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Effects of Ventral Intermediate Nucleus Deep Brain Stimulation Across Multiple Effectors in Essential Tremor

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Abstract

Objective: Essential tremor (ET) prominently affects the upper-limbs during voluntary movements, but can also affect the lower-limbs, head, and chin. Although deep brain stimulation (DBS) of the ventral intermediate nucleus (VIM) of thalamus improves both clinical ratings and quantitative measures of tremor, no study has quantified effects of DBS on tremor across multiple body parts. Our objective was to quantify therapeutic effects of DBS across multiple body parts in ET.

Methods: We performed quantitative assessment of tremor in ET patients who had DBS for at least one year. We assessed tremor on and off VIM-stimulation using triaxial accelerometers on the upper-limbs, lower-limbs, head and chin during seated and standing tasks.

Results: VIM-DBS significantly reduced tremor, but there was no statistical difference in degree of tremor reduction across the measured effectors. Compared to healthy controls, ET patients treated with DBS showed significantly greater tremor power (4-8 Hz) across all effectors during seated and standing tasks.

Conclusions: VIM-DBS reduced tremor in ET patients. There was no significant difference in the degree of tremor reduction across the measured effectors.

Significance: This study provides new quantitative evidence that VIM-DBS is effective at reducing tremor across multiple parts of the body.

Keywords

essential tremor; deep brain stimulation; thalamus; accelerometer

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Conflict of Interest Statement

None of the authors have potential conflicts of interest to be disclosed.

1. Introduction

Essential tremor (ET) is a progressive, heterogeneous neurological syndrome characterized by tremor that is most pronounced in the upper-limbs, and may also spread to involve other areas of the body such as the lower-limbs, head and chin. ET is the most prevalent movement disorder, with estimates suggesting it affects approximately 2.2% of the population in the United States (Louis and Ottman, 2014). Treatment of ET is often approached with pharmacological agents, however pharmacologically resistant and carefully selected severe cases may be treated using deep brain stimulation (DBS).

DBS of the ventral intermediate nucleus (VIM) of the thalamus has been demonstrated to be effective in reducing clinical ratings of tremor severity (Barbe et al., 2018). Fewer studies, however, have performed quantitative assessment of tremor reduction from DBS. A small number of studies have demonstrated quantitative measures of tremor reduction in the upper-limbs (Milosevic et al., 2018; Shah et al., 2017; Vaillancourt et al., 2003; Wastensson et al., 2013) and the head and neck (Chockalingham et al., 2017), but the degree of tremor reduction achieved by DBS in other areas (e.g., lower-limbs) is not known. Most importantly, it is unclear whether VIM DBS has a differential effect across affected areas of the body. The VIM thalamus has been shown to have functionally connectivity to upper-limb, lower-limb, and head areas in the primary motor cortex in both individuals with ET and healthy controls (Fang et al., 2016). Thus, we hypothesize that the effects of VIM DBS should improve tremor in multiple affected areas of the body simultaneously, and that the degree of tremor reduction will not differ across these areas of the body.

In this study, we performed quantitative assessment of tremor in ET patients off and on VIM DBS using wireless triaxial accelerometers placed on the head, chin, hands, and legs. We also compared ET participants treated with DBS to a control group. The goals of this study were to determine: 1) the effect of DBS across multiple affected areas in ET patients, 2) the degree of tremor in ET patients with DBS off across multiple effectors compared to a group of healthy control (HC) participants, and 3) the degree to which residual tremor was observed in ET patients on DBS across these multiple effectors as compared to HC participants.

2. Methods

2.1. Participants

The present study included 20 individuals with ET and 20 HC between 47 and 83 years of age (Table 1). All procedures were approved by the Institutional Review Board at the University of Florida, and written informed consent was obtained from all subjects in accordance with the Declaration of Helsinki. Participants in the ET group included 12 males and 8 females, all of which had a VIM DBS device for at least one year. The ET participants included in this study are the first 20 subjects that met inclusion/exclusion criteria. There may have been other subjects that had DBS during that year, but those included were the first 20 who volunteered. Participants were not pre-selected based on improvement. Out of the 20 ET participants, 9 had bilateral DBS, and 11 had unilateral DBS. Details on DBS

device settings and laterality for ET participants are described in Table 2. Participants in the HC group included 11 males and 9 females.

