Quantifying Stridor associated with Parkinsonism and Deep Brain Stimulation- a case report

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We present a patient with a diagnosis of Parkinson's disease with an atypical presentation of stridor responsive to medication. The patient was treated with Subthalamic nucleus Deep Brain Stimulation (STN-DBS) for medically refractory motor symptoms. The stridor deteriorated following DBS and novel parameter adjustments were used to improve it. Laryngoscopy was performed pre and post adjustment but not in each test condition for reasons of patient comfort. A Laryngograph (1) was instead used to provide an objective measure of vocal fold closure and stridor during adjustment along with a perceptual speech rating- the DAB scale (2).

Case Report

Stridor is a recognisable harsh and high pitched irregular inspiratory sound (3) associated with impaired vocal fold abduction. Though cases have been reported (4), it is uncommon in Parkinson's disease (PD) and raises the suspicion of Multiple System Atrophy (MSA) (5).

A 54-year-old male with a history of Parkinsonism, presented initially with L-sided tremor, reduced arm-swing and shoulder pain. He was diagnosed with PD and treated with Levodopa and a dopamine agonist. Ten years after onset he was assessed for DBS due to medically-refractory motor fluctuations and dyskinesia (UPDRS-III 32 OFF and 12 ON). At this time whilst inspiration was markedly audible, the stridor was not present in speech. Improvements in respiration and phonation were responsible for the higher on medication speech score (OFF Medication DAB score 28/42, ON medication 35/42). A history of mild stridor was reported (4yr), raising the suspicion of MSA. No evidence of autonomic dysfunction or imaging

features of MSA were identified and he had a sustained motor response to L-dopa. The patient reported that the stridor was partially responsive to L-dopa.

He was treated with bilateral STN-DBS with a Boston Gevia™ device, with a good motor response (UPDRS-III reduction of 50% with stimulation in off-medication state), and reduction in motor fluctuations.

Following DBS, the stridor became audible on exertion and intrusive in speech. At night the stridor was audible but did not interrupt his sleep. Laryngoscopy 6 months post DBS found a maximum abduction of 4-5mm and at 9 months 2.5mm, after which tracheostomy was discussed. Due to the stridor's responsiveness to medication, stimulation adjustment was attempted to prevent or delay a tracheostomy.

Our group previously demonstrated how novel stimulation techniques incorporating short pulse width and directional stimulation can ameliorate adverse effects including stimulation induced dysarthria, dyskinesia and pyramidal side effects (7). A systematic monopolar review aiming to reduce stridor while maintaining motor function was carried out, using both conventional (60 us & 130Hz) and novel approaches including frequency modulation, the use of shorter pulse width (30us), and directional screening at the vertical level of the chronically used contacts.

Stridor severity was assessed in the context of speech, after exertion. Four conditions were tested 1) off-medication/off-stimulation (OFF-OFF), 2) on-medication/off-stimulation (ON-OFF), 3) on-medication/on-baseline settings (ON-BL)

and 4) on-medication/ optimised settings (ON-OP). A 6-week follow-up assessment was carried out (ON-OP-CHRONIC) on optimised parameters.

Baseline STN-DBS settings were of a standard ring mode configuration: 2.1mA, -60μs, 130Hz at contacts 2-3-4 and 10-11-12. The optimised settings were 5.9mA, 30μs, 79Hz bilaterally at segmental contacts 3- at the left STN and 11-,12- (50% each) at the right STN. UPDRS-III scores on stimulation pre- and post-optimisation (off/on medication) were 28/18 and 25/17 respectively.

The impact of stimulation was quantified with baseline settings (ON-BL) and subsequently optimised settings, utilising short pulse width and directional stimulation (ON-OP). Audio recordings available as Supplementary files.

Perceptual speech scores improved with medication (see Table 1). Although stridor remained intrusive, vocal fold irregularity (IFx%) decreased with medication (see Table 1) in regions indicative of high-frequency stridor.

With optimised stimulation settings, perceptual speech scores improved with more precise, scaled, swift articulation as exemplified by decreased reading duration and IFx reduced further (see Table 1), with high frequency stridor all but absent (Figure 1). Voice quality (Mean, Qx%) also improved reflecting a greater mean duration of closure throughout the vocal fold cycle.

At 6-week review (ON-OP CHRONIC), benefits to speech persisted and stridor improved. The patient confirmed improvement yet felt his voice was higher. Modal frequency (F0) was found to be elevated.

Repeat Laryngoscopy following optimisation revealed the glottis to have increased to 7mm. This was sustained for 10 months following the initial adjustment but ultimately declined, eventually necessitating tracheostomy placement.

