



Neuropsychologic Effects of Dual Lead Thalamic DBS to Treat Severe Multiple Sclerosis Tremor

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Introduction

Surgical treatment of severe multiple sclerosis (MS) tremor via lesioning or deep brain stimulation (DBS) has proven more difficult than for essential or parkinsonian tremor, resulting in mixed and often disappointing results. This may be due to tremor pathophysiology beyond the cerebello-thalamo-cortical loop targeted by these procedures, or due to involvement of a relatively wide somatotopic distribution that cannot be fully captured from a single point.

Methods

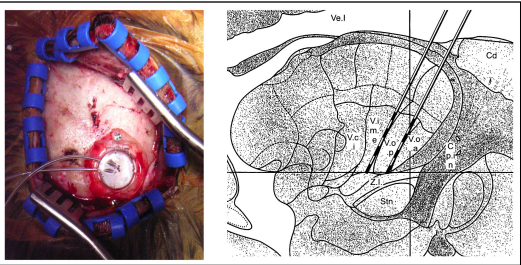
Inclusion criteria: clinical diagnosis of MS tremor, age 18-79, tremor refractory to medical therapy, stable medical regimen

Exclusion criteria: medical comorbidity precluding surgery, evidence of atypical movement disorder, structural brain abnormality precluding DBS, dementia, major psychiatric illness

12 patients were enrolled:

ID	Age at implant	Sex	MS subtype	Disease Duration (y)	Tremor Duration (y)	Baseline TRS
2	30	F	relapsing-remitting	7	6	53
4	27	M	relapsing-remitting	19	1.5	66
6	49	F	relapsing-remitting	15	7	50
7	54	F	primary progressive	8	8	50
9	47	F	relapsing-remitting	28	17	68
10	51	F	relapsing-remitting, gradual progression	18	17	60
11	26	M	primary progressive	1.5	1.5	62 **
12	72	F	primary progressive	13	3	81
13	23	F	primary vs secondary relapsing-remitting, progressing to secondary	3	2	55
14	40	F	relapsing-remitting	20	11	50
15	36	F	relapsing-remitting	7	5	76
16	58	F	relapsing-remitting	30	8	46

** this patient did not complete the protocol due to wound infection requiring DBS explantation



Methods, continued

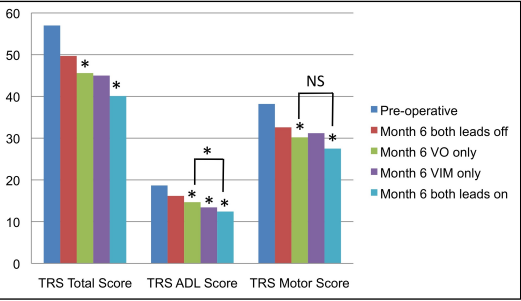
All patients underwent standard VIM DBS lead placement followed by parallel VO lead placement 2 mm anterior to the VIM tract, via a single burr hole

Patients were randomized to either VIM- or VO-only stimulation for 3 months, then both leads were activated and optimized for 3 more months. Patients and evaluators were blinded to stimulation conditions

TRS was measured at baseline and 3 months. At 6 months TRS was performed in all 4 possible conditions (Both Off, Both On, VIM On, VO On). Mood and neuropsychological batteries were also performed at each time point.

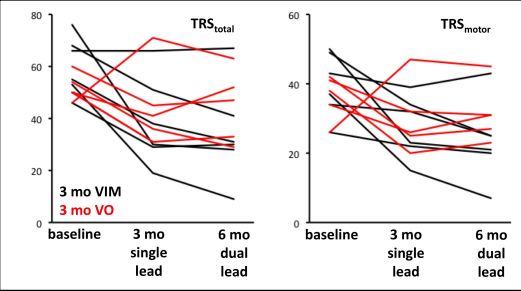
Results

Mean TRS Scores:

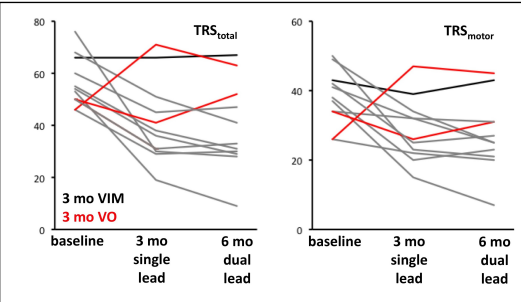


Results, continued

Individual TRS scores:



For many subjects, DBS had a profound effect. Additional improvement often observed with dual lead stimulation. 3 nonresponders were observed: 2 with severe ataxic tremor component, one with worsening likely due to MS progression.



Adverse Events:

- 1 hardware infection requiring explantation
- 1 superficial wound infection
- 1 transient altered mental status
- 1 sudden death 2 years postoperatively, IRB determined unrelated to procedure
- 1 fractured extension 1 year postop
- 1 postop MS exacerbation (new plaque), progressive hemiparesis and spasticity, > 1 year postop

