Critical Review:
What is the effect of subthalamic deep brain stimulation on swallowing in persons with Parkinson’s disease?

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This critical review examines the effects of subthalamic nucleus (STN) deep brain stimulation (DBS) on swallowing in persons with Parkinson’s disease (PD) in 8 studies. Study designs include: within group, pre/post-test studies and case reports. The evidence from this review indicates that STN DBS did provide positive outcomes for swallowing function in persons with PD; however, a large degree of variability was seen among these improvements. Recommendations for further research and clinical practice are provided.

Introduction

Canada has an aging population and as the baby boomers become seniors, they will begin to outnumber children and adults (Statistics Canada, 2011). Between 2006 and 2011, the senior age group increased by 14.1% and it will continue to grow at this accelerated rate (Statistics Canada, 2011). As Parkinson’s disease (PD) has an average on-set age of 62 years, the senior population is most affected by this disease (National Parkinson Foundation (NPF), 2013). Currently, estimates suggest 4-6 million people worldwide suffer from PD (NPF, 2013). As the population continues to age, the number of persons diagnosed with PD will continue to rise.

PD is a neurodegenerative disease where dopamine producing neurons deteriorate in the brain stem and basal ganglia. This can lead to symptoms of muscle rigidity, bradykinesia, resting tremor and muscular instability (Kulneff, Sundstedt, Olofsson, Van Doorn, Linder, Nordh & Blomstedt, 2012). Of all persons who develop PD, 90% will also experience some amount of swallowing challenges including, but not limited to, silent aspiration (Fagbami & Donato, 2011).

Bilateral high-frequency deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective procedure that is used to alleviate symptoms in advanced PD when medical management has failed to do so (Kleiner-Fisman, Herzog, Fisman, Tamma, Lyons and Pahwa, 2006). Although studies have shown that STN DBS manages a wide range of symptoms that mostly respond to levodopa, the effect of STN DBS on swallowing function is still unclear (Tassorelli, Buscone, Sandrini, Paccetti, Furnari, Zangalia, Bartolo, Nappi & Martignoni, 2009).

Objectives

The primary objective of this paper is to critically examine the current literature regarding the impact of STN DBS on swallowing in persons with PD. The secondary objective is to provide evidence-based recommendations for future clinical practice and research in the area of DBS.

Methods

Search Strategy

Computerized databases, including PubMed, CINAHL, Scopus and Embase were searched using the following search strategy:

((Parkinson’s disease) OR Parkinsonism) AND (deep brain stimulation) AND (subthalamic nucleus) AND ((swallowing) OR (deglutition) OR (dysphagia)).

Selection Criteria

Studies selected for inclusion in this critical review were required to evaluate swallowing in persons with PD using an instrumental swallowing assessment. Participants were required to have bilateral electrode implantation. No limits were set on when the participant received DBS implantations in comparison to disease on-set and stage.

Data Collection

Results of the literature search yielded the following types of articles that met the selection criteria: within group, pre/post-test study (6) and case report (2).

Results

Since DBS is a relatively new and growing area of interest and not all persons with PD are treated with DBS, the studies in this critical review have small sample sizes. Therefore, statistical power is reduced, generalization is limited and conclusions must be interpreted with caution.

Within Groups, Pre/Post-test Studies

This type of design is beneficial because it reduces variability between participants and allows for an
examination of performance over time. However, this design lacks the use of control subjects and randomization of participants into different treatment groups.

Ciucci, Barkmeier-Kraemer and Sherman (2008) examined the effects of STN DBS on the oral and pharyngeal stages of deglutition in 12 male and 2 female subjects with PD. The participants received a videofluoroscopic swallowing study (VFSS) that looked at the effects of three independent variables: DBS state (ON/OFF), bolus state (5 or 10 mL water or 7 grams of cracker – in this order) and trial state (1, 2 or 3). Participants were tested following 12 hours without levodopa medication and 1 hour was given between changes in DBS states. Measures of pharyngeal transit time (PTT), maximal hyoid bone excursion (MHE), oral composite score (OCS) and pharyngeal composite score (PCS) were rated. The OCS included: number of swallows per bolus, number of festinated tongue movements, range of tongue movement, oral residue and premature loss of bolus to the pharynx. The PCS included: decreased velar elevation, decreased posterior pharyngeal wall displacement, laryngeal penetration, aspiration, vallecular residue, pyriform sinus residue and upper esophageal sphincter dysfunction.

