhage. CONCLUSION: In this randomized controlled trial of patients with advanced PD, deep brain stimulation was more effective than best medical therapy in improving on time without troubling dyskinesias, motor function, and quality of life at 6 months, but was associated with an increased risk of serious adverse events.

Non-Randomized Studies


We report the 5 to 6 year follow-up of a multicenter study of bilateral subthalamic nucleus (STN) and globus pallidus internus (GPI) deep brain stimulation (DBS) in advanced Parkinson’s disease (PD) patients. Thirty-five STN patients and 16 GPI patients were assessed at 5 to 6 years after DBS surgery. Primary outcome measure was the stimulation effect on the motor Unified Parkinson’s Disease Rating Scale (UPDRS) assessed with a prospective cross-over double-blind assessment without medications (stimulation was randomly switched on or off). Secondary outcomes were motor UPDRS changes with unblinded assessments in off- and on-medication states with and without stimulation, activities of daily living (ADL), anti-PD medications, and dyskinesias. In double-blind assessment, both STN and GPI DBS were significantly effective in improving the motor UPDRS scores (STN, P < 0.0001, 45.4%; GPI, P = 0.008, 20.0%) compared with off-stimulation, regardless of the sequence of stimulation. In open assessment, both STN- and GPI-DBS significantly improved the off-medication motor UPDRS when compared with before surgery (STN, P < 0.001, 50.5%; GPI, P = 0.002, 35.6%). Dyskinesias and ADL were significantly improved in both groups. Anti-PD medications were significantly reduced only in the STN group. Adverse events were more frequent in the STN group. These results confirm the long-term efficacy of STN and GPI DBS in advanced PD. Although the surgical targets were
Deep Brain Stimulation for Parkinson's Disease and Neurological Movement Disorders

not randomized, there was a trend to a better outcome of motor signs in the STN-DBS patients and fewer adverse events in the GPI-DBS group.


Whereas numerous studies document the effects of dopamine medication and deep brain stimulation on motor function in patients with Parkinson's disease, few have investigated deep brain stimulation-induced changes in sensory functions. In this study of 13 patients with Parkinson's disease, we tested the effects of deep brain stimulation on the somatosensory temporal discrimination threshold. **To investigate whether deep brain stimulation and dopaminergic medication induce similar changes in somatosensory discrimination, somatosensory temporal discrimination threshold values were acquired under four experimental conditions: (i) medication ON/deep brain stimulation on; (ii) medication ON/deep brain stimulation off; (iii) medication OFF/deep brain stimulation on; and (iv) medication OFF/deep brain stimulation off.**

Patients also underwent clinical and neuropsychological evaluations during each experimental session. Somatosensory temporal discrimination threshold values obtained in patients were compared with 13 age-matched healthy subjects. **Somatosensory temporal discrimination threshold values were significantly higher in patients than in healthy subjects. In patients, somatosensory temporal discrimination threshold values were significantly lower when patients were studied in medication ON than in medication OFF conditions. Somatosensory temporal discrimination threshold values differed significantly between deep brain stimulation on and deep brain stimulation off conditions only when the patients were studied in the medication ON condition and were higher in the deep brain stimulation on/medication ON than in the deep brain stimulation off/medication ON condition.** Dopamine but not subthalamic nucleus deep brain stimulation restores the altered somatosensory temporal discrimination in patients with Parkinson's disease. Deep brain stimulation degrades somatosensory temporal discrimination by modifying central somatosensory processing whereas dopamine restores the interplay between cortical and subcortical structures.


