Deep brain stimulation – effects on swallowing function in Parkinson's disease.

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Word count: 1971 words

Abstract

Objective

In patients with Parkinson's disease (PD), deep brain stimulation of the subthalamic nucleus (STN DBS) is well recognized in improving limb function, but the outcome on swallowing function has rarely been studied. The aim of this work was to evaluate the effect of STN DBS on pharyngeal swallowing function in PD patients using self-estimation and fiberoptic endoscopic evaluation of swallowing.

Methods

Eleven patients (aged 41-72, median 61 years) were evaluated preoperatively and at 6 and 12 months after STN DBS surgery. All patients were evaluated with self-estimation on a visual analogue scale and eight of them with a fiberoptic endoscopic examination with a predefined swallowing protocol including Rosenbek's Penetration-Aspiration Scale, Secretion Severity Scale, preswallow spillage, pharyngeal residue and pharyngeal clearance.

Results

The self-assessments of swallowing function revealed a swallowing improvement with STN DBS stimulation whereas the data from the swallowing protocol did not show any significant effect of the STN DBS treatment itself. The prevalence of aspiration was not affected by the surgery.

Conclusions

The results show that swallowing function was neither improved nor negatively affected by STN DBS and the risk of aspiration did not increase. Self-estimation of swallowing function showed an improvement due to stimulation.

Key words: Deep brain stimulation, subthalamic nucleus, dysphagia, Parkinson's disease, FEES, swallowing function, aspiration, L-dopa.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease mainly affecting the dopamine producing cells in the substantia nigra pars compacta (1,2). The prevalence is about 150-200/100 000 (3). The disease is clinically characterized by bradykinesia, tremor at rest, rigidity, and postural instability but also subcortical dementia, depression, autonomic dysfunctions, sialorrhea and dysphagia (2,4). Pneumonia is a common cause of death in PD patients (5), and it has been concluded that aspiration pneumonias yield the highest mortality risk of all co-morbidities (6).

Swallowing dysfunction in PD patients covers the clinical area from mild dysphagia to life threatening aspiration-induced pneumonias (7–9). The cause of swallowing dysfunction is often not known for PD patients, but a dysfunctional regulation pattern in the medulla oblongata (10) has been speculated (11). Studies of dysphagia have shown inconsistencies between objective-, and self-estimated swallowing dysfunction with low numbers of deglutition abnormalities when self-reported data are used (12–15).

Swallowing can be divided into four phases: pre-oral, oral, pharyngeal and esophageal phases. The oral and pre-oral phases are voluntarily controlled; the pharyngeal phase can be initiated either voluntarily or by reflexes, whereas the esophageal phase is under autonomic control. Abnormalities reported in the oral phase include labial bolus leakage, lingual tremor, poor bolus formation and control, resulting in slowed oral transit time (OTT) and preswallow spillage (5,11,14,15). Pharyngeal abnormalities are stated as penetration and aspiration of bolus, delayed initiation of the swallowing reflex, slowed pharyngeal transit time (PTT), and retention in the valleculae and pyriform sinuses (5,11,15). Penetration is defined as bolus entering the airway, remaining above the vocal folds, whereas aspiration is defined as bolus entering the airway and passing below the vocal folds (16).

Deep brain stimulation (DBS) is an established treatment for PD and the subthalamic nucleus (STN) is currently the target of choice. The efficacy of DBS on motor symptoms has been documented in several studies (17-21). Few studies have however focused on DBS and swallowing function, and no longitudinal study objectively monitoring swallowing function has been conducted. In one study video fluoroscopy was used to determine swallowing function three months postoperatively, comparing stimulation on and off in a medication on state. Stimulation seemed to improve some aspects of

pharyngeal swallowing while the oral stage was unaffected (22). In other reports, the effects of DBS surgery on swallowing functionality varies from unchanged (23,24), to a clear-cut deterioration (25). Dysphagia has further been reported as a rare complication after STN DBS, which in some of the cases was clearly related to the stimulation (26–29). The studies mentioned above did not examine swallowing function objectively in combination with self-estimated evaluation. The purpose of this study was to examine the effect of STN DBS surgery on pharyngeal swallowing function in PD patients using self-estimation and fiber optic endoscopic evaluation of swallowing (FEES).

