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Severe subthalamic stimulation-induced dysarthria alleviated by a novel paradigm: a case report

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Fumin Jia-conception, organization, and execution of research project; writing of the first draft; Yi Guo-implantation of DBS systems; Sen Wan-execution of research project; writing a part of first draft; Luming Li-conception and organization of research project; design; the corresponding author of this article.

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Dear Editor:

High frequency stimulation (HFS) of the subthalamic nucleus (STN) improves Parkinson's disease (PD) motor symptoms, such as bradykinesia, tremor and rigidity [1]. Dysarthria in PD is characterized by monotony of pitch and loudness, imprecise consonants, and a breathy and harsh voice [2], which may be induced or even aggravated by deep brain stimulation (DBS) [3,4]. While previous studies have shown that dysarthria can be alleviated by low-frequency stimulation (LFS) [5,6], this can often lead to the reappearance of motor symptoms over time. Strategy to overcome this clinical problem remains to be developed. Here, we describe the results of a PD patient with dysarthria who received variable frequency stimulation (VFS) i.e. a stimulation pattern of high and low alternating frequencies.

A 37-year-old woman with PD was treated with bilateral deep brain stimulation (DBS) (PINS Medical, Beijing, China) targeting the STN (December 2012). The patient developed parkinsonian motor symptoms in 2002, with the onset of tremor in her right hand, followed by rigidity and bradykinesia. In 2003, she was diagnosed with PD according to the UK Parkinson Disease Brain Bank Criteria.

Over time, her daily dopaminergic medication of levodopa was increased from 250 mg to 500 mg plus 0.375 mg pramipexole. With the development of severe motor fluctuations, DBS was considered.

The patient's motor symptoms were significantly improved following HFS. This was reflected with a reduction of daily levodopa equivalent dose to 125 mg. At 14 months post-surgery, the patient developed strained, strangled, very effortful speech with short maximum phonation time (MPT), which improved OFF stimulation, a phenotype classified as strained voice dysarthria according to Tsuboi et al [7]. Dysarthria was alleviated in both OFF and bipolar stimulation conditions. However, these parameters would lead to the re-appearance of PD motor symptoms. Severe dysarthria and dyskinesia in this patient was presented as the stimulation amplitude was increased and frequency was set > 130 Hz. Symptoms remained unresponsive to modulation of active stimulation contacts, amplitude and frequencies.

The application of a VFS paradigm was applied upon informed consent. Frequency parameters were set to a high frequency of 130 Hz, followed by successive tests

alternating to 60, 70 or 80 Hz. The patient's dysarthria and axial symptoms were best improved with parameters of 130 and 60 Hz. Thereafter, time duration for each cycle (total duration < 1 minute) and ratio of frequency were tested. Dizziness and imbalance was reported by the patient when duration for each frequency was set <10 s. Final parameters were set to 130 Hz and 60 Hz, for 30 s and 20 s, respectively, per cycle. Amplitude and pulse width were set to 2.2 V, 60 μs and 2.5 V, 90 μs for the left and right hemispheres, respectively, as used previously for HFS.

Following VFS, speech was more intelligible in comparison to HFS (UPDRS III, item 18, score 1) (Table 1). Acoustic aerodynamic measurements were evaluated using Phonolaryngeal Graph SH01 (Rion, Japan). Under VFS, there were increases in maximum phonation time (1.97 to 6.88 s) and mean sound pressure levels (55.43 to 63.86 db), demonstrating improvement in hypophonia. The benefit of VFS for the treatment dysarthria was also seen in aerodynamic efficiency, power and resistance, while the patient's improved motor symptoms remained stable at 12 months follow-up.

Discussion.

Although speech intelligibility in PD patients with early-stage dysarthria can be partially improved by HFS STN-DBS, the therapeutic effects are less pronounced than those seen for motor symptoms, with initial benefits decreasing over time [7]. The strained voice type of dysarthria may be caused by abnormal tonic laryngeal muscle contraction, induced by current diffusion to the corticobulbar fibers [7]. LFS has been used to alleviate dysarthria [5] but a short duration of therapeutic benefit and lack, or even worsening, of cardinal symptoms limits its wide clinical application. However, LFS remains clinically useful when it lessens the detrimental effects of HFS [6].