Patients with Parkinson's disease (PD) show impairment in generating random motor sequences reflecting a higher order motor deficit in set-shifting and suppression of perseverative behavior. The impact of deep brain stimulation (DBS) of the subthalamic nucleus (STN) on motor perseverations has not yet been elucidated. In 35 patients with PD, we **evaluated the effect of STN-DBS and levodopa on motor perseverations using the Vienna perseveration task.** The task was performed 6 months after implantation of stimulation electrodes in the following three conditions: Stimulation off/medication off (Stim OFF/Med OFF), Stim ON/Med OFF, and Stim OFF/Med ON. Perseverations were measured by redundancy of second order (R(2)) with higher values indicating more severe perseverations. **ANCOVA analysis revealed that influence of STN-DBS on R(2) significantly depended on R(2) severity during Stim OFF/Med OFF (F = 4.69,
P = 0.035). Accordingly, we classified patients with PD into two groups based on the R(2) value during off treatment. In patients with mild perseveration (R(2) < 35) neither STN-DBS nor levodopa changed perseverations. By contrast, in patients with severe perseveration (R(2) > 35), STN-DBS significantly reduced R(2) by 9.7 +/- 2.6 (P < 0.001) whereas levodopa had no impact (R(2) reduction 3.7 +/- 1.6, P = 0.081). This demonstrates that STN-DBS, by reducing motor perseveration, influences higher order aspects of motor behavior of patients with PD.


BACKGROUND/AIMS: To quantify aperiodic phonation, nonlinear dynamic methods of acoustic voice analysis, such as correlation dimension, have been shown to be useful. The purpose of this study is to evaluate the validity of nonlinear dynamic analysis as a voice analysis tool for the effects of deep brain stimulation (DBS) and levodopa on patients with Parkinson's disease (PD). METHODS: In this study, the effects of DBS and levodopa treatment on patients with PD were measured using perturbation, nonlinear dynamic, and perceptual analysis. Nineteen PD patients that received bilateral (n = 9), left (n = 7), or right (n = 3) DBS performed sustained vowel phonations, which were recorded before and after medication with the stimulator off and on. Recordings were also taken of 10 PD patients who did not receive DBS surgery before and after medication to provide a baseline. RESULTS: A mixed two-way ANOVA (surgery, medication) generated significant positive treatment effects of DBS only in mean log-transformed D2, which was supported by mean log-transformed shimmer, vF0 (variability in fundamental frequency), and vAm (peak-to-peak amplitude variation). CONCLUSION: These findings may indicate the validity of nonlinear dynamic analysis as a complement to perceptual analysis in clinical PD voice studies.

Economic Evaluations


Many expensive treatments have been developed for Parkinson's disease (PD), and a good cost-utility analysis is required. Quality-adjusted life-years (QALY) allows comparison of the cost-utility of different medical conditions. If a treatment strategy gives a patient an extra but unhealthy year, the QALY he obtained will be less than one. When a therapeutic strategy is more effective, but causes higher costs, it is mandatory to calculate the incremental cost-effectiveness ratio (ICER). In keeping with guidance from the UK National Institute for Health and Clinical Excellence (NICE), a therapy that delivers QALYs of £20,000 or less are likely to be approved. The threshold used by NICE for the maximum it is prepared to pay for a QALY, which lies between £20,000 and £30,000, will be reviewed case by case. Subthalamic deep brain stimulation (STN-DBS) is an effective therapy, which can improve the quality of life in PD patients immediately, but has not been approved by the Bureau of National Health
Insurance here. It has been estimated that the ICER/QALY in STN-DBS patients was of 34,389€, which is within appropriate limits to consider STN-DBS as an efficient therapy. We expect that we can have a decision-making mechanism similar to that of NICE that, according to the ICER of each medical condition, medical resource can be redistributed openly and justly.


Deep brain stimulation of the subthalamic nucleus is the standard of care for treating medically intractable Parkinson's disease. Although the adjunct of microelectrode recording improves the targeting accuracy of subthalamic nucleus deep brain stimulation in comparison with image guidance alone, there has been no investigation of the financial cost of intraoperative microelectrode recording. This study was performed to address this issue. A comprehensive literature search of large subthalamic nucleus deep brain stimulation series (minimum, 75 patients) was performed, revealing a mean operating room time of 223.83 minutes for unilateral and 279.79 minutes for simultaneous bilateral implantation. The baseline operating room time was derived from the published operating room time for subthalamic nucleus deep brain stimulation without microelectrode recording. The total cost (operating room, anesthesia, neurosurgery) was then calculated based on hospitals geographically representative of the entire United States. The average cost for subthalamic nucleus deep brain stimulation implantation with microelectrode recording per patient is $26,764.79 for unilateral, $33,481.43 for simultaneous bilateral, and $53,529.58 for staged bilateral. For unilateral implantation, the cost of microelectrode recording is $19,461.75, increasing the total cost by 267%. For simultaneous bilateral implantation, microelectrode recording costs $20,535.98, increasing the total cost by 159%. For staged bilateral implantation, microelectrode recording costs $38,923.49, increasing the total cost by 267%.

