

Critical Review:
The Effects of Subthalamic Nucleus Deep Brain Stimulation on Speech Production in Parkinson's Disease

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Abstract

This systematic review examined the effects of subthalamic nucleus deep brain stimulation (STN-DBS) on speech in individuals with Parkinson's disease in nine studies. Study designs included: four non-experimental studies (one case study, one survey study, one systematic review, one expert opinion) and five quasi-experimental studies (one case control study, three treatment studies, one clinical trial study). The evidence from this review indicated that STN-DBS did not appear to provide positive outcomes for speech production in Parkinson's disease.

Introduction

Canada's population is aging and will continue to do so at an accelerated pace between 2009 and 2031; a period during which all baby boomers will become seniors (≥ 65 years). Between the years 2015 and 2021, the number of seniors is projected to surpass the number of children (≤ 14 years), a first in Canadian population history. Seniors will represent 23-25% of the population by 2036 (Stats Canada 2009). Although Parkinson's disease (PD) only affects about 2-3% of Canadians over the age of 60 (Parkinson's Society Canada), the number of people affected by PD will continue to increase as the senior population grows.

Parkinson's disease is a neurodegenerative disease caused by the deterioration of dopaminergic neurons in the brain stem and the basal ganglia. The primary symptoms of PD include muscle rigidity, bradykinesia, resting tremor, and impaired balance (Brookshire, 2007). Motor speech difficulties are commonly associated with PD. In fact 60% or more of PD patients will develop symptoms of hypokinetic dysarthria. Hypokinetic dysarthria is characterized by monopitch, monoloudness, reduced stress, short phrases, variable rate, short rushes of speech, imprecise consonants, inappropriate silences, harsh voice quality, a constant breathy voice, and low pitch (Duffy, 2005).

The treatment of PD with the drug, levodopa, is effective for reducing the motor symptoms in many patients, but is not consistently associated with improvements in speech. The effects of levodopa can fluctuate as a function of the drug cycle and increases in dosage can cause abnormal uncontrolled muscle movements (Duffy, 2005). Alternatively, deep brain stimulation (DBS), which sends electrical impulses to a specific area of the brain, has been shown to improve motor difficulties experienced by individuals with PD,

but with variable effects on speech (Frost et. al, 2010). The subthalamic nucleus (STN) is currently the preferred surgical target of DBS for the treatment of PD (Murdoch, 2010).

Objectives

The primary objective of this paper was to summarize and systematically evaluate studies that have examined the effects of STN-DBS on speech production in patients with PD.

Methods

Search Strategy

The computerized database CINAHL and the University libraries search engine were searched using the following search strategy: (Subthalamic Nucleus) OR (Deep Brain Stimulation) AND (dysarthria) OR (dysphonia) or (voice) OR (Speech). The search was limited to English language, and journal articles or reviews published after 2007 and before February 2011. (Note: Relevant papers published prior to 2007 were reviewed in the systematic review included in this paper).

Selection Criteria

Studies included in the systematic review involved an investigation of the effects of subthalamic nucleus deep brain stimulation in patients with Parkinson's disease. No limits were set on the demographics (age, gender, culture, race, socioeconomic status, or geographic location) of research participants or type of speech parameter examined.

Data Collection

Results of the literature search produced nine articles consistent with the search criteria: four non-experimental studies (one case study, one survey study,

one systematic review, one expert opinion) and five quasi-experimental studies (one case control study, three treatment studies, one clinical trial study). Articles included in the systematic review were not included as separate individual studies in this review.

Results

Nonexperimental

Expert Opinion

Murdoch (2010) reviewed and evaluated the literature related to the effects of surgical interventions for PD. Of greatest concern to this paper was the section titled “Effects of deep brain stimulation on speech” (p. 381). Based on the author’s review of the literature insufficient evidence existed regarding speech outcomes in PD patients with DBS. DBS has been reported to have no effect, minor positive effects as well as negative effects on speech. The results highlighted the variable influence STN-DBS had on speech function. The author suggested that an improvement in speech due to STN-DBS was not clinically significant, while the negative side-effects were possibly due to the spread of electrical stimulation to the cerebello-thalamic tracts.