Interestingly, dysarthria is often associated with the (re)occurrence of gait disorders [8]. The axial motor symptoms of PD i.e. freezing of gait (FOG) and swallowing function have been seen to improve following LFS (60 Hz) of the STN [9]. We have recently reported that VFS can successfully improve FOG in a patient with PD [10]. The application of VFS may be extended to PD patients with dysarthria, overcoming

the present clinical challenges. However, further investigations in large sample groups are warranted.

References:

1 Limousin P, Krack P, Pollak P, Benazzouz A, Ardouin C, Hoffmann D, et al. Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 1998;339:1105-1111.

2 Pinto S, Ozsancak C, Tripoliti E, Thobois S, Limousin-Dowsey P, Auzou P. Treatments for dysarthria in Parkinson's disease. LANCET NEUROL. 2004;3:547-556.

3 Tripoliti E, Zrinzo L, Martinez-Torres I, Frost E, Pinto S, Foltynie T, et al. Effects of subthalamic stimulation on speech of consecutive patients with Parkinson disease. NEUROLOGY. 2011;76:80-86.

4 Wertheimer J, Gottuso AY, Nuno M, Walton C, Duboille A, Tuchman M, et al. The impact of STN deep brain stimulation on speech in individuals with Parkinson's disease: The patient's perspective. PARKINSONISM RELAT D. 2014;20:1065-1070.

5 Moreau C, Pennel-Ployart O, Pinto S, Plachez A, Annic A, Viallet F, et al. Modulation of dysarthropneumophonia by low-frequency STN DBS in advanced Parkinson's disease. Mov Disord. 2011;26:659-663.

6 di Biase L, Fasano A. Low-frequency deep brain stimulation for Parkinson's disease: Great expectation or false hope? Mov Disord. 2016;31:962-967.

7 Tsuboi T, Watanabe H, Tanaka Y, Ohdake R, Yoneyama N, Hara K, et al. Distinct phenotypes of speech and voice disorders in Parkinson's disease after subthalamic nucleus deep brain stimulation. Journal of Neurology, Neurosurgery & Psychiatry. 2015;86:856-864.

8 Moreau C, Ozsancak C, Blatt JL, Derambure P, Destee A, Defebvre L. Oral festination in Parkinson's disease: biomechanical analysis and correlation with festination and freezing of gait. Mov Disord. 2007;22:1503-1506.

9 Xie T, Vigil J, MacCracken E, Gasparaitis A, Young J, Kang W, et al. Low-frequency stimulation of STN-DBS reduces aspiration and freezing of gait in patients with PD. NEUROLOGY. 2015;84:415-420.

10 Jia F, Guo Y, Wan S, Chen H, Hao H, Zhang J, et al. Variable frequency stimulation of subthalamic nucleus for freezing of gait in Parkinson's disease. Parkinsonism Relat Disord. 2015;21:1471-1472.

Table 1. Motor and Dysarthria evaluation.

	HFS	VFS 1 day	VFS 6 months	VFS 12 months	Normal	SD
Motor function						
UPDRS Ⅲ (0-108)	19	19	17	16		
UPDRS Ⅲ item 18 (0-4)	4	2	2	1		
Voicing efficiency						
Peak air pressure (cm H_20)	/	3.9	2.58	4.92	6.65	1.96
Aerodynamic Power (watts)	/	0.06	0.012	0.017	0.06	0.04
Aerodynamic Resistance (cm H_2O/(L/s))	/	23.03	46.6	111.43	55.18	30.64
Acoustic Ohms (dyne•s/cm^5)	/	23.48	47.53	113.63	56.27	31.24
Aerodynamic Efficiency (ppm)	/	16.06	45.42	112.79	103.66	57.29
Maximum sustained phonation						
Mean SPL During Voicing (db)	55.43	68.59	66.01	63.86	78.73	3.93
Maximum phonation Time (s)	1.97	13.63	9.76	6.88	22	5.74
Mean Expiratory Airflow (L/s)	0.16	0.07	0.05	0.05	0.13	0.06

Note: In the voicing efficiency examination, peak air pressure and aerodynamic efficiency were used to assess the loudness and efficiency of voicing. In the maximum sustained phonation examination, the maximum phonation time (MPT), the mean sound pressure levels (SPL) and the mean expiratory airflow were used to assess the speaking efficiency and loudness. '/' means characteristic could not be detected in this station.