The researchers used a 2x3x3 ANOVA and a Bonferonni t-test to examine the results. PTT: PTT significantly decreased in the DBS ON state. As the bolus changed and trials progressed the PTT increased. MHE: No significant changes were seen during the DBS and trial states. There was a significant increase as the bolus changed from liquid to solid. OCS: There was no change noted during either DBS state. However as the bolus changed and the trials progressed the OCS significantly decreased. PCS: The PCS significantly increased across all conditions when DBS was ON. Therefore, DBS of the STN demonstrated improvements in the pharyngeal swallow; however the bolus state affected the oral and pharyngeal stages of the swallow independent of the DBS state.

Limitations of this study include the disproportionate gender representation. Thus the findings cannot be generalized as readily to all persons with PD who have DBS. Also random presentation of the bolus state was not considered, making it difficult to determine patterns of interaction. Furthermore, pre-operative measures were not considered and therefore pre and post comparisons could not be made. Although this study has strong inter/intrarater reliability there was no mention of who rated the VFSS results and what their experience level in regards to swallowing parameters was. Another limitation includes not looking at effects on swallowing in comparison to time since implantation as all participants were seen at different times post-implantation. Lastly, the participants were only tested while off their medications, but persons with PD and DBS STN typically require some amount of levodopa medication.

Even with these limitations, the findings provide suggestive evidence due to the detailed analysis and discussion, strong inter/intrarater reliability and the thorough description of methods.

Galazky, Vorwerk and Voges (2010) aimed to evaluate the pharyngeal stage of swallowing in 7 persons with PD using the fiberoptic endoscopic evaluation of swallowing study (FEES). Participants were evaluated in a medication OFF state both prior to surgery and again after surgery while in the DBS ON state. The FEES results were assessed for retention, penetration, aspiration and leaking when considering solid, mashed and liquid food. Of the 7 participants, 71% reported symptoms of dysphagia pre-surgery. Retention was noted in 85% prior to surgery, of which 50% improved during the DBS ON state. Leaking was found in 57% of the participants and all of these participants noted improvements post-surgery. No aspiration was observed pre/post-surgery and penetration was determined to be normal. Overall, swallowing improved to a variable degree with the use of DBS.

Limitations of this study include the unclear gender representation in the small sample size and the unclear distinction of unilateral versus bilateral DBS implantation. Thus this study has limited statistical power and a weak ability to generalize. Also this study does not consider the implication of medication states (ON/OFF), but rather looks at participants only OFF medication. Another limitation of this study is the poor description of the methods and results (i.e. limited information about the bolus conditions, raters, reliability, statistical analysis, measurements taken and data presentation). These limitations make it very difficult to replicate this study. Therefore this study is of equivocal importance in determining the effect of STN DBS on swallowing function.

Kitashima, Umemoto, Tsuboi, Higuchi, Baba and Kikuta (2012) examined the effect of STN DBS on swallowing function in persons with PD. Participants in this study included 8 males and 10 females who had advanced PD and swallowing problems. 10 participants received VFSS pre-operatively in both medication states (ON/OFF). All participants received VFSS 6 months post-operatively with DBS ON and OFF states. Medication state was ON for all post-operative measures. Swallowing function was evaluated using the VF Dysphagia Scale which looked at oropharyngeal
transit time, tongue movement and laryngeal elevation delay time. The Unified Parkinson’s Disease Rating Scale (UPDRS) was also used to evaluate the swallowing function of these participants. The test foods included: 5ml of jelly, honey-thickened water, nectar-thickened water and plain water.