This article did not provide a description of search strategies or article selection criteria. This expert opinion reflects the analyses and conclusions of only one author. However, the author appears to be a well-regarded expert in the field. This expert opinion provided suggestive evidence that STN-DBS has variable effects on speech outcomes.

Systematic Review

Iulianella, Adams, and Gow (2008) conducted a systematic review of the effects of STN-DBS on speech production in PD. Eight articles were identified by searching various computerized databases for English language articles published prior to February 2007. All articles included participants with levodopa responsive PD; otherwise no type of research parameter or demographic limitations were set. Of the eight articles, one was a case study and seven were group studies using quasi-experimental designs. Results of the critical review indicated that evidence within the eight articles should be interpreted with caution due to their fairly small sample sizes. It was also noted that methodologies varied across studies, leading to difficulty making comparisons. However, several important trends still emerged.

Six of the seven group studies were unsuccessful in finding a beneficial effect of bilateral STN-DBS on a range of speech production measures. Four of the seven group studies reported negative effects of STN-DBS on

speech production. Moreover, three of these studies suggested that left STN-DBS had a greater negative effect on speech production compared to right STN-DBS. Only two studies (one being a case study) provided evidence of a positive effect of STN-DBS. However, an insufficient report of statistical information did not allow for an accurate evaluation.

This systematic review included a comprehensive and clearly described search for relevant articles as well as adequate inclusion and exclusion criteria. The validity of the study was strengthened by its weighting of results by sample size. However, the study was based on one individual’s evaluation of the data and no quantitative analyses were performed. Overall, this study provides suggestive evidence that STN-DBS has no beneficial effect or in some cases a negative effect on speech production.

Survey Study

Frost, Tripoliti, Hariz, Pring, & Limousin (2010) investigated whether patients perceived the changes in their speech following STN-DBS to be different than that of non-surgical PD patients. Also of interest was determining whether objective measures for movement and speech impairment correlated with subject Voice Handicap Index (VHI) scores before and after surgery. The study included 40 patients with PD, 20 had STN-DBS surgery 6-12 months prior to the study (surgery group) and 20 were potential candidates for STN-DBS surgery (non-surgical group). Patients completed two VHIs, one with reference to their current status (i.e., post-surgery for the surgery group) and the other relative to either pre-surgery (surgery group) or their last prior appointment (non-surgery group). For 18 of the 20 surgery participants, additional information was available from their medical charts, such as pre- and post-surgery UPDRS-III scores as well as voice recordings from pre-surgery while off medication and post-surgery without medication, but stimulation on.

Data were appropriately analyzed using 2-factor mixed ANOVAs, t-tests, and correlations. The results revealed that 14/20 participants in each group scored their current voice higher (or worse) than their voice prior to surgery or last appointment. The surgical group had higher scores on the VHI and the UPDRS, but the differences were statistically not significant and did not interact with time. As well, changes in VHI scores and UPDRS scores for the surgical group were not significant.

This study included appropriate participant inclusion and exclusion criteria, an adequate number of subjects, and a thorough description of the methods. The validity of the study was strengthened by its high response rate

and use of a standardized measure. However, the study was based on participant perception only and had very few quantitative measures. Overall, this study provides suggestive evidence that STN-DBS has no significant effect on perceived voice outcomes.

Case Study

Narayana, Jacks, Robin, Poizner, Zhang, Franklin, Liotti, Vogel, & Fox (2009) conducted a case study, with some treatment manipulations, to investigate an exacerbated speech impairment following STN-DBS in a 59-year-old man with PD. The bilateral STN-DBS was implanted two years prior to the study.

