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The effect of subthalamic deep brain stimulation on gastric motility in Parkinson's disease

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ABSTRACT

Objective: Deep brain stimulation of the subthalamic nucleus (STN-DBS) is well established for treating the motor symptoms for advanced Parkinson's disease (PD) but its effects on gastric myoelectrical activity and gastrointestinal symptoms have not been well studied. The aim of this study was to evaluate the effect of STN-DBS on gastric motility using electrogastrography (EGG).

Methods: Twenty patients with PD (5 females, 15 males; mean aged 58.0 ± 9.0 years) who underwent STN-DBS were studied. EGG was performed in fasting and postprandial conditions before STN-DBS and 3 months after the surgery. We also evaluated the frequency and severity of gastrointestinal symptoms based on a structured gastrointestinal dysfunction questionnaire.

Results: After STN-DBS the percentage of normogastria (47.8 ± 20.7 vs 51.3 ± 15.1) and period dominant power (PDP) (11.8 ± 1.2 vs 12.3 ± 0.9) significantly increased, the percentage of arrhythmia decreased compared to the baseline during fasting and postprandial state. Abnormal response to a meal (power ratio of PDP <1 after meal) decreased from 70% to 55% after 3 months follow-up. The abnormal EGG (the percentage of normogastria <70%) decreased in both fasting (from 80% to 65% patients) and postprandial state (from 80% to 60% patients), respectively after the surgery. The most common GI symptoms reported prior to the surgery were constipation 95%, difficulty with defecation 85% and dysphagia 50%. After STN-DBS all gastrointestinal symptoms improved, the greatest improvement was observed in difficulty with defecation.

Conclusion: Our results suggest that STN-DBS improves gastric motility as well as gastrointestinal symptoms in PD. Further studies of gastrointestinal motility in PD are warranted.

1. Introduction

Gastrointestinal (GI) dysfunction is one of the most common non-motor symptom of Parkinson's disease (PD) [1]. The majority of symptoms such as constipation, bloating, early satiety, delayed gastric emptying and abdominal discomfort result from abnormal motility of the GI tract [2,3]. Abnormal gastric motility and delayed gastric emptying occur in early-stage PD even prior to pharmacological treatment [4–7] and increase in the advanced stage of the disease [7]. This argues that disease intrinsic mechanisms are responsible for the disturbed motility [8]. Delayed gastric emptying may lead to erratic absorption of levodopa contributing to abnormal motility and the occurrence of motor fluctuations in advanced stages of PD when the bioavailability of orally administrated drugs is impeded [9]. According to Braak's studies α-synuclein pathology involves several brain regions including dorsal motor nucleus [10] and neurons of the gastric myenteric and submucosal plexus [11].

The presence of α-synuclein deposition at all levels of the gastrointestinal tract and in the dorsal vagal nucleus implicates involvement of the brain and gut, the so-called brain-gut axis [12]. Deep brain stimulation of the subthalamic nucleus (STN-DBS) is well established for treating the motor symptoms for advanced PD but its effects on gastrointestinal dysfunction have not been well

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studied. It has previously been shown that some autonomic function may improve following STN-DBS [13]. A recent study reported improvement in gastric emptying and gastrointestinal function after STN-DBS [14].

EGG is a noninvasive method for the measurement of gastric myoelectrical activity that uses abdominal surface electrodes [15]. The aim of this study was to evaluate gastric motility and the frequency and severity of gastrointestinal symptoms before STN-DBS and after surgery in PD patients.

2. Materials and methods

The study included 20 patients (5 females, 15 males) aged 58.0 ± 9.0 years with PD treated with bilateral STN-DBS at the Department of Neurosurgery Jagiellonian University between 2009 and 2014. Duration of PD was 10.9 ± 4.7 years. The results of EEG assessment were compared with a healthy, asymptomatic, age and gender matched control group (5 females and 15 males, age range 57.4 ± 11years). The inclusion criteria for surgery included diagnosis of PD according to the UK Parkinson's Disease Society Brain Bank Clinical diagnostic criteria [16]: disease duration >5 years, age under 70 years, responsiveness to levodopa and medication – resistant motor fluctuations, dyskinesia or tremor. Exclusion criteria included significant cognitive impairment, psychiatric or behavioral disturbances (score on the Mini-Mental State Examination <24), or significant abnormalities on neuroimaging (MRI). None of the patients had a history of a gastrointestinal or endocrinological disorder known to affect gastric emptying (e.g. gastrointestinal surgery, diabetes mellitus, thyroid disorders). Patients on current or recent (28-day period) pharmacological treatment that could possibly alter gastric motility (apart from dopamimetic antiparkinsonian drugs) were excluded (e.g. anticholinergic drugs, tricyclic antidepressants, antiemetic drugs). The study protocol was approved by the Jagiellonian University Bioethical Committee (no. KBET/240/B/2012). All the subjects included in this study were instructed about its purpose and gave their written consent of participation.