A paired t-test was used to compare oropharyngeal transit time (OTT), speed of tongue movement and laryngeal elevation delay time (LEDT). The Mann-Whitney U-test was used to analyze the UPDRS and VFSS scaled scores. Results indicate there was no difference between VFSS scores pre and post-operatively with DBS ON; however UPDRS scores significantly improved. Although there was no difference between DBS ON vs. OFF states, there was a significant decrease in OTT and LEDT when DBS was ON for jelly and honey-thickened water.

This study has limitations. With a small heterogeneous participant group, these findings cannot be generalized to all persons with PD who have STN DBS. Also, the researchers noted that participants with greater dysphagia symptoms should have been included. The participants in this study presented with limited dysphagia symptoms only. Another limitation of this study is that the DBS states (ON/OFF) were not completed with both medication states (ON/OFF) to determine the interaction of DBS with levodopa medications. As well, this study only allowed 10 minutes between the change in DBS states. Literature suggests this is not enough time (Cooper, McIntyre, Fernandez & Vitek, 2013). There is also no discussion about the inter/intrarater reliability for the neurologist evaluating the VFSS. Lastly, this study did not include randomization of bolus presentation, nor of DBS states which could confound the results.

Beyond these limitations, this study has several strengths. The design and statistical analysis were appropriate for this study. The post-operative measures were all taken at 6 months post-surgery. Certified neurologists completed the evaluations and adequate details were given about participant selection and methods used. Compared to other studies in this critical review it has the largest sample size, but it examined a limited number of parameters and fairly general aspects of the swallowing function to determine the effect of STN DBS on swallowing. Therefore, the findings of this study are suggestive at most.

Kulneff et al. (2012) evaluated the effects of STN DBS on the pharyngeal swallowing function in individuals with PD. The 8 males and 3 females in this study were evaluated using FEES while swallowing, in this order, a thin liquid, semi-viscous liquid, a viscous liquid, a solid and lastly water. Blind raters evaluated the swallowing functions using the Rosenbek’s Penetration-Aspiration Scale, Secretion Severity Scale, and parameters regarding pre-swallow spillage, pharyngeal residue and pharyngeal clearance. Afterwards, the participants completed a self-estimation of their swallowing function. This visual-analogue scale was defined as the percent deterioration of swallowing function (%DSF). Each participant was seen pre-operatively after fasting from their medications for 12 hrs and again while on 1.5 times their ordinary medication dose. Post-operatively participants were seen at 6 months and 12 months. They were tested on ordinary doses of medications in DBS ON and OFF states.

The Friedman repeated measures test by ranks was used to determine differences between the different conditions. The Wilcoxon signed rank test was used for pairwise post hoc comparisons. Significant differences were noted for %DSF when comparing pre-operative conditions (medication ON better than OFF) pre/post-operative conditions (6 months post, DBS ON better than medication OFF pre) and post-operatively (at 6 and 12 months post, DBS ON better than OFF). Across all other measures and conditions there were no significant differences found. Therefore, the subjective measure (%DSF) suggested less deterioration of swallowing with STN DBS. However FEES demonstrated no change in swallowing function due to surgery or STN DBS. Researchers reasoned this discrepancy could be due to changes that were not seen through FEES (i.e. changes in the oral/esophageal stages of swallowing, subtle changes of the swallow or overall improvement in well-being caused by STN DBS).

Limitations of this study include the missing FEES results of 3 participants. Thus the power of this study and generalizability is even less than it could have been. Researchers suggested a larger sample population and greater variation in dysphagia symptoms would strengthen this study. Another limitation of this study is that the DBS states (ON/OFF) were not completed during both medication states (ON/OFF) to determine further interactions and impacts on self-estimation scores and FEES results. Further, the researchers stated a more specific self-estimation tool (i.e. SWAL-QOL) should have been used. As well, participants had either unilateral or bilateral DBS implants, but there was no discussion about how this could impact the results. Lastly, bolus, DBS and medication states were not randomized among participants.

This study has several strengths. This is 1 of 2 studies in this critical review that compared subjective and objective measures and that looked at short-term and long-term time frames post-operatively. Overall this
study’s findings are compelling due to its statistical analysis, presentation of results, discussion of the strengths and weaknesses of the findings, and strong inter/intrarater reliability.