Microelectrode recording more than doubles the cost of subthalamic nucleus deep brain stimulation for Parkinson's disease and more than triples the cost for unilateral and staged bilateral procedures. The cost burden of microelectrode recording to subthalamic nucleus deep brain stimulation requires the clinical efficacy of microelectrode recording to be proven in a prospective evidence-based manner in order to curtail the potential for excessive financial burden to the health care system.

Guidelines and Recommendations


Ten years ago deep brain stimulation (DBS) has been introduced as an alternative and promising treatment option for patients suffering from severe Tourette syndrome (TS). It seemed timely to develop a European guideline on DBS by a working group of the European Society for the Study of Tourette Syndrome (ESSTS). For a narrative review a systematic literature search was conducted and expert opinions of the guidelines group contributed also to the suggestions. Of 63 patients reported so far in
the literature 59 had a beneficial outcome following DBS with moderate to marked tic improvement. However, randomized controlled studies including a larger number of patients are still lacking. Although persistent serious adverse effects (AEs) have hardly been reported, surgery-related (e.g., bleeding, infection) as well as stimulation-related AEs (e.g., sedation, anxiety, altered mood, changes in sexual function) may occur. At present time, DBS in TS is still in its infancy. **Due to both different legality and practical facilities in different European countries these guidelines, therefore, have to be understood as recommendations of experts.** However, among the ESSTS working group on DBS in TS there is general agreement that, at present time, DBS should only be used in adult, treatment resistant, and severely affected patients. It is highly recommended to perform DBS in the context of controlled trials.

NGC summary: http://www.guideline.gov/content.aspx?id=15087&search=%22deep+brain%22

**PREPARED BY:**
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca
APPENDIX – FURTHER INFORMATION:

Review articles


OBJECTIVE: To provide recommendations to patients, physicians, and other health care providers on several issues involving deep brain stimulation (DBS) for Parkinson disease (PD). DATA SOURCES AND STUDY SELECTION: An international consortium of experts organized, reviewed the literature, and attended the workshop. Topics were introduced at the workshop, followed by group discussion. DATA EXTRACTION AND SYNTHESIS: A draft of a consensus statement was presented and further edited after plenary debate. The final statements were agreed on by all members. CONCLUSIONS: (1) Patients with PD without significant active cognitive or psychiatric problems who have medically intractable motor fluctuations, intractable tremor, or intolerance of medication adverse effects are good candidates for DBS. (2) Deep brain stimulation surgery is best performed by an experienced neurosurgeon with expertise in stereotactic neurosurgery who is working as part of an interprofessional team. (3) Surgical complication rates are extremely variable, with infection being the most commonly reported complication of DBS. (4) Deep brain stimulation programming is best accomplished by a highly trained clinician and can take 3 to 6 months to obtain optimal results. (5) Deep brain stimulation improves levodopa-responsive symptoms, dyskinesia, and tremor; benefits seem to be long-lasting in many motor domains. (6) Subthalamic nuclei DBS may be complicated by increased depression, apathy, impulsivity, worsened verbal fluency, and executive dysfunction in a subset of patients. (7) Both globus pallidus pars interna and subthalamic nuclei DBS have been shown to be effective in addressing the motor symptoms of PD. (8) Ablative therapy is still an effective alternative and should be considered in a select group of appropriate patients.


