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Review

Swallowing and deep brain stimulation in Parkinson's disease: A systematic review

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ABSTRACT

The purpose of this review is to assess the current state of the literature on the topic of deep brain stimulation (DBS) and its effects on swallowing function in Parkinson's disease (PD). Pubmed, Cochrane review, and web of science searches were completed on all articles addressing DBS that contained a swallowing outcome measure. Outcome measures included the penetration/aspiration scale, pharyngeal transit time, oropharyngeal residue, drooling, aspiration pneumonia, death, hyolaryngeal excursion, epiglottic inversion, UPDRS scores, and presence of coughing/throat clearing during meals. The search identified 13 studies specifically addressing the effects of DBS on swallowing. Critical assessment of the 13 identified peer-reviewed publications revealed nine studies employing an experimental design, (e.g. "on" vs. "off", pre- vs. post-DBS) and four case reports. None of the nine experimental studies were found to identify *clinically significant* improvement or decline in swallowing function with DBS. Despite these findings, several common threads were identified across experimental studies and will be examined in this review. Additionally, available data demonstrate that, although subthalamic nucleus (STN) stimulation has been considered to cause more impairment to swallowing function than globus pallidus internus (GPi) stimulation, there are no experimental studies directly comparing swallowing function in STN vs. GPi. Moreover, there has been no comparison of unilateral vs. bilateral DBS surgery and the coincident effects on swallowing function. This review includes a critical analysis of all experimental studies and discusses methodological issues that should be addressed in future studies.

1. Introduction

Deep brain stimulation (DBS) is a common treatment modality for individuals with advanced Parkinson's disease (PD) who have become refractory to oral medications [1–3]. It is particularly effective against motor fluctuations and tremor. The procedure involves placement of quadripolar electrical leads through a trajectory that traverses the frontal lobe and extends into the deep structures of the basal ganglia, specifically the subthalamic nucleus (STN), globus pallidus internus (GPi), or thalamus ventralis intermedius nucleus (VIM) [1,4,5]. Unilateral or bilateral leads can be implanted to deliver continuous electrical impulses of variable intensity to the STN, GPi, or VIM regions. Following optimal lead implantation, programming, and medication adjustments, DBS effectively ameliorates motor fluctuations, dyskinesia, and medication refractory tremor [3,6,7]. In some cases there may also be a concomitant medication reduction.

DBS implantation, like any surgery, is associated with adverse events and complications which can be acute and/or long-term. As will be highlighted in this review, most studies reporting negative effects of DBS on swallowing are not experimental studies and do not test changes in swallowing as a function specifically of DBS. Instead, these findings have been extrapolated from case reports or from larger, single or multi-center longitudinal studies where aspiration pneumonia, percutaneous gastrostomy (PEG) tube placement, and drooling were listed among other reported complications and/or adverse events. Reports of swallowing-related adverse events following STN DBS vary. There are some reports of minimal swallowing-related adverse events where, for example, only one or two study participants developed dysphagia or

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aspiration pneumonia post-STN DBS implantation [8–14]. Other studies have observed the occurrence of more frequent swallowing specific adverse events with 15% or more of the study population developing dysphagia post-STN DBS [15–19]. Similarly, there are varied reports of adverse events when comparing STN and GPi targets for DBS in PD. Some have reported more dysphagia-related adverse events with STN DBS [14] and others have alternatively reported more dysphagia related adverse events with GPi DBS [19].

Dysphagia, or disordered swallowing, is an inevitable result of the disease progression in PD [20]. Aspiration pneumonia secondary to dysphagia is a leading cause of death in PD [21–23]. A limited amount of literature exists on the potential effects of DBS on swallowing function in PD. Within the available studies, there has been little consensus and conflicting reports as to whether swallowing function improves or declines following implantation. Therefore, research detailing the specific impact of DBS on swallowing function is both timely and of critical importance. The purpose of this manuscript is to critically review the current literature (published in English) on DBS and swallowing function in PD.

2. Methods

A Pubmed, Cochrane review, and Web of Science search of all available DBS studies which included a swallowing related outcome was completed. Selected swallowing related outcomes included: the penetration/aspiration scale, pharyngeal transit time, pre-swallow spill, oropharyngeal residue, drooling, aspiration pneumonia, death, hyolaryngeal excursion, swallowing severity score, epiglottic inversion, Unified Parkinson's disease rating scale (UPDRS) scores, and presence of coughing/throat clearing during meals. The six search words included were: DBS, deglutition, dysphagia, swallow, aspiration pneumonia, and Parkinson's disease (disorder). Ethical and IRB approval was waived for completion of this review article.

Once the studies were identified, they were critically assessed for: 1) presence of an experimental design with proper control of extraneous variables confounding effects of DBS on swallowing function, 2) presence of clinically relevant findings based on inclusion of proper outcome measures and robustness of results, and 3) contribution of the study to the body of literature on swallowing in DBS.