The study consisted of three experiments. Experiment 1 manipulated the level of stimulation (bilateral DBS on, left DBS on, right DBS on, bilateral DBS off) in order to conduct perceptual ratings (7-point equal interval scale) of 38 perceptual dimensions by two SLPs (blinded to condition and to the others rating) while reading "The Rainbow Passage" at each level of stimulation. The SLPs achieved an acceptable 97% interrater reliability for identification of deviant dimensions across all conditions. Acoustic contrastivity measures as well as broad durational measures of tone groups and intergroup intervals were reported. Experiment 2 manipulated the speech task (rest, reading, and sustained phonation) while stimulation was on as well as off. Neuroimaging methods involving standard techniques were employed. Experiment 3 used transcranial magnetic stimulation (TMS) to virtually lesion a specific area of the brain that was identified in Exp. 2. STN-DBS remained off for the duration of this phase. The level of TMS (on and off) was manipulated while the perceptual, acoustic contrastivity and broad durational were reported and qualitatively compared to the outcomes from Exp. 1. In addition, speech intelligibility (percent of produced words identifiable to authors 2 and 3) was measured during TMS on and off conditions.

The main results of Exp. 1 indicate that the subject's speech production was impaired in all conditions; however, left STN-DBS was associated with perceptually inferior and acoustically less contrastive speech as compared to no stimulation. Right STN-DBS resulted in higher (less impaired) ratings than no stimulation for the perceptual dimensions of breathiness, strained/strangled, and short phrases. Exp. 2 identified the left dorsal premotor cortex (PMd) as having the most significant increase in cerebral blood flow during STN-DBS. Exp. 3 results indicated that virtual lesioning of the left PMd resulted in perceptually similar speech as left STN stimulation. The authors hypothesized that the impaired speech production

associated with STN-DBS may be due to the unintended activation of the PMd.

This case study included an appropriate description of the participant and a detailed description of the methods. The validity of the case study was strengthened by the experimental manipulations and the quantitative analyses. However, the results are based on only one participant and would require specific technology in order for the study to be replicated in other research settings. Overall, this case study provides compelling evidence that STN-DBS has negative effects on speech production outcomes.

Quasiexperimental

Case Control Study

Lee, Zhou, Rhan III, Wang, & Jiang (2008) investigated whether PD subjects without STN-DBS have significantly higher correlational dimension (D2) values than healthy control subjects and PD subjects with STN-DBS. The study recruited 19 PD patients (surgery group) to undergo STN-DBS surgery, 10 PD patients who did not undergo surgery (non-surgical control group), and 11 healthy subjects (non-pathologic control group). The PD participants were selected to be homogeneous within each group and well-matched between groups. They were also subject to strict exclusion criteria. The non-pathologic control group was part of another study using identical voice testing protocol in addition to having a similar average age.

The surgery group recorded five sustained /a/ phonations at each level of stimulation (on and off). Three sustained /a/'s were randomly selected to be analyzed. Control participants were recorded once. All participants were off medication. One-second segments from the middle of the selected vowels were examined using correlational dimension procedure measures. Perturbation analysis (using Cspeech 4.0 software and The Multi-Dimensional Voice Program) were also conducted. Appropriate unpaired Wilcoxon rank sum tests were used to compare the mean D2 values and each of the perturbation indices for the surgery, non-surgery, and non-pathogenic groups. The Bonferroni correction was appropriately used during additional analyses. Double-blinding was achieved for all phases of the study reducing potential for bias. The mean D2 value of the non-surgical group was significantly higher compared to the non-pathological and surgical groups. Also, many PD subjects produced type 2 signals containing subharmonics, with PD control subjects producing stronger subharmonics than PD patients under stimulation.

This study included appropriate participant inclusion and exclusion criteria, a reasonable number of subjects,

and a thorough description of the methods. The validity of the study was strengthened by its use of two control groups, well-matched PD groups, and double-blind procedures. The results suggested STN-DBS may provide measurable improvement in patients with severe vocal impairment; however, it was not stated whether the improvements were noticeable perceptually. Overall, this study provides compelling evidence that STN-DBS has a beneficial effect on voice outcomes.

Treatment Studies (3)

Fasano, Romito, Daniele, Piano, Zinno, Bentivoglio, & Albanese (2010) investigated the long-term motor and cognitive outcomes in 20 consecutive PD patients who underwent bilateral STN-DBS implantation 8 years prior to the study.