Motor complications impair quality of life and cause severe disability in patients with advanced Parkinson's disease (PD). Since they are often refractory to medical therapy, interventional therapies have been developed, which can provide a considerable reduction of daily off-time and dopaminergic dyskinesias. Continuous dopaminergic drug delivery (CDD) is based on the steady stimulation of striatal dopamine receptors by subcutaneous apomorphine or duodenal L-DOPA infusions via portable minipumps. Advances in the understanding of basal ganglia functioning and in neurosurgical, electrophysiological and neuroimaging techniques have led to a renaissance of neurosurgery for advanced PD. Deep brain stimulation of the subthalamic nucleus (STN-DBS) is the most invasive procedure promising great benefit and the highest level of independency for suitable patients, but is definitely associated with surgical risks and DBS-related side effects. Each of these more or less invasive therapy options has its own profile, and
a thorough consideration of its advantages and drawbacks for the individual situation is mandatory. In this paper, we **summarize relevant facts for this decision and provide some guidelines for a responsible counseling of eligible patients.**


Deep brain stimulation (DBS) has developed during the past 20 years as a remarkable treatment option for several different disorders. Advances in technology and surgical techniques have essentially replaced ablative procedures for most of these conditions. Stimulation of the ventralis intermedius nucleus of the thalamus has clearly been shown to markedly improve tremor control in patients with essential tremor and tremor related to Parkinson disease. Symptoms of bradykinesia, tremor, gait disturbance, and rigidity can be significantly improved in patients with Parkinson disease. Because of these improvements, a decrease in medication can be instrumental in reducing the disabling features of dyskinesias in such patients. Primary dystonia has been shown to respond well to DBS of the globus pallidus internus. The success of these procedures has led to application of these techniques to multiple other debilitating conditions such as neuropsychiatric disorders, intractable pain, epilepsy, camptocormia, headache, restless legs syndrome, and Alzheimer disease. The literature analysis was performed using a MEDLINE search from 1980 through 2010 with the term deep brain stimulation, and several double-blind and larger case series were chosen for inclusion in this review. The **exact mechanism of DBS is not fully understood. This review summarizes many of the current and potential future clinical applications of this technology.**


Deep brain stimulation (DBS) is a widely employed therapeutic modality for the treatment of movement disorders. Full FDA approval or humanitarian device exemption has been made for Parkinson's disease, tremor, and dystonia. In this review, we **describe the indications and selection criteria, target selection, and outcomes for each of these conditions. In addition, we describe the operative techniques utilized in DBS surgery and look forward to new developments in DBS on the horizon.**

Additional references


Parkinson’s disease (PD) affects speech in the majority of patients. Subthalamic nucleus deep brain stimulation (STN-DBS) is particularly effective in reducing tremor and rigidity. However, its effect on speech is variable. The **aim of this pilot study was to quantify the effects of bilateral STN-DBS and medication on articulation, using electropalatography (EPG).** Two patients, PT1 and PT2, were studied under four
conditions: on and off medication and ON and OFF stimulation. The EPG protocol consisted of a number of target words with alveolar and velar stops, repeated 10 times in random order. The motor part III of the Unified Parkinson Disease Rating Scale (UPDRS) indicated significantly improved motor scores in the ON stimulation condition in both patients. However, PT1’s articulation patterns deteriorated with stimulation whereas PT2 showed improving articulatory accuracy in the same condition. The results revealed different effects of stimulation and medication on articulation particularly with regard to timing. The study quantified less articulatory undershoot for velar stops in comparison to alveolars. Furthermore, the findings provided preliminary evidence that stimulation with medication has a more detrimental effect on articulation than stimulation without medication.


Deep brain stimulation (DBS) is an established treatment for essential tremor (ET). The nucleus ventralis intermedius thalami (Vim) is the target of choice, but promising results have been presented regarding DBS in the posterior subthalamic area (PSA). The aim of this study was to evaluate the possible influence of gender, age and severity of disease on the outcome of these procedures. Sixty eight patients (34 Vim, 34 PSA) with ET were included in this non-randomised study. Evaluation using the Essential Tremor Rating Scale (ETRS) was performed before, and one year after surgery concerning PSA DBS, and at a mean of 28 +/- 24 months concerning Vim DBS. Items 5/6 and 11-14 (hand tremor and hand function) were selected for analysis of tremor outcome. The efficacy of DBS on essential tremor was not related to age or gender. Nor was it associated with the severity of tremor when the percentual reduction of tremor on stimulation was taken into account. However, patients with a more severe tremor at baseline had a higher degree of residual tremor on stimulation. Tremor in the treated hand and hand function were improved with 70% in the Vim group and 89% in the PSA group.