Discussion

We report a gentleman with L-dopa and STN-DBS responsive Parkinsonism who exhibited worsening stridor following DBS that responded to stimulation adjustment. The Laryngograph may be a useful tool in the assessment of stridor and its impact on the irregularity of voice.

The increase in mean modal pitch (F0) and shift to periodic stridor (Figure 2) points to increased laryngeal tone in optimised stimulation. In an analysis of stridor in MSA (3), increased periodicity was associated with enhanced laryngeal tone and greater stenosis. For our patient, the periodic stridor was accompanied by a wider glottis post adjustment and at 6-week review, however, this did not persist.

While the mechanisms underlying stridor in Parkinsonian disorders have not been fully elucidated, dystonia in the laryngeal adductor muscles has been a suggested cause. The worsening of stridor with conventional stimulation may represent a stimulation induced side effect such as dystonia or hyperadduction of the vocal cords by corticobulbar tract stimulation (6) and the use of novel stimulation techniques has

been shown to alleviate these (7) , corresponding to the improvement in stridor demonstrated in this case.

While there are previous reports of stridor being induced by STN-DBS in PD (8) (9), to our knowledge this is the first reported case illustrating the utility of neuromodulation in partially alleviating stridor and delaying invasive measures, and the usefulness of the laryngograph in quantifying stridor severity.

Author roles

1) Research project: A. Conception, B. Organization, C. Execution;

2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique;

3) Manuscript: A. Writing of the first draft, B. Review and Critique.

TG: 1BC, 2AB, 3A

VD: 1BC, 2AB, 3AB

AF: 3AB

CM: 1A, 3B

PL: 2C, 3B

TF: 3B

Ethical compliance statement section.

The authors confirm that the approval of an institutional review board was not required for this work. Verbal and written consent was obtained from the patient for the publication of this case study. We confirm that we have read the Journal's

position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Disclosures

1) Funding Sources and Conflict of Interest:

P.L. has received honoraria and travel expenses from Medtronic and Boston Scientific for speaking at meetings.

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2) Financial Disclosures for the previous 12 months: The authors declare that there are no additional disclosures to report.

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Legends

Figure 1. DFx1&2- A more similar DFx1 & 2 is indicative of better pitch control

DFx1 (red) - Probability distribution for the frequency of each vocal fold cycle.

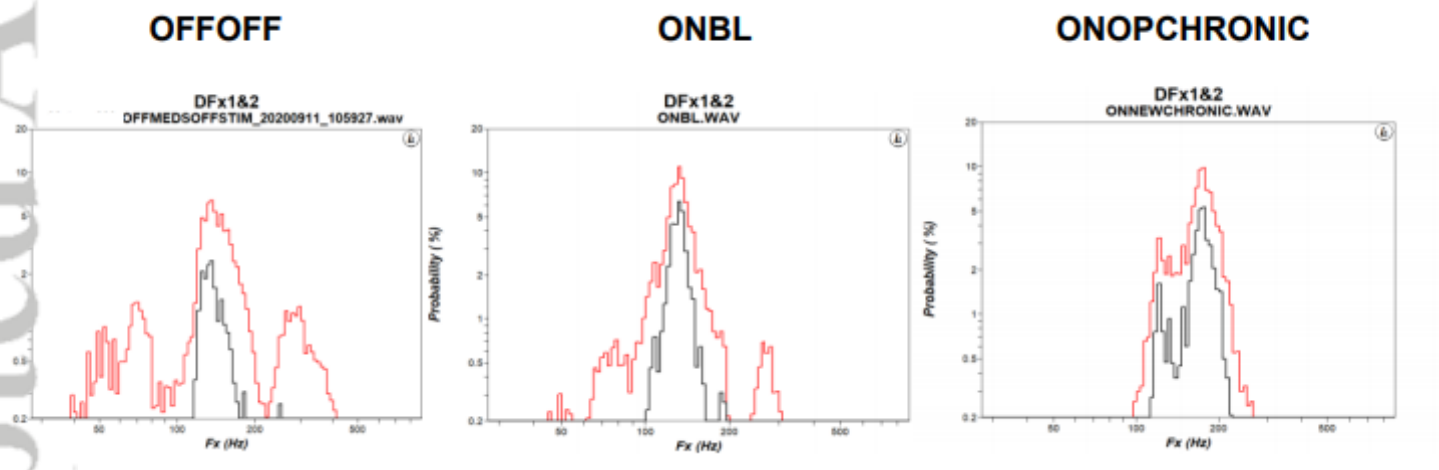
DFx2 (black) - Successive adjacent periods with the same frequency

