

Microlesion effects and tremor outcome in Ventrointermediate Deep Brain Stimulation (VIM-DBS)

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ABSTRACT

Objective: To investigate the relationship between the microlesion effect (MLE) and the subsequent tremor response and parameter settings of VIM DBS. **Background:** A microlesion effect is defined by the abolition or reduction of tremor after insertion, but before activation, of DBS electrodes. The MLE might predict eventual outcome, although formal data is lacking. **Design/methods:** Nineteen thalami in 12 patients (11 Essential tremor (ET) and 1 Parkinson's disease (PD), who underwent unilateral (n=5) and bilateral VIM DBS (n=7) were assessed at pre and 24-hour post operation, initial DBS activation and at 6 month follow-up. The severity of tremors was rated (0-4) including hand tremor at rest, outstretched, wing beating, finger-nose-finger, dot approximation and spiral drawing (total score 0-24). The difference of tremor scores before and 24-hours after electrode implants (MLE) were segregated into 3 groups: mild (0 - 2), moderate (>2-4), and marked (>4). **Results:** The mean percent change of OFF tremor scores between pre and 24-hour postoperative DBS in group 1, 2, 3 were -9.35%, -22.65%, -50.76%. The OFF tremor score percent difference at 6-month follow-up in group 1, 2, 3 4.32% (p= 0.853), 0% (p=0.616) and 8.33%. The percent difference of mean DBS ON tremor scores at initial activation in groups 1, 2 and 3 were -34.5% (p=0.006, n=5), -48.4% (p=0.005, n=7), -85.6% (n=7), but at 6 months were; -64%(0.726, n=5), -48.4% (p=0.410, n=4), -61.4% (n=4). The mean ON DBS settings at 6-month were 3.26(0.7) V,145Hz,90 μs; 3.1(0.8) V,157.5Hz,60 μs;2.8(0.9) V,172.5Hz, 60 μs.(NS). **Conclusion:**The effect of microlesion on tremor disappears by 6-months,however DBS settings including amplitude and pulse width tended to lower in those with a marked MLE.

METHODS

Eleven ET and two tremor-dominant PD subjects were recruited. All subjects signed a consent approved by the BCM IRB. All subjects had DBS surgery with the lead model 3387, Medtronic with IPG model 7426, Soletra at the Methodist hospital in Houston by the same surgeon. One PD patient was dropped because he underwent coronary artery bypass surgery after stage 1 DBS lead implant. The subjects were assessed at pre- and 24-hour post-operative DBS, initial activation, and at 6-month follow up during ON and OFF DBS stimulation. The DBS was adjusted by the same programmer. The severity of tremor was rated by using Tremor Research Group Rating Scale (TRG) The difference of tremor scores before and 24-hours after electrode implants were segregated into 3 groups based on improvement of tremor scores: mild (0 - 2), moderate (>2-4), and marked (>4). The demographic data, tremor rating scores during ON-OFF stimulation and DBS settings were recorded.

Table 1 : Demographic data

Subject	Age (yr.)	Sex	Diagnosis	Duration from onset to implant	Site	IPG
1	59.4	M	ET	45.9	Unilateral	Soletra
2	38.9	F	ET	7.0	Unilateral	Soletra
3	67.3	M	ET	8.9	Bilateral	Soletra
4	92.1	M	ET	16.0	Unilateral	Soletra
5	80.2	M	ET	16.0	Bilateral	Soletra
6	80.1	M	ET	10.0	Unilateral	Soletra
7	70.5	F	ET	40.5	Bilateral	Soletra
8	81.6	F	ET	33.6	Bilateral	Soletra
9	67.6	F	PD	4.0	Unilateral	Soletra
10	67.2	M	ET	41.2	Bilateral	Soletra
11	80.7	F	ET	5.7	Bilateral	Soletra
12	61.3	M	ET	43.3	Bilateral	Soletra

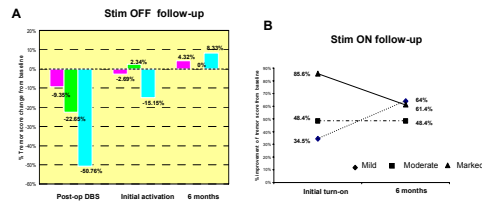


Figure 1 : (A) Mean percent change in tremor scores during Stim OFF at post-operation, initial activation and 6-month follow-up from baseline (pre-operative DBS) in the mild MLE, moderate, and marked groups (B) Mean percent change in tremor scores during Stim ON at the initial activation and 6-month follow-up from baseline in the mild MLE, moderate and marked groups.