3. Results

The search identified 13 studies specifically addressing the effects of DBS on swallowing. Critical assessment of the 13 identified peer-reviewed publications revealed nine studies employing an experimental design, (e.g. "on" vs. "off", pre- vs. post-DBS) [5,24–31] and four case reports [32–35]. None of the nine experimental studies were found to identify *clinically significant* improvement or decline in swallowing function with DBS (Table 1). To follow, we will first present a brief overview of findings from case reports describing swallowing changes in patients post-DBS. We will then present the experimental studies in chronological order, providing a critical analysis of the methods and results, and highlighting the contributions of each experimental study to the body of literature on DBS and swallowing.

4. Case reports

Kataoka and colleagues [33] reported the case of an 87-year-old man with PD who underwent bilateral STN DBS implantation, requiring lead revision one month post-surgery. Following this surgery, the patient developed hallucinations, sleep apnea, stridor, dyspnea, and increased walking difficulty. Due to respiratory distress, a fiberoptic endoscopic evaluation of swallowing (FEES) was performed and revealed a rigid epiglottis that remained fixed during breathing and swallowing. By manipulating STN stimulator settings, the researchers discovered that the rigidity of the epiglottis was aggravated by increasing the voltage of stimulation, and it was relieved by decreasing the voltage.

A case study reported by Allert and colleagues [34] described a woman with a history of PD and oculo-pharyngeal muscle dystrophy who they followed for several years and who at the age of 67 years was first considered for DBS surgery. At that time she was reporting significant dysphagia with a 7 kg weight loss. More specifically, she had pharyngeal residue, evidence of choking, and the need for repeated swallows. Given her high aspiration risk, a PEG tube was placed. One month following STN DBS surgery a FEES was completed which revealed severe pharyngeal residue with saliva, puree, and solid consistencies, but no aspiration or penetration. The PEG tube was removed nine months post-DBS. As time went on the patient's swallowing continued to be impaired, but she reported that it was better than before DBS. Despite this claim, she continued to lose weight and the PEG was re-inserted at 21 months post-surgery.

Fagbami and Donato [32] evaluated a 74-year-old man with PD post-bilateral STN DBS implantation who subsequently reported a weak cough, stridor, tachypnea, and aspiration. His swallowing function was assessed "on" stimulation during videofluoroscopic (VFS) examination and revealed aspiration of thin liquids. VFS is considered by most speech-language pathologists to be the gold standard for visualization of oropharyngeal swallowing function. Following a 1 h washout period in the stimulation "off" condition, aspiration was not observed, and the patient reported a subjective 80% improvement of cough and swallowing function. Similarly, he experienced a 15% improvement in pulmonary function testing with stimulation in the "off" condition. The researchers postulated that the marked improvement with DBS "off" may have resulted from dystonia or dyskinesia of the upper airway muscles, secondary to DBS stimulation.

Finally, Asahi et al. [35] published a case study of a 43-year-old male with young onset PD and a history of severe dysphagia, who received bilateral STN DBS implantation. Prior to DBS surgery, a PEG tube was placed secondary to aspiration pneumonia. The patient was evaluated pre- and post-DBS surgery using VFS while swallowing a pudding consistency (yogurt). The baseline evaluation revealed piecemeal deglutition, oral residue, residue in the vallecculae and pyriform sinuses, delayed hyolaryngeal excursion, aspiration, coughing, and inadequate cricopharyngeal opening. The evaluation three years post-DBS surgery revealed improved swallowing function as the "contrast medium smoothly moved to the esophagus," and the patient was consuming "the foods of his choosing." No post-DBS information regarding PEG tube status or any other swallowing outcomes was provided.

5. Experimental studies

Zibetti and colleagues [30] prospectively compared the motor and non-motor symptoms of 36 participants with PD pre- and post-bilateral STN DBS implantation. The swallowing-specific outcome variables analyzed were the UPDRS item six (salivation) and item seven (swallowing) obtained from clinical neurological evaluations. Baseline evaluations were conducted pre-DBS surgery both "on" and "off" dopamine medication (where a 12 h washout period was required for "off" medication testing). The participants were then tested again 12 and 24 months post-DBS "on" STN stimulation and "on" dopamine medication. Results revealed that pharmacological treatment significantly improved salivation and swallowing in the pre-DBS condition. This improvement was maintained when comparing UPDRS scores pre-DBS "off" dopaminergic therapy to UPDRS scores "on" STN stimulation and "on" dopaminergic therapy. The authors highlighted that post-DBS, participants required reduced levels of dopaminergic therapy. Participants were not tested in the "off" medication condition following STN DBS. Because swallowing remained better than baseline after DBS and with reduced pharmacological intervention, Zibetti and colleagues postulated that DBS may have improved bradykinesia at the pharyngeal level. Although the authors utilized a reasonably sized cohort ($n = 36$), appropriate medication wash-out periods (12 h),