Figure 2. Sections of stridor taken in isolation across conditions. The waveform becomes progressively more periodic with a shift from semi-rhythmic stridor to rhythmic across conditions 1) OFF-OFF, 2) ON-OFF, 3) ON-BL, 4) ON-OP, 5) ON-OP-CHRONIC

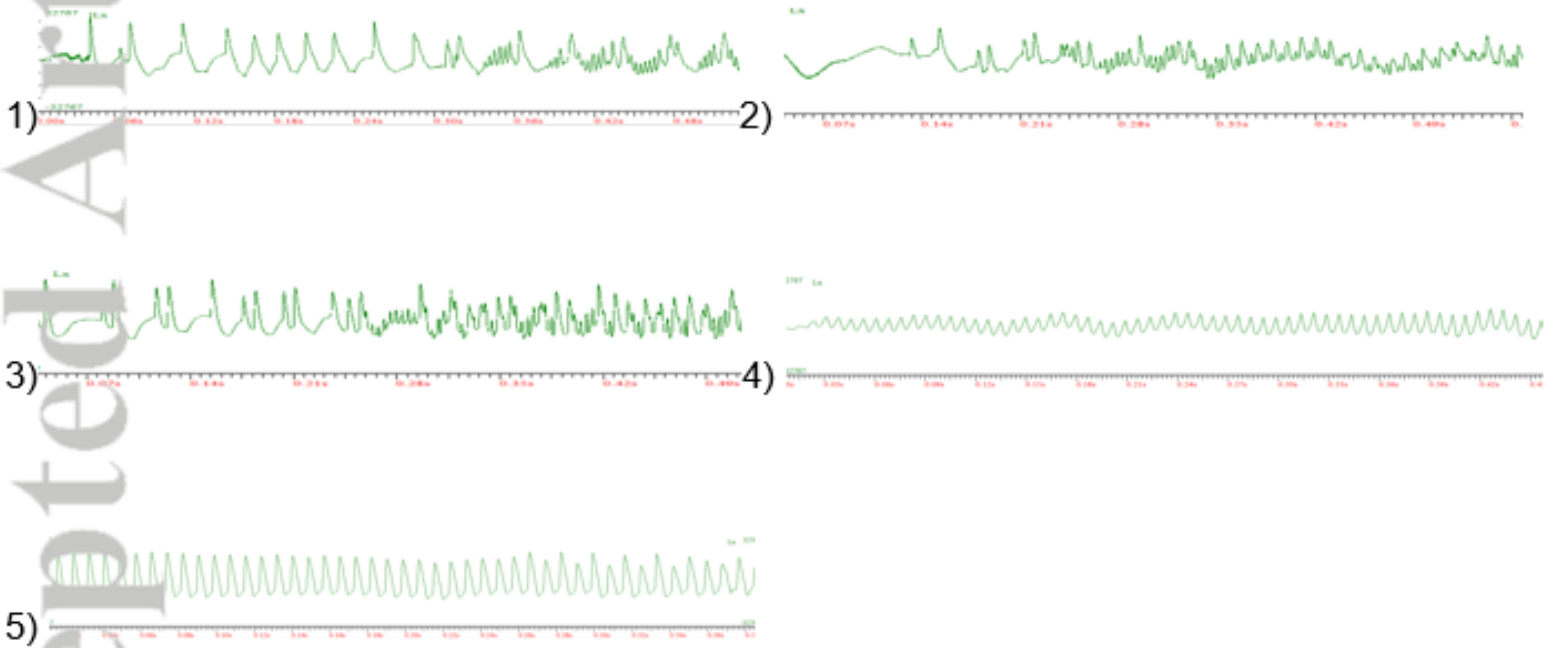
Supplemental Audio file 1- A recording of Stridor in the context of speech in the OFF medication and OFF stimulation condition (OFF-OFF).

Supplemental Audio file 2- A recording of Stridor in the context of speech in the ON medication and OFF stimulation condition (ON-OFF).

Supplemental Audio file 3- A recording of Stridor in the context of speech in the ON medication, OPTIMISED stimulation condition (ON-OP).



MDC3_13368_Figure 1 stridor.png



MDC3_13368_Figure 2 periodic stridor.png

Table 1. Measures of speech and stridor in each medication and stimulation condition

	OFFOFF	ONOFF	ONBL	ONOP	ONOPChronic
Speech score DAB /42	14	25	24	30	28
Reading Duration (secs)	164	154	164	127	129
IFx % irregularity	49.91	37.89	33.67	34.35	21.91
F0 Hz	136.6	125.27	132.72	121.1	177.2
Stridor only IFx %	85.29	68.83	70.63	15.63	8.89