Concurrent Bilateral ViM and STN DBS in a Patient with ET/PD

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BACKGROUND

- Deep brain stimulation (DBS) of the ventralis intermedius (ViM) thalamic nucleus improves a variety of tremor types that are severe or medication-refractory.[1]
- ET and Parkinson's disease (PD) may co-exist in the same patient[2] and each may be treated with DBS, though often at different targets.
- ViM DBS improves both essential tremor (ET) and parkinsonian tremor, but without benefit on other cardinal PD symptoms or motor complications.[3]
- Subthalamic nucleus (STN) DBS improves parkinsonian tremor along with rigidity, bradykinesia and certain gait difficulties.[4]
- We report a patient with long-standing ET previously treated with bilateral ViM DBS who underwent adjunctive bilateral STN DBS for treatment of new onset PD (ET/PD).

CASE REPORT

- 77yo RH M with alcohol-responsive bilateral hand tremors since his 20s and family history of tremors in his father and two sons.
- Symptoms included bilateral rest and action tremors, head and chin tremors, and difficulty in performing tandem gait. No parkinsonism was evident.
- Standard oral medications failed to provide significant tremor control. Bilateral ViM DBS was performed at another institution in July 2008 with initial good tremor control.
- One year after ViM surgery, tremor control was limited by side effects including stimulation-dependent slurred speech and gait unsteadiness with bilateral stimulation.
- The patient turned off one DBS electrode when speaking or ambulating and turned both electrodes on when better tremor control was needed.
- Multiple DBS programming sessions provided partial improvement in tremor without complete resolution of side effects.
- Examination in 2011: **DBS off:** wide based cautious gait with good initiation. **DBS on:** difficulty standing and with gait initiation, stooped posture, shuffling gait but good tremor control. **After reprogramming:** slight gait instability and good tremor control. No evidence of rigidity or bradykinesia.
- Examination in 2012: persistent gait shuffling and impaired balance even with the DBS turned off, also bradykinesia, rigidity and a stooped posture.
- MRI showed adequate bilateral VIM lead placement (Fig. 1A) and DaTscan (Fig. 1B) was abnormal, consistent with a diagnosis of ET with co-existing PD.
- Gait, bradykinesia and rigidity, but not tremor, improved with levodopa, but this was poorly tolerated. He underwent b/l STN DBS in 2013 without complications.

SURGICAL PROCEDURE

- Electrodes were implanted using a Leksell frame in a staged procedure.
- Target coordinates: 14 mm left and right of AC-PC midpoint, 3 mm behind the AC-PC midpoint, and 6 mm deep to the AC-PC midpoint (Fig. 1C).
- Intra-operative micro-electrode recording (MER) and test stimulation were performed.
- MER showed appropriate STN recordings correlating with tremor frequency ("tremor cells").
- Stimulation of either STN electrode in isolation failed to yield immediate tremor control. Combined ViM and STN stimulation on the left but not the right side yielded marked suppression of contralateral rest, kinetic and postural tremor. There were no apparent side effects of STN and/or ViM stimulation.
- MDS-UPDRS off medications was performed after the first programming session (one month, un-blinded), two months (un-blinded) and at six months (blinded video rater) under different stimulation conditions lasting 30 minutes each (Fig. 2A-C).

RESULTS

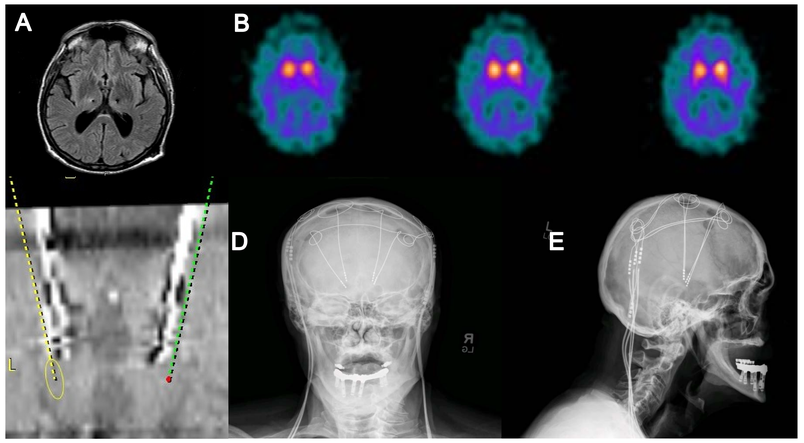
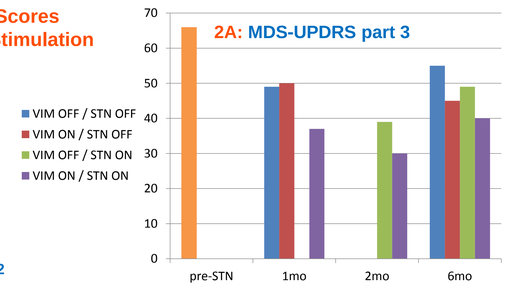