Materials and methods

Participants

In this study 11 consecutive patients (8 males), median age 61 years (range 41 - 72); median duration of disease 6.5 years (range 1-13), were selected on clinical grounds for STN DBS (30). Data from FEES was analyzed for 8 of the 11 patients because FEES video material was not available for three of them. Self-estimation data was analyzed for all of the patients (Table 1). Main indication for surgery, information about unilateral or bilateral stimulation and medications are presented in Table 1. None of the patients used anticholinergic medications. Six patients were implanted bilaterally. One patient had unilateral STN DBS before inclusion in the study, and was after implantation of the second electrode included in the bilateral group. A perioperative CT fused with the preoperative MRI confirmed correct location of the electrodes in all patients. The general motor function was recorded according to Unified Parkinson's Disease Rating Scale – motor part (UPDRS-III). All patients gave their written informed consent after receiving information on the details of the study according to the Helsinki declaration. The study was approved by the Regional Ethical Review Board in Umeå (08-0934M).

Testing of the patients

Patients were evaluated before and at six and 12 months after STN DBS surgery. The preoperative evaluation was performed in a medication off state after an abstinence period of about 12 hours, while the evaluation in the medication on state was done with 1.5 times the ordinary dose of L-dopa equivalents. The postoperative evaluations were performed

within the optimal time in the patient's usual medication cycle, with stimulation on and off (after 60 min of stimulation on and off, respectively) (Table 2).

It would have been desirable to also examine the patients in "medication off, stimulation off". However, this design was not considered ethically justifiable, with respect to the high levels of discomfort associated with absence of stimulation and with consideration to the number of other tests performed on these patients in the off/off condition.

Evaluation of swallowing

The FEES were conducted and recorded using an Olympus ENF P4 transnasal flexible endoscope and a Wolf endocam 5502. The patients were asked to swallow one solid and four different liquid consistencies, all colored with green dye. Each bolus size was estimated to one table spoonful (10 ml) and the consistencies were water, thin liquid (5 ml of jellification powder in 500 ml of water), semi-viscous (10 ml of powder/500 ml water), and viscous liquid (15 ml of powder/500 ml water). The solid test food was a biscuit with a smear of the thickest liquid consistency on top. The order of bolus intake was the same for all examinations, starting with the thin liquid, going towards thicker and solid consistencies, and finishing with the water.

After the test meal, the patients were asked to evaluate their swallowing function, using a 100 mm linear visual analogue scale. One of the endpoints of the scale represented 100% functional swallowing while the other represented a total loss of swallowing function. The distance in mm from the maximum point to the patient's mark was defined as percentage deterioration of swallowing function (%DSF). This measure was used as the patients' subjective perception of their swallowing function.

The endoscope recordings were de-identified and randomly ordered and the swallowing function was evaluated according to a predefined protocol. Rosenbek's Penetration-Aspiration Scale (16) (range 1-8 points), Secretion Severity Scale (31) (range 0-3) and parameters regarding preswallow spillage, pharyngeal residue and pharyngeal clearance were included in the protocol (Table 3). There had to be a clearly visible pool of bolus in order to account for residual, spillage or defective clearance. All patients underwent the test meal but the FEES video material from three patients was not available when the data analysis was done.

Twelve percent of the data was judged for intra-rater reliability and 16% was judged for inter-rater reliability. If both evaluators for each parameter gave the same scores, they were considered to agree. Both inter and intra reliability was 95% and all parameters had similar levels of agreement.

Data Analysis

A mean score from the five different food consistencies was calculated for each and one of the swallowing parameters, in order to enable statistical comparisons concerning possible effects of testing condition. The scores from the swallowing parameters were transformed so that the lowest score was always 0. E.g. the minimum transformed Penetration/Aspiration score was 0p when there was no penetration or aspiration for any consistency. The maximum transformed score was 7p. Secretion Scale ranged between 0-3p and pharyngeal residue, preswallow spillage and clearance between 0-1p.

Friedman repeated measures test by ranks was used for statistical analyses of differences between conditions. Wilcoxon signed rank test was used for pair wise post-hoc testing. A p-value <0.05 was considered as statistically significant.

Results

Individual scores for %DSF, Penetration/Aspiration and UPDRS III are seen in Table 4. Group medians and means for the different swallowing parameters and the results from the Friedman test by rank are seen in Table 5. Post-hoc comparisons for the %DSF are seen in Table 6.

Preoperatively the subjective %DSF score revealed significantly improved swallowing function with test dose of L-dopa medication compared to medication off condition ($z = -2.50$, $p=0.01$). The swallowing parameters from the FEES including Penetration/Aspiration, Secretions scale, pharyngeal residual, preswallow spillage and clearance showed no significant differences between the test dose of L-dopa and the medication off condition ($p>.05$).