Mood battery scores at baseline and in post-DBS testing conditions.						
Measure	Baseline (B)	Both Off (T1)	Both On (T2)	VIM On (T3)	VO On (T4)	Results of Paired Sample t-tests
BDI	4.80 (2.27)	3.73 (5.85)	6.08 (4.32)	3.17 (6.01)	3.85 (5.41)	—
STAI-State Total	31.9 (8.72)	34.7 (15.4)	30.9 (9.97)	28.1 (8.82)	31.5 (11.7)	Both On > VIM On (p = 0.05)
YAMS						
Anxious	8.50 (4.1)	12.7 (15.7)	13.5 (15.2)	6.83 (10.2)	14.7 (15.0)	—
Confused	16.2 (18.8)	17.5 (17.8)	17.8 (24.3)	9.90 (12.8)	17.8 (28.4)	—
Sad	9.21 (11.0)	16.5 (27.5)	18.1 (28.5)	7.40 (9.70)	17.1 (14.2)	VIM On < VO On (p = 0.03)
Angry	5.58 (8.30)	10.2 (16.7)	11.8 (18.4)	6.50 (9.31)	12.7 (28.1)	—
Energetic	34.8 (14.1)	49.4 (38.3)	49.4 (30.0)	42.3 (14.2)	45.5 (28.9)	—
Tired	45.9 (33.9)	35.4 (28.1)	31.1 (20.3)	44.2 (16.5)	34.2 (28.8)	—
Happy	75.4 (27.6)	62.9 (31.4)	85.8 (33.8)	60.1 (23.8)	67.0 (25.2)	B > Both On (p = 0.03), VIM On (p = 0.02)
Tense	11.6 (16.1)	13.0 (18.1)	18.4 (21.8)	11.8 (13.0)	20.7 (23.4)	—
POMS						
Tension/Anxiety*	1.83 (3.38)	5.08 (4.21)	4.67 (3.08)	4.02 (4.12)	5.08 (5.11)	—
Depressed/Down	2.07 (4.50)	3.77 (4.80)	5.42 (6.49)	4.08 (4.81)	3.79 (7.40)	—
Anger/Hostility	4.83 (4.04)	1.90 (1.80)	1.92 (2.78)	2.17 (2.76)	2.75 (4.05)	B > Both Off (p = 0.02), Both On (p = 0.009), B > VIM On (p = 0.05)
Vigil/Activity	10.5 (8.19)	6.77 (5.59)	7.58 (8.45)	6.75 (13.1)	7.30 (8.80)	—
Fatigue/Anxiety	3.17 (2.37)	5.98 (4.17)	5.90 (2.97)	5.17 (3.76)	5.42 (6.02)	—
Confusion/Revol	15.3 (7.20)	15.7 (8.10)	14.4 (7.99)	16.4 (7.40)	16.7 (9.82)	B < Both Off (p = 0.05), VIM On (p = 0.07)
POMS Total Score	19.3 (16.1)	24.3 (8.54)	24.8 (9.67)	26.0 (8.88)	26.2 (16.9)	—

Note: Mean (SD) are provide for each variable. **Bolded** values indicate a significant difference (p ≤ 0.05) for a given variable across testing conditions based on results of paired sample t-tests.

*Post-DBS testing conditions for this variable differ significantly (p < 0.05) with baseline scores employed as a covariate.

*Education used as a covariate.

*Age at testing used as a covariate.

Neuropsychological battery scores at baseline and in post-DBS testing conditions.						
Measure	Baseline (B)	Both Off (T1)	Both On (T2)	VIM On (T3)	VO On (T4)	Results of Paired Sample t-tests
Stroop						
Word*	55.7 (24.0)	54.4 (20.1)	58.7 (14.7)	56.1 (22.7)	56.5 (15.9)	—
Color	46.7 (18.4)	41.1 (16.4)	40.0 (15.3)	39.6 (21.2)	39.2 (14.3)	B > VO On (p = 0.02)
Color-Word Interference*	30.4 (16.3)	25.9 (12.0)	26.1 (11.5)	26.8 (14.4)	23.8 (12.1)	VIM On > VO On (p = 0.02)
PASAT						
Trial b	24.3 (13.1)	24.7 (15.0)	26.2 (15.3)	25.1 (15.8)	27.5 (16.9)	—
Total	41.4 (25.6)	47.3 (30.8)	50.3 (28.5)	47.4 (30.5)	43.8 (27.8)	—
Fluency						
Letter	31.1 (7.61)	28.2 (8.60)	29.3 (6.60)	28.4 (5.50)	28.4 (5.63)	—
Semantic	14.5 (5.16)	21.6 (13.2)	16.1 (4.35)	14.8 (6.65)	16.1 (5.26)	—
HVLT						
Trial 1	6.42 (1.62)	6.75 (1.76)	6.67 (1.88)	6.83 (1.34)	6.92 (2.43)	—
Total Recall	24.1 (3.85)	25.3 (5.21)	25.2 (4.65)	25.7 (3.65)	23.9 (6.45)	—
Delayed Recall*	6.83 (3.35)	8.58 (3.32)	8.33 (3.65)	7.75 (3.67)	7.91 (2.60)	—
Percent Recession	68.0 (11.9)	86.1 (25.2)	79.4 (27.5)	75.8 (31.8)	84.4 (16.1)	Both Off > VIM On (p = 0.04)
BDI	10.3 (1.82)	11.0 (2.00)	10.9 (1.42)	10.9 (2.27)	10.3 (2.49)	B < Both Off (p = 0.05), Both On (p = 0.01)

Note: Mean (SD) are provide for each variable. **Bolded** values indicate a significant difference (p ≤ 0.05) for a given variable across testing conditions based on results of paired sample t-tests.

*Post-DBS testing conditions for this variable differ significantly (p < 0.05) with baseline scores employed as a covariate.

*Education used as a covariate.

*Age at testing used as a covariate.

Conclusions

Dual VIM plus VO DBS significantly improved tremor rating scale scores at 6 months compared to baseline. Vim and VO stimulation alone achieved equivalent tremor suppression. Major adverse events were infrequent and similar to routine DBS implantation. No major deleterious mood or cognitive changes were observed during extensive testing at each time point. There were 3 nonresponders in this cohort, who illustrate pitfalls of DBS for MS tremor including severe comorbid ataxia and underlying MS disease progression. We conclude that, for carefully selected patients, dual lead thalamic DBS is safe and efficacious for treatment of severe, refractory MS tremor.