Lengerer, Kipping, Rommel, Weiss, Breit, Gasser and Wachter (2012) retrospectively examined pre and post-operative STN DBS VFSS of 7 female and 11 male individuals with idiopathic PD (according to the British Bank criteria). Pre-operatively no participants reported any signs of dysphagia. VFSS records include examination of 3 consistencies (viscous, fluid and solid) and 3 conditions (pre-operatively, 20 month post-operatively DBS ON and 20 months post-operatively DBS OFF). The participants took their ordinary doses of medications for each condition. There was 10 minutes between DBS ON and OFF states during post-operative examinations. Participants with the most affected deglutition (7/18 considered to have mild impairment) were isolated to further explore the effects of DBS on the severity of the deglutition impairment.

T-tests were used to compare clinical parameters in between groups or conditions. Further the Friedman test for non-parametric data in SPSS with alpha <0.05 compared pre-surgery and post-surgery DBS ON and OFF. Significant results were examined using post hoc pairwise comparison using sign test for the qualitative data and the Wilcoxon tests for the quantitative measures. Qualitative measures were gathered with the New Zealand Index of Multidisciplinary Evaluation of Swallowing (NZIMES). On a scale of 0 (no impairment) to 4 (profound impairment) it examined lingual control, palatal closure, position of bolus at onset of swallow, relative timing of onset of swallow, velopharyngeal closure, pharyngeal contraction/bolus propulsion, laryngeal excursion, bolus propulsion through UES, clearance of pyriform sinus residual, upper esophageal parameters, aspiration/penetration and airway reaction. Researchers found across all three conditions there were no clinically relevant signs of dysphagia. A significant (p=0.012), but marginal decrease of NZIMES scores for pharyngeal contraction and bolus propulsion were seen between pre-operative and post-operative DBS OFF. No significant differences were seen for the subgroup of participants with mild deglutition.

Quantitative measures were evaluated with the Logemann-MBS parameters. The oral, pharyngeal, laryngeal and velar timing parameters were determined by the number of images from an acquisition rate of 15/s. MHE was determined with a computer program (Magic Web). With DBS ON, findings suggested a significant decrease of the pharyngeal delay time (PDT) (up to 70%), PTT (16%), pharyngeal response time (PRT) (18%) and the cricopharyngeal opening duration (CPOD) (21%) when compared to the pre-operative and post-operative DBS OFF conditions. This difference was seen more prominently in the pre-operative condition in fluid consistency. The subgroup of participants with mild deglutition demonstrated a significant decrease of PRT only (8%) with DBS ON compared to pre-operative and DBS OFF conditions.

Overall, the findings of this study demonstrate no clinically relevant changes in deglutition after STN DBS in PD persons without pre-existing deglutition with a 20 month follow-up.

Although this study has the largest sample size of all studies in this critical review, it still has a small sample size. Thus generalizability is difficult. Another limitation of this study is that it was completed retrospectively and therefore VFSS results were only recorded at 15/s rather than the standard 30/s that is suggested for scientific approaches. This also means bolus presentation and DBS conditions could not be randomized among participants. Also, the VFSS recordings only allowed 10 minutes between DBS ON and OFF states, which is too short for the effect of DBS to fully subside (Cooper, et al., 2013). Furthermore, the interaction of both medication states on deglutition was not included and therefore it is difficult to know if and what the possible interaction between medication and DBS might be. Lastly, this study only included participants who presented with very mild deglutition issues.

Despite these limitations, this study used blind raters to evaluate the VFSS. The researchers also expressed and discussed the limitations of this study thoroughly and provided a detailed description of their analysis. Additionally, this study further explored the effects of DBS on severity of deglutition by subdividing the participants by their degree of deglutition impairment. Overall, this study provides suggestive evidence that STN DBS has a small positive impact on swallowing in persons with PD.