Preoperative and postoperative comparison regarding %DSF between medication off and six months postoperative stimulation on showed statistically significant improvement in the subjective evaluation of the swallowing function after DBS surgery ($z= -2.49$, $p= .01$). No other significant %DSF differences between pre- and postoperative conditions were

found, $p>.05$. There were no significant differences between test dose of L-dopa and stimulation on at six and 12 months, $p>.05$. Regarding the swallowing parameters from the FEES no significant differences between pre- and postoperative conditions were found, $p>.05$.

Postoperatively at six months as well as at 12 months the subjective %DSF score showed significantly improved swallowing function with stimulation on compared to stimulation off, ($z= -2.54$, $p=0.01$). There were no clear-cut differences between stimulation on and stimulation off at six and 12 months for any of the swallowing parameters from the FEES, $p<.05$.

Discussion

The aim of this study was to examine the effect of STN DBS surgery on swallowing function using self-estimation and FEES. The results show that the effect of the STN DBS differs between the subjective measure and the swallowing parameters. The self-estimations showed that the PD patients evaluated their swallowing function as improved by STN DBS, when comparing preoperative to postoperative function and stimulation on and off postoperatively. However, the results from the FEES showed that neither the STN DBS stimulation nor the surgery itself seemed to have a negative or positive effect on the Penetration/Aspiration score, Secretion Scale score, the pharyngeal residue, the preswallow spillage or the clearance. This is of importance as dysphagia has been reported as an adverse side effect of DBS (26–29). STN DBS has further been reported to improve some aspects of the pharyngeal swallowing function (22). Ciucci et al used video fluoroscopy to examine swallowing function. Our study did not show any improvement regarding the FEES parameters and the findings are similar to the results from our parallel study including patients with caudal Zona Incerta DBS (24). However, neither the discrepancy between the self-estimation and the FEES parameters nor the subjective improvements was seen in the caudal Zona Incerta study.

Discrepancy between self-perception and objective findings regarding swallowing function has been seen in dysphagic patients (8,14,15,32,33). In this study the discrepancy could have several explanations. A possible explanation could be that the improvements reported are manifested in the oral or esophageal phase of the swallowing and hence not examined in the FEES of the pharyngeal swallowing phase. Another explanation would be that the

improvements are subtle and only recognized over time. A FEES including just a couple of boluses might not be enough to discover such a subtle improvement. A third explanation might be an overall improvement in well being brought on by the STN DBS that could affect the experience of the swallowing function.

A visual analogue scale has been shown to be a valid tool to examine swallowing function (34), but to further examine the subjective improvement of DBS a more specific self-assessment instrument or questionnaire would be suitable. SWAL-QOL was not available in Swedish at the commencement of the study (35).

The number of patients included is relatively small, especially in the FEES, and this has to be taken in to consideration when interpreting the results. The findings need to be confirmed in larger materials. One should also consider that all postoperative examinations were done in a medication on state.

Taken together the results show that the swallowing function was not negatively affected by STN DBS. It also showed that neither the DBS nor the surgery itself increased the risk for aspiration in this sample. Self-assessments indicated an improvement in subjective swallowing function due to the stimulation.

Acknowledgements

The concerning patient handling by Anna Fredricks and skilful technical assistance of Anders Asplund is gratefully acknowledged. The project was supported by grants from Magnus Bergvall's Foundation and the Parkinson Foundation in Sweden. A visiting professorship at the Rehabilitation Research Chair, King Saud University, Riyadh, Saudi Arabia, to one of the authors (E.N.) is gratefully acknowledged.

Full Financial Disclosures of all Authors for the Past Year:

Linda Kulneff: none

Stina Sundstedt: none

Katarina Olofsson: none

Jan van Doorn: none

Dr Linder received lecture honoraria from Medtronic Inc., Orion Pharma, UCB Pharma, Abbott and Nordic Infu Care.

Dr Erik Nordh received lecture honoraria from IPSEN and Pfizer.

Patric Blomstedt: none

The authors report no potential conflicts of interest.