2.2. Experimental Design

Participants were first administered a series of clinical rating scales. The Montreal Cognitive Assessment (MOCA) and Beck Depression Inventory (BECK) were administered to screen for potential comorbid cognitive decline or depression. Two clinical scales of tremor were also administered: the Fahn, Tolosa, Marin Tremor Rating Scale (FTM-TRS) and TRG Essential Tremor Rating Assessment Scale v3.1 (TETRAS). Next, a total of six triaxial accelerometers were placed on the following areas: forehead, chin, left hand, right hand, left leg, and right leg (Figure 1).

Data were collected with the Delsys Trigno Wireless System (Delsys Inc., Boston, MA) using MotionMonitor software (Innovative Sports Training, Inc., Chicago, IL) at a sampling rate of 1000 Hz. Participants were asked to perform three trials, each lasting 20 seconds, for each of the following tasks: 1) seated rest tremor, 2) seated postural tremor, 3) standing postural tremor. Since our goal was to assess the effects of DBS on multiple areas across the body, we used different tasks that would allow us to measure tremor in different body positions. For seated rest tremor (1), participants were instructed to sit upright in a chair with head unsupported, hands placed resting on the seat of the chair, feet touching the floor, and relax. For seated postural tremor (2), participants were instructed to sit upright in a chair with head unsupported, arms and hands outstretched at 90 degrees from vertical, and feet touching the floor. For standing postural tremor (3), participants were instructed to stand, unsupported, with arms and hands outstretched at 90 degrees from vertical, and to maintain an upright posture. For all tasks, participants were asked not to attempt to suppress tremor.

ET participants were administered the FTM-TRS, TETRAS, and performed these three tasks with both DBS-On and DBS-Off conditions while tremor was recorded with triaxial accelerometers. DBS-On and DBS-Off assessments were performed in separate sessions during the same day and the order of which was counterbalanced across participants, with at least an hour between sessions to allow for the change in DBS stimulation to take effect. Prior work suggests that one hour is sufficient time for observing changes to tremor severity induced by changing DBS devices either “off” or “on” in patients with tremor (De Jesus et al., 2018; Temperli et al., 2003). For ET participants with bilateral DBS devices (see Table 2), stimulation was delivered bilaterally.

2.3. Data analysis

Acceleration data from the six sensors were analyzed using a custom MATLAB script. Representative acceleration data (left hand) over a single trial from an ET participant with DBS-Off and a HC are depicted in Figure 2. Data were bandpass filtered between 1 and 50 Hz (Butterworth 4th order dual pass), followed by Fourier transform. Group mean spectral power for x, y, and z directions of each sensor during the standing postural task are depicted in Figure 3.

Using acceleration data, we assessed the sum of power between 4-8 Hz and 8-12 Hz for each trial, and the median value across 3 trials was recorded for each sensor. The sum of power

between 4-8 Hz and 8-12 Hz was used as the index of tremor from each area tested (Elble et al., 1994; Neely et al., 2015; Vaillancourt et al., 2004). As an additional measure of tremor, we also calculated amplitude from the acceleration signal of each sensor and assessed the standard deviation of amplitude signal. This was performed for each plane of acceleration (x, y, z). We observed no effect of plane (x, y, z), nor interactions with other variables. Thus, we averaged across the three axes of acceleration for all subsequent analyses.

For ET participants, we calculated the percent reduction of tremor power during DBS-On trials compared to DBS-Off trials as follows:

$$\frac{\text{OFF}-\text{ON}}{\text{OFF}} * 100$$

The percent reduction of tremor power was used as input data for a two-factor (3×6) repeated measures ANOVA, with task and sensor as within-subject factors, covarying for age, sex, and DBS-Off TETRAS score. This was performed for both the acceleration data, as well as amplitude. In these models, the effectiveness of DBS was interpreted as a significant non-zero intercept for the model.