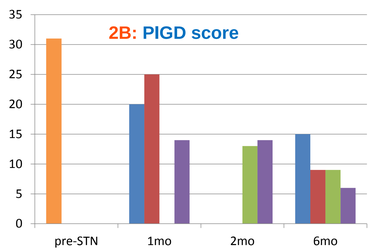
Figure 1: **A**- Pre-operative MRI showing bilateral ViM electrodes in good position. **B**- DaTscan showing presynaptic dopamine deficiency. **C**- Coronal view, 15 degrees from mid plane, showing pre-operative planned trajectories for bilateral STN DBS in relation to bilateral ViM electrodes previously in place (Medtronic StimPilot™). **D, E-** X-ray of the skull in antero-posterior and lateral views showing the 4 lead placements.

Figure 2A-C: MDS-UPDRS Part 3 Scores and Sub-scores Under Different Stimulation Conditions



Total tremor score = sum of items 3.15-3.17

PIGD score = sum of items 3.3-3.8, 3.10, 3.12



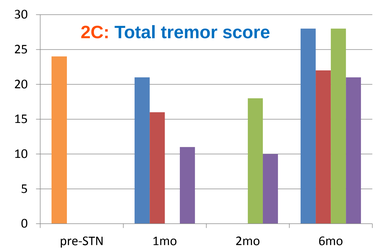


Table 1: DBS Parameters after the First Programming Session (1 Mo.) and at 6 Months.

After First Programming	Contacts		Amplitude (V)	Pulse width (μs)	Frequency (Hz)
Left ViM	Interleaved ViM1	C+ 0-	1.5	90	125
	Interleaved ViM2	2+ 1-	2.0	60	125
Right ViM	10+ 9-		2.0	80	125
Left STN	C+ 3-		2.2	60	180
Right STN	C+ 10-		2.5	60	180
At 6 Months					
Left ViM	Interleaved ViM1	C+ 0-	1.5	70	125
	Interleaved ViM2	2+ 1-	1.9	60	125
Right ViM	10+ 9-		1.4	60	125
Left STN	Interleaved STN1	C+ 3-	3.0	60	125
	Interleaved STN2	C+ 2-	2.7	60	125
Right STN	C+ 10-		3.2	60	125

DISCUSSION

- To our knowledge, this is the first reported case of concurrent ViM and STN DBS in a patient with ET/PD.
- Previous cases of STN DBS 3-14 years after ViM DBS in patients with PD were performed to better address motor complications;[3] in these cases, ViM stimulation was discontinued.
- There is one reported case of concurrent bilateral ViM and STN in a patient with "Holmes tremor" and parkinsonism with improvement in rest, postural and kinetic tremors as well as rigidity.[5]
- Concurrent bilateral ViM and STN DBS was safe and well-tolerated in our patient with ET/PD.
- ViM stimulation alone caused clear worsening of rigidity and postural stability, which improved after addition of STN stimulation. The mechanism of worsening parkinsonism with ViM stimulation is unclear.
- ViM (but not STN) stimulation affected tremor control at six months.
- STN stimulation controlled other parkinsonian symptoms and allowed for reduction of ViM stimulation settings, resulting in reduced stimulation side effects.
- The improvement in parkinsonism remained stable at six months, and is attributable to STN stimulation. However there was worsening of tremor at six months likely due to a combination of reduced VIM settings and habituation of tremor suppression.
- "Tremor cells" are present in both ViM and STN, and correspond to tremor frequency in patients with ET or PD. ET is thought to be caused by a dysfunction of the cerebello-thalamocortical pathways while dysfunction in striato-pallidal circuitry triggers resting tremor in PD, and is further modulated by cerebello-thalamocortical networks.[7]
- It is possible that combined network effects may improve tremor control via independent mechanisms when the ViM and STN are stimulated together in patients with dual disease pathophysiology.[8]
- In our patient, the lack of sustained contribution to tremor control with STN stimulation at six months could be due to the predominance of ET pathophysiology (especially since tremor did not worsen when obvious parkinsonism emerged), or patient-specific factors such as habituation of tremor suppression.

CONCLUSIONS

- Concurrent bilateral ViM and STN DBS may be considered in patients with ET/PD, but caution should be exercised when considering the potential for additive effect on tremor.
- STN DBS can improve parkinsonism in patients also receiving concurrent ViM stimulation for tremor control.
- Mechanisms of tremor in patients with ET/PD should be investigated further. Additional studies should be undertaken to understand the network effects of isolated and combined ViM and STN simulation in patients with ET/PD.

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