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Tables

Table 1 Stimulation, medication and main indication of surgery

Patient	Stimulation	Indication for surgery	Medication
1	*unilateral, left*	*tremor right hand*	*L-dopa,*
2	*bilateral*	*tremor, on-off fluctuations, dyskinesia*	*L-dopa, pramipexole, entacapone*
3	*unilateral, left*	*tremor right side*	*L-dopa, pramipexole,*
4	*bilateral*	*wearing-off, dyskinesias*	*L-dopa, pramipexole, amantadine*
5	*bilateral*	*tremor bilteral*	*L-dopa, pramipexole, entacapone*
6	*unilateral, right*	*tremor bilteral*	*L-dopa, pramipexole, selegelin*
7	*bilateral*	*on-off fluctuations*	*L-dopa, pramipexole, entacapone*
8	*unilateral, left*	*tremor right side, wearing-off*	*L-dopa, pramipexole*
9*	*unilateral, left*	*tremor right side*	*L-dopa, pramipexole*
10*	*bilateral*	*tremor bilateral*	*L-dopa, entacapone*
11*	*bilateral*	*on-off fluctuations, dyskinesia*	*L-dopa, pramipexole, entacapone, amantadine*

* Only data from the slef-estimations, no FEES parameters.

Table 2 Testing conditions

Surgical status	Condition	Treatment status
Preoperative	Medication *off* Test dose of L-dopa	Dopaminergic medication witheld for 12 hours or overnight 1,5 hours after a test dose of L-dopa 1,5 times higher than normal
6 months Postoperative	Stimulator *off* Stimulator *on*	Stimulator turned off for 60 min. Patient's ordinary medication. Stimulator turned on for 60 min. Patient's ordinary medication.
12 months Postoperative	Stimulator *off* Stimulator *on*	Stimulator turned off for 60 min. Patient's ordinary medication. Stimulator turned on for 60 min. Patient's ordinary medication.

Table 3 Evaluation of preswallow spillage, pharyngeal residue and pharyngeal clearance

Parameter	Operationalization
Pre- swallow spillage	Green bolus is seen before white-out
Pharyngeal residue	Residue in the sinus piriformis or vallecula
Pharyngeal clearance	No residue after the first deglutition

Table 4 Individual data for %DSF, Penetrattion/Aspiration and UPDRS-III scores

	%DSF						Penetration and aspiration scores						UPDRS-III					
	Preoperative		6m Postoperative		12m Postoperative		Preoperative		6m Postoperative		12m Postoperative		Preoperative		6m Postoperative		12m Postoperative	
Patient	Med off	Test dose L-dopa	Stim off	Stim on	Stim off	Stim on	Med off	Test dose L-dopa	Stim off	Stim on	Stim off	Stim on	Med off	Test dose L-dopa	Stim off	Stim on	Stim off	Stim on
1	25	20	5	16	30	13	2.8	0.0	0.0	0.0	0.2	0.0	31	24	24	12	-	17
2	53	27	46	35	76	65	0.8	0.8	0.8	0.4	3.0	1.2	52	24	-	-	30	20
3	25	28	25	3	8	19	0.0	0.6	0.0	0.0	0.0	0.0	33	16	12	4	11	8
4	32	11	39	23	14	8	0.0	0.4	0.2	0.5	0.0	0.2	39	18	21	17	30	-
5	34	10	3	1	15	11	0.0	0.0	0.0	0.0	0.0	0.0	40	16	6	6	57	38
6	4	2	49	7	6	3	0.0	0.0	0.0	0.0	0.0	0.0	54	37	21	11	34	12
7	26	14	24	10	25	0	0.0	0.0	0.0	0.2	0.0	0.2	32	6	-	-	19	19
8	5	3	3	3	25	8	0.4	0.2	0.0	0.0	0.0	0.0	19	4	-	-	30	12
9	0	0	11	6	52	31	-	-	-	-	-	-	35	22		20	-	21
10	48	38	40	35	44	27	-	-	-	-	-	-	57	36		28	35	14
11	71	55	34	5	19	6	-	-	-	-	-	-	44	21		21	28	21
Mean	**29.4**	**18.9**	**25.36**	**13.1**	**28.5**	**17.4**	**0.5**	**0.2**	**0.1**	**0.1**	**0.4**	**0.2**	**39.6**	**20.4**	**16.8**	**14.9**	**30.4**	**18.2**
Median	**26**	**14**	**25**	**7**	**25**	**11**	**0**	**0**	**0**	**0**	**0**	**0**	**39**	**21**	**21**	**14.5**	**30**	**18**

%DSF= self-reported percentage deterioration of swallowing function

Table 5 Scores from swallowing evaluation and self-reported assessment of swallowing function. Means of the five consistencies. Median, range, mean and standard deviation. Friedman test comparing differences among conditions. The lower scores the better the function.