Silbergleit, Lewitt, Junn, Schultz, Collins, Beardsley and Schwalb (2012) compared dysphagia before and after STN DBS surgery in 2 females and 12 males with PD. Participants had to be Hoehn and Yahr stage > || and score >30 on the UPDRS Part 3. Participants completed a VFSS within 1 month prior to DBS surgery and again 3 and 12 months post-surgery. During the VFSS, participants had to complete 3 trials sitting upright and swallowing 10 cc of thin liquid by cup, 10 cc thick liquid by cup, 1 tsp vanilla pudding and ¼ of a graham cracker. The first trial followed a 12hr fast from medications and the second and third trials occurred 30
minutes after medication administration. During post-operative testing, participants did as described above, however DBS ON and OFF states were introduced for each trial as well (with 15 minutes allowed between DBS changes). Swallows were judged by a blinded diagnostic radiologist and two blinded speech language pathologists. They looked for the presence or absence of impaired oral preparation, delayed oral phase, delayed swallowing response, reduced pharyngeal contractions, laryngeal vestibule penetration, tracheal aspiration with cough and tracheal aspiration without cough (scores between 0-3 for each item).

Within each consistency of swallow material, t-tests were used to determine the differences between times and between DBS/medication states. Results were not included for laryngeal vestibule penetration, tracheal aspiration with cough and tracheal aspiration without cough because few participants experienced these. Evaluation of impaired oral preparation, delayed oral phase, delayed swallowing response and reduced pharyngeal contractions found there was a trend towards higher mean responses at 12 months post-operative compared with baseline and 3 months post-operative. STN DBS may improve oropharyngeal coordination with solid boluses as well as oral preparation of thin liquids 12 months after surgery (DBS OFF/medication OFF).

Participants also completed the Dysphagia Handicap Index (DHI) after each VFSS. The DHI included a physical, functional, emotional, total and patient reported severity score. Trends towards improvement were seen in the emotional and functional subscales and the total score. These trends became significant improvements after 12 months post-operative.

Limitations of this study include unequal gender distribution that is greater than the 1.5M:1F ratio typically found in PD. These results have less power and are less generalizable to the female population. Another limitation is the small time given between switching DBS ON/OFF states. Some literature suggests 15 minutes is not adequate to see complete washout of DBS ON effects (Cooper, et al., 2013). Lastly, this study did not randomize the order or conditions of the trials and there was no discussion of randomized presentation of swallow material.

Despite these limitations, this study provided sufficient detail to allow for replication. There was a very specific selection criteria for the PD participants. In addition, this was the only study to compare DBS ON/OFF states and medication ON/OFF states together. It has a relatively large sample size and is 1 of 2 studies that compare subjective and objective measures. Inter/intrarater reliability was strong (Cohen’s kappa analysis revealed 80%-100%). Overall, this study provides compelling evidence that there is a trend towards swallowing improvement following STN DBS.

Case Report
Asahi, Inoue, Hayashi, Araki and Endo (2011) examined the alleviation of dysphagia following STN DBS in a 43-year-old man with PD. He had pronounced swallowing challenges before the DBS surgery and was given a PEG to decrease his risk of developing aspiration pneumonia. Pre-operative VFSS demonstrated the participant could only swallow small quantities of material, there was pooling in the oral cavity, valleculae and pyriform sinuses, there was delayed laryngeal elevation and there was insufficient upper esophageal sphincter (UES) opening. The participant could only swallow a medium the consistency of yogurt. The patient had 31/58 on the UPDRS in the medication ON/OFF state respectively. Post-operative (3 years) VFSS examination demonstrated a noticeably improved swallow with the bolus moving smoothly into the esophagus and the participant was able to eat anything he wanted. The participant had 11/17 on the UPDRS in the medication ON/OFF state respectively.

This case report included an appropriate description of the participant and his presenting symptoms. Compared to other studies, this case report looks at a patient with PD who presented with severe dysphagia before STN DBS. However, limitations of this case report include inadequate description of methods (i.e. how VFSS was rated and by who), and a sample size of one, making it difficult to generalize or replicate this study. Overall, this study provided equivocal evidence that STN DBS improves dysphagia up to three years post-DBS.