3. Clinical assessment

Evaluation of signs of PD was performed using the motor components of the Unified Parkinson's disease rating scale (UPDRS). Assessment of the motor scale was carried out at baseline (before STN-DBS), both in the 'on' condition with medication, and without medication after withdrawal overnight in the 'off' condition, and for 3 months following the surgery. After the surgery, the motor score was performed in 'off' medication and stimulation 'on' condition. All patients were evaluated by the same movement disorder specialist at baseline and during the 3 month follow-up visit (Table 1). Data concerning gastrointestinal dysfunction were collected from the patients at baseline (before STN-DBS) and for 3 months following the surgery.

Also a structured gastrointestinal dysfunction questionnaire was specifically designed for the study and was used to collect information from patients in order to assess gastrointestinal symptoms (Appendix). We did not use the Non Motor Symptom Scale (NMSS) and the Non Motor Symptoms Questionnaire (NMS QUEST) because one of the aims of our study was to determine the appearance and severity of all gastrointestinal symptoms such as bloating, feeling of fullness in the upper abdomen, difficulty with defecation, rectal burning during or after defecation, heartburn, which are not addressed by the NMSS and NMS QUEST questionnaires [17,18]. In addition the NNMSS and the NMS QUEST questionnaires have not been validated in the Polish population.

The questionnaire used in this study was addressing the following symptoms: (1) dysphagia, (2) sialorrhea, (3) bloating, (4) heartburn, (5) constipation, (6) difficulty with defecation, (7) rectal burning during or after defecation, (8) feeling of fullness in the upper abdomen. Definition of the GI symptoms assessed: dysphagia – difficulty swallowing solids, liquids or saliva, with or without choking, sialorrhea – feeling of excessive saliva in the mouth, bloating and early satiety – postprandial discomfort manifested by sensation of stomach fullness or inability to finish a meal or abdominal distention, heartburn – burning sensation in the chest behind the sternum, usually occurring shortly after eating lasting a few minutes to several hours, constipation – was defined as less than three bowel movements per week, difficulty with defecation – difficulty with the act of defecation, straining and/or sense of incomplete evacuation, rectal burning during or after defecation, feeling of fullness in the upper abdomen – feeling uncomfortably after a meal [3,19].

For each symptom we assessed its presence over the last month. The severity of each of these symptoms was scored (0–4 points) as: none (0), slight (1), mild (2), moderate (3) or severe (4).

4. Surgical procedure

Pre-operative 1.5T MRI (T2. T1 with contrast enhancement) was performed. The targeting of the subthalamic nucleus (STN) was performed on surgical planning workstation (Stealth. Medtronic Inc., Minneapolis, MN) and software (Framelink, Medtronic Inc.). The target site (STN) was identified on MRI with reference to a standard stereotactic atlas and coordinates. On the day of the surgery the RM stereotactic frame was placed on the head of the patient under local anesthesia and CT with contrast enhancement was performed. Fusion of CT and MRI was then performed. Patients received a short-term sedation during drilling of the burr hole and introducing 3–5 microelectrodes. Microelectrode recordings were carried out to identify the neuronal signals of STN. Macrostimulation was t performed to confirm the appropriate location for rigidity, bradykinesia and tremor control and to assess the adverse effects of stimulation. When the best location had been established a permanent electrode (Medtronic 3389, Medtronic Inc) was inserted in the same position. Under general anesthesia an internal pulse generator (IPG) was placed into a subcutaneous pocket in the subclavicular region and connected to the electrode. The next day, CT was performed and IPG was turned on. Implantation of the second electrode and IPG, on the other side of the body, was usually

Table 1
Clinical characteristic of patients before and 3 months after STN-DBS.

	Before STN-DBS	3 months after STN-DBS	Changes (%)	p Wilcoxon's test
Unified Parkinson's disease Rating Scale –III part (points)				
"on"	37.1 ± 6.6	10.4 ± 3.2	78.0	**p < 0.002**
"off"	57.5 ± 7.0	18.5 ± 5.2	67.8	**p < 0.003**
Scale UPDRS II part (points)	17.9 ± 2.6	6.6 ± 3.2	63.1	**p < 0.004**
Scale UPDRS IV part (points)	16.6 ± 2.8	2.3 ± 0.9	86.1	**p < 0.005**
LED (mg/24 h)	1190 ± 416.3	178.6 ± 147.1	85.0	**p < 0.001**

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