RESULTS

Eleven ET with 1 tremor - dominant PD were studied. The demographic data was shown in Table 1. Using the difference of the mean tremor scores segregated thalamic sites into mild MLE (n=5, 26.4%), moderate (n=7, 36.8%) and marked (n=7, 36.8%) groups. The average duration from DBS surgery to initial activation was 23.4 ± 3.7 days, and to 6-month follow-up was 180.2 ± 27.1 days. Within 24-hour post-operation, the mean improvement of tremor scores from baseline was 1.3 ± 0.8 (9.35%); 2.9 ± 0.7 (22.65%); 6.7 ± 2.3 (50.76%); and 4.3 ± 2.9 (32.3%) in mild, moderate, marked and total groups. (P value 0.000; 0.001, mild vs. marked; moderate vs. Marked group) (Table 2) At the initial adjustment before electrode activation, the tremor improvement was less compared to 24 hours after operation. The tremor score difference from baseline was -0.4 ± 2.3 (-2.69%); +0.3 ± 1.1 (+2.34%); -2.0 ± 1.6 (-15.15%); and -1.0 ± 1.9 (-7.5%) in the mild, moderate, marked and total groups (P value 0.262; 0.009, mild vs. marked; moderate vs. marked group). The microlesion effect disappeared at 6-month follow-up in each group (total n=13). (Table 2, Figure 1A)

Table 2: Mean difference of tremor score at post-operative, initial activation and 6-month follow up Stim ON-OFF from baseline

	Mild	Moderate	Marked	Total	P-value
24-hr.post-op	-1.3 ± 0.8(-9.4%)	-2.9 ± 0.7(-22.7%)	-6.7 ± 2.3(-50.8%)	-4.3 ± 2.9(32.3%)	0.000;0.001
Stim OFF					
1 st activation	-0.4 ± 2.3(-2.7%)	+0.3 ± 1.1(+2.3%)	-2.0 ± 1.6(-15.1%)	-1.0 ± 1.9(-7.5%)	0.262;0.009
6-month	+0.6 ± 5.0(+4.3%)	0.0 (0%)	+1.1 ± 3.7(+8.3%)	+0.6 ± 3.4(+4.5%)	0.853;0.616
Stim ON					
1 st activation	-4.8 ± 2.6(-34.5%)	-6.2 ± 2.0(-48.4%)	-11.3 ± 3.5(-85.6%)	-5.8 ± 3.1(-43.6%)	0.006;0.005
6-month	-8.9 ± 3.4(-64%)	-6.2 ± 4.0(-48.4%)	-8.1 ± 2.5(-61.4%)	-7.4 ± 3.4(-55.6%)	0.726;0.410
DBS settings					
1 st activation					
Amp(V)	2.9 ± 0.5	3.2 ± 0.7	2.8 ± 0.7	2.9 ± 0.6	0.793;0.334
Freq(Hz)	160	160	135	140	0.087;0.383
PW(μs)	60	60	60	60	0.546;0.546
6 th month					
Amp(v)	3.3 ± 0.7	3.1 ± 0.8	2.8 ± 0.9	3.1 ± 0.8	0.450;0.704
Freq(Hz)	145	157.5	172.5	160	0.836;0.961
PW(μs)	90	60	60	60	0.865;0.662

CONCLUSIONS

- At the initial electrode activation, the mean tremor score improvement was greater in the marked MLE group compared to the mild, moderate and total groups. (Table 2)
- At 6-month ON stimulation, the tremor score improvement was similar among groups.
- The DBS settings, including amplitude (mean ± SD), frequency (median) and pulse width (median) at the initial activation were similar among groups. At 6 months they were statistically similar but tended to be lower in the marked MLE group (Table 2)
- The initial DBS activation achieved a superior tremor reduction in the group with the greatest MLE, however by 6 months the effects were similar, albeit with a trend towards lower DBS settings including amplitude and pulse width. (Table 2)
- The lower power use for DBS stimulation in the marked MLE group may increase the longevity of the battery. (Ondo WG et al, 2007)