The UPDRS was used to evaluate motor function beginning at baseline (prior to surgery) and continuing until 8 years post-surgery. UPDRS item 18 evaluated speech. The motor assessment was completed under two conditions: condition A was stimulation with no medication and condition B was stimulation with medication. The student t-test (unpaired and paired) or the Wilcoxon signed rank test was appropriately used to analyze the motor data depending on the distribution. At 5 years the majority of PD motor symptoms improved, but speech did not. At 8 years speech did not improve, but also did not decline further.

This study included appropriate participant inclusion and exclusion criteria and an adequate description of the methods. The validity of the study was strengthened by its prospective longitudinal design. However, the results are limited by the study's use of the UPDRS item 18 as its only speech measure. Overall this study provides highly suggestive evidence that STN-DBS has no effect on speech outcomes.

A second treatment study by Jones, Kendall, Okun, Wu, Velozo, Fernandez, Spencer, & Rosenbek (2010) investigated the differences in speech response time (SRT) for word production in maintenance and switch conditions at the each level of stimulation (on and off) in PD patients with DBS of the STN and globus pallidus pars interna (GPi). Twelve participants were included in this study; five with GPi-DBS and seven with STN-DBS. A total of eight participants had bilateral implants and four had unilateral implants. The stimuli used in the study were 16 prime-target pairs. Seventy-five percent of the prime-target trials were identical (maintenance condition) and 25% were mismatched (switch condition). Participants were asked to say the prime word aloud as quickly and accurately as possible upon the presentation of the target. The

onset of SRT was signaled by the presentation of the target, and phonation signaled offset.

Participants with bilateral DBS had their right stimulation turned off for the duration of the study. The non-parametric Wilcoxon signed-rank test was correctly used to determine differences in SRT between on and off stimulation in maintenance and switch tasks. Fisher's Combination Method was appropriately used for post-hoc analyses in order to correct p-values for multiple comparisons. SRTs were significantly faster with maintenance as compared to switch tasks regardless of stimulation on or off. Specifically, SRT was faster in the maintenance task when stimulation was on. Unexpectedly, no significant difference in SRT was found in the switch task with stimulation on or off. It was concluded that DBS helped to improve speech motor program maintenance but not switching.

This study included specific inclusion and exclusion criteria as well as an adequate description of the methods. The validity of the study is strengthened by its double-blinded procedures, random assignment of participants to their initial condition, and counterbalancing of conditions. However, the results are limited by the small sample size, the incorporation of two DBS target sites, and the face validity of the switch task. Overall, the results of this study provide suggestive evidence that STN-DBS has a beneficial effect on in motor speech outcomes.

A third treatment study was conducted by D'Altri, Paludetti, Contarino, Galla, Marchese, & Bentivoglio (2008) to assess speech in PD patients with STN-DBS using objective measures and to follow the patients longitudinally. Included in the study were 12 PD patients with STN-DBS and 25 healthy controls. Perceptual speech ratings (UPDRS item 18) and acoustic data were collected within 2-5 years after surgery. Participants produced a sustained vowel /a/, varying intonation patterns, and diadochokinetics under four conditions: (1) medication off-stimulation on; (2) medication off-stimulation off; (3) medication on-stimulation on; and (4) medication on-stimulation off. Several well-defined articulation and phonation-related parameters were measured. Medians of Wilcoxon's matched pairs test were used to statistically analyze UPDRS item 18 and acoustic parameters across the four conditions.

Variations in perceptual scores (UPDRS item 18) were not statistically significant across the four conditions. However, jitter and noise-to-harmonics ratio values significantly decreased in response to med off-stim on vs. med off-stim off. There was also a significant decrease in magnitude of the amplitude tremor and

magnitude of the frequency tremor for med-off-stim vs. med off-stim off. Together these results indicate an improvement in vocal tremor and glottal vibration. No significant variation in acoustic measures was observed for prosody, articulation or intensity.

This study included appropriate inclusion and exclusion criteria as well as an adequate description of the methods. The validity of the study was limited by its small sample size. Furthermore, the improvements noted in this study did not lead to improved intelligibility. Overall, this study provides somewhat suggestive evidence that STN-DBS improves speech production outcomes.