Median ± Range (Mean ± SD)	**Preoperative**		**6m Postoperative**		**12m Postoperative**		**Friedman test (n=8-11)**		
	Med off	Test dose of L-dopa	Stim off	Stim on	Stim off	Stim on	*N*	*Fr*	*p*
P/A	0.1 ± 0.8 (0.3 ± 0.3)	0.0 ± 2.8 (0.5 ± 1.0)	0.0 ± 0.8 (0.1± 0.3)	0.0 ± 0.5 (0.1 ± 0.2)	0.0 ± 3.0 (0.4 ± 1.1)	0.0 ± 1.2 (0.2 ± 0.4)	8	1.80	*p* =0.88
Phr	0.2 ± 0.6 (0.2± 0.2)	0.0 ± 0.2 (0.1± 0.1)	0.0 ± 1.0 (0.1 ± 0.1)	0.0 ± 0.4 (0.1 ± 0.2)	0.2 ± 0.4 (0.2 ±0.1)	0.1 ± 0.8 (0.2 ± 0.3)	8	7.22	*p* =0.21
PS	0.0 ± 1.0 (0.2 ± 0.4)	0.0 ± 0.8 (0.2 ± 0.4)	0.0 ± 1.0 (0.1 ±0.4)	0.1 ± 0.7 (0.2 ± 0.2)	0.0 ± 1.0 (0.2 ± 0.4)	0.0 ± 1.0 (0.2 ± 0.4)	8	3.63	*p* =0.60
CC	0.0 ± 1.0 (0.1 ± 0.4)	0.0 ± 0.8 (0.1 ± 0.3)	0.0 ± 1.0 (0.2 ± 0.4)	0.1 ± 1.0 (0.1 ± 0.4)	0.0 ± 1.0 (0.1 ± 0.4)	0.0 ± 1.0 (0.1 ± 0.4)	8	3.32	*p* =0.65
SS	0.5 ± 2.0 (0.9 ± 1.0)	0.0 ± 2.0 (0.4 ± 0.7)	0.0 ± 3.0 (0.8 ± 1.2)	0.5 ± 3.0 (1.0 ± 1.2)	1.5 ± 3.0 (1.4 ± 1.3)	0.0 ± 2.0 (0.4 ± 0.7)	8	5.52	*p* =0.36
% DSF	26.0 ± 71.0 (29.4 ± 21.9)	14.0 ± 55.0 (19.8 ±17.7)	25.0 ± 46.0 (25.4 ± 17.6)	7.0 ± 34.0 (13.1 ± 12.6)	25.0 ± 70.0 (28.5 ± 21.2)	11.0 ± 65.0 (17.4 ± 18.5)	11	15.6.0	***p* =0.08**

P/A: Penetration and Aspiration scale, 0-7p. Phr: pharyngeal residual, 0-1p. PS: preswallow spillage, 0-1p. CC: clearance, 0-1p. SS: Secretions scale, 0-3p. %DSF: Self-reported percentage deterioration of swallowing function. 0-100%.

Table 6 Pairwise comparison of subjective scores of the percentage deterioration of swallowing function. Median, range, mean and standard deviation. Preoperatively, 6 months and 12 months after surgery. N=11

			Preoperative		6m Postoperative		12m Postoperative	
			Med off	Med on	Stim off	Stim on	Stim off	Stim on
		Mean ± SD	26.0 ± 71.0	14.0 ± 55.0	25.0 ± 46.0	7.0 ± 34.0	25.0 ± 70.0	11.0 ± 65.0
		Median±range	29.4 ± 21.9	19.8 ±17.7	25.4 ± 17.6	13.1 ± 12.6	28.5 ± 21.2	17.4 ± 18.5
Preop	Med off	26.0 ± 71.0	-					
	Med on	14.0 ± 55.0	p =0.01	-				
6m	Stim off	25.0 ± 46.0	*n.s*	*n.s*	-			
Postop	Stim on	7.0 ± 34.0	p =0.01	*n.s*	p =0.02	-		
12m	Stim off	25.0 ± 70.0	*n.s*	*n.s*	*n.s*	p =0.01	-	
Postop	Stim on	11.0 ± 65.0	*n.s*	*n.s*	*n.s*	*n.s*	p =0.01	-

Value is significant at $P < 0.05$ (two-tailed). Wilcoxon signed rank test. *n.s* : Non significant.