Fagbami et al. (2011) examined stridor and dysphagia as a result of STN DBS in a 74-year-old man with refractory PD (14 years post onset). He presented with an 8 month history of paroxysmal, non-productive cough that became acutely worse following DBS adjustments. He also noted shortness of breath and a FEES evaluation identified aspiration of thin liquids. Tests were repeated with the DBS OFF. Cough and respiratory symptoms immediately resolved and no aspiration was noted. The researchers suggest that although there is improvement in transit time with DBS, there is no improvement in the oral stage of deglutition due to DBS.

This case report included an appropriate description of the participant. A strong discussion rationalizing the results strengthened the validity. However, the case report did not have a detailed description of the methods.
and the findings are based on one participant and therefore difficult to generalize. Furthermore, Cooper, et al. (2013) suggested once DBS is turned off there is a washout period. This case report suggests the participant noticed immediate improvements when his DBS was turned off. Greater detail in the types of improvements and a definition of immediate would strengthen this case report. Overall, this study provides suggestive evidence that STN DBS has negative effects on swallowing in persons with refractory PD.

Discussion

Overall, the results of this critical review suggest that the effects of STN DBS on swallowing in persons with PD are positive, but limited. The evidence from these 8 studies needs to be interpreted with some caution due to the:

- **a) small sample sizes:** Given the nature of the area being studied small sample sizes are understandable and most studies took this into consideration; however as STN DBS is increasing in use for treating persons with PD, it is suggestive studies with larger samples be completed.
- **b) inconsistent findings:** Of the 8 studies, 5 suggested there was an improvement seen in the swallowing function following STN DBS, 2 suggested no change and 1 suggested a negative impact on swallowing function following STN DBS.
- **c) large range of improvements seen:** Of the 6 studies that suggested an improvement in swallowing function following STN DBS, 2 suggested an overall improvement, 2 indicated the pharyngeal swallow improved and 2 suggested the oral swallow improved.

Studies only including an instrumental swallowing assessment were included in this critical review making it easier to compare and contrast the findings of each study. However each study chose to evaluate this instrumental assessment in a different manner. The different measurements made included: oral preparation, transit time, residue, number of swallows per bolus, tongue movement and control, spillage/leakage, velar/laryngeal/hyoid bone elevation, posterior pharyngeal wall movement, penetration, aspiration, UES function, position/propulsion of bolus throughout swallow, timing of swallow and airway reaction. Several studies also included specific rating scales, which included: Rosenbek’s Penetration-Aspiration Scale, Secretion Severity Scale, New Zealand Index of Multidisciplinary Evaluation of Swallowing (NZIMES) and Logemann-MBS parameters.

Although some studies had measures that overlapped, no studies replicated the exact same results for the same measure. The only exception to this was that 2 studies indicated an improved pharyngeal transit time following STN DBS. Subjective (self-report) measures were taken in 2 of the studies and these measures were consistent throughout – persons with PD who were given STN DBS felt like their swallowing had improved. This was especially interesting when no objective improvements were found.

Following this critical review, it is suggested that further studies be completed to look at the effect of STN DBS on swallowing function in persons with PD. These studies should include:

- a) Larger sample sizes
- b) Longitudinal studies to see long-term effects
- c) Patient self-ratings, clinical ratings, and physical measures of swallowing function
- d) A larger range of dysphagia severity among participants

Conclusion

While STN DBS may be beneficial for persons with PD, positive outcomes for dysphagia are possible but guarded. Although most studies reveal improvements in swallowing functions following STN DBS, some do not.

Clinical Implications

The results suggest that STN DBS is generally associated with small improvements in swallowing functions. Such evidence could have valuable clinical implications for Speech Language Pathologists (SLPs). As more knowledge is gathered about the effects of STN DBS on swallowing function in persons with PD, it may be possible to use STN DBS as an intervention for dysphagia. Understanding the diverse outcomes of STN DBS on swallowing will allow SLPs to better assess and treat the patient following the DBS surgery.

References