Clinical Trial Study with healthy controls

Putzer, Barry, & Moringlane (2008) compared the performance of speech subsystems (glottal-supraglottal articulation & phonation) in nine PD patients with STN-DBS and 20 healthy control subjects. EEG and behavioral recordings of vowel productions were measured, and several well-defined articulation and phonation-related parameters were measured during on and off stimulation conditions. All parameter measures were appropriately converted to z-scores and analyzed using ANOVA and ANOVA with repeated measures.

The results indicated that the duration of the voiced segments in the three syllable-cycles was greater under stimulation due to longer vowel duration, continued voicing in the oral closure phase, and shorter voice onset times. Conversely, the syllable-cycles (i.e., speed of syllable repetition) as a whole were shorter under stimulation due to significantly shorter duration of stop closures in the /p/- and /t/-syllables. In general, four subjects showed improvements in articulation and five showed reduced precision. When compared to the control group, PD participants under stimulation demonstrated negative differences for the following EEG-parameters: start of the closing phase, end of the closing phase, and the contact phase. However, stimulation induced positive differences for the following EEG-parameters: open quotient and skewness of the whole opening phase. In general, participants equally demonstrated improvement, impairment, and no change under stimulation.

This study included inclusion and exclusion criteria as well as an adequate description of the methods. The validity of this study is strengthened by its use of a control group and its simultaneous recording of EEG and acoustic signals during speech tasks. However, the study is based on a small sample size. Overall, these results provide suggestive evidence of improvement and impairment (at times occurring within the same individual) of speech production outcomes.

Discussion

Overall, the results of this review suggest that the positive effects of STN-DBS on speech production in Parkinson's disease are limited. The evidence from these nine studies can be interpreted with some confidence because most of the studies included adequate samples sizes given the nature of the area being studied. The sample sizes of the participants with STN-DBS for the six group studies ranged from 7 to 20 subjects and only two of these studies had less than ten subjects. Several of the studies implemented bias reducing procedures. Four of the six studies had a PD non-surgery control group and/or a healthy control group. One study used randomization to assign participants to their initial treatment group as well as counterbalancing. Three studies used blinding procedures.

The speech tasks and outcome measures used in these studies were quite varied, making it difficult to compare results across studies. Speech tasks included: reading, conversational speech, sustained phonation, maintenance and switch tasks, varying intonation patterns, and diadochokinetics. Outcome measures included: speech response time, perturbation values, EEG measures, correlational dimension values, VHI scores, UPDRS item 18 scores, perceptual ratings, acoustic contrastivity measures, broad durational measures of tone group and intergroup intervals, blood flow, and acoustic measures. Despite the variation in experimental methodologies, several important trends became apparent.

First, four of the studies failed to find evidence to support a beneficial effect on STN-DBS on speech outcomes, two of which reported negative effects of STN-DBS (perceptual and acoustic contrastivity measures) and two reported no effect of STN-DBS on speech outcomes (perceptual voice and perceived voice). Second, of the remaining studies two reported variable effects of STN-DBS on speech outcomes (positive and negative effects across participants and within the same participants). Finally, three of the nine studies reported a positive effect of STN-DBS on speech outcomes. These included correlational dimension values, subharmonics, speech response time, speech maintenance, jitter, noise-to-harmonics ratio, vocal tremor, and glottal vibration. However, none of these studies reported improved intelligibility scores (i.e., intelligibility scores were unimproved or were not reported at all). Therefore, the positive effects of STN-DBS on speech are considered very limited.

Conclusion

While STN-DBS may be medically useful for PD patients, positive outcomes for speech do not appear to be observed. In fact, several studies report negative effects of STN-DBS on speech.

Clinical Implications

The results analyzed suggest that STN-DBS is not generally associated with positive effects on speech. Such evidence has important clinical implications for speech language pathologists (SLPs). Understanding the effects STN-DBS have on speech will help SLPs to provide their clients with realistic speech outcomes following surgery. Additionally, it would allow SLPs to collect speech recordings and perceptions prior to their client's surgery in order to monitor any speech changes. Knowledge of the diverse outcomes of STN-DBS on speech would help SLPs to better assess and treat the changes that may result from the procedure.

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