We also compared both DBS-Off and DBS-On trials from ET participants to HC participants. In both DBS-Off and DBS-On comparisons, data were not normally distributed, and thus we performed a Mann-Whitney U test for each of the six sensors across each of the three tasks. The resulting p-values were then corrected for multiple comparisons using a false discovery rate (FDR) of 5% (Benjamini and Hochberg, 1995).

We investigated the possibility of tremor coupling across the measured effectors in two ways. We assessed cross-correlations and coherence of the acceleration across the following pairs of sensors: (1) Left Hand – Head, (2) Left Hand – Left Leg, (3) Right Hand – Head, (4) Right Hand – Right Leg, (5) Head – Chin. For the cross-correlation analysis we first identified the plane (x, y, z) with greatest tremor amplitude, for each sensor during each trial. We then cross-correlated the accelerometer signal from the plane with greatest tremor amplitude for those sensor pairings during each trial, and then averaged across the 3 trials. This was done for both 0-millisecond lag, as well as the largest magnitude correlation within a –100 to +100 millisecond window. Means for these cross-correlations were calculated for DBS on/off and HC groups. For the coherence analysis we calculated the average magnitude squared coherence (MSC; Halliday et al., 1995) between 4 to 12 Hz for each of the four sensor pairs, in each plane (x, y, z), for each trial. We then averaged MSC across the three trials within each plane, and then averaged across the three planes of acceleration. We additionally calculated MSC at the frequency with peak tremor power in the y-plane (*i.e.*, plane with greatest tremor amplitude) for each participant. For both cross-correlations and MSC we compared DBS-Off to DBS-On, DBS-Off to controls, as well as DBS-On to controls, and corrected for multiple comparisons using FDR at 5%.

3. Results

ET patients with DBS turned off showed tremor across all measured effectors (Figure 2). As seen in Figure 3, greatest tremor power was observed in the y-plane (medial-lateral) for all

sensors, with less power in the z-plane (inferior-superior) and x-plane (anterior-posterior). For all measured effectors, ET patients with DBS off showed the most tremor power, with lower tremor power while DBS was turned on, and healthy controls showed the least (Figure 3).

The model assessing percent reduction of 4-8 Hz tremor power in ET participants had a significant non-zero intercept [$F(1,16)=6.47$, $p<.05$], indicating that across all sensors and tasks, there was a DBS induced reduction in 4-8 Hz tremor power (*i.e.*, percent reduction of tremor power > 0). The mean percent reduction of 4-8 Hz tremor power across all tasks and effectors was 25.4%. The model assessing percent reduction of 8-12 Hz tremor power in ET participants also had a significant non-zero intercept [$F(1,16)=4.89$, $p<.05$], indicating that across all sensors and tasks, there was a DBS induced reduction in 8-12 Hz tremor power. The mean percent reduction of 8-12 Hz tremor power across all tasks and effectors was 18.0%. There was no significant effect for the within subject factors of task, sensor, TETRAS score, nor any interaction between these factors for either the 4-8 Hz or 8-12 Hz analysis. For the model using tremor amplitude to assess percent reduction of tremor in ET participants, there was also a significant non-zero intercept [$F(1,16)=4.66$, $p<.05$], similarly indicating that across all sensor and tasks, there was a DBS induced reduction in tremor amplitude (*i.e.*, percent reduction of tremor amplitude > 0). The mean percent reduction of tremor amplitude across all tasks and effectors was 20.4%. Figure 4 depicts percent reduction of tremor power across all sensors and tasks for ET participants with DBS off and on within 4-8 Hz (A-C) and 8-12 Hz (D-F) frequency bands, as well as the percent reduction of tremor amplitude (G-I).

Comparing 4-8 Hz power between ET and HC participants, ET participants with DBS-Off had greater 4-8 Hz tremor power than HC across all sensors and tasks, with the exception of right hand during seated rest task (Table 3). ET participants with DBS-On showed greater 4-8 Hz tremor power than HC across all sensors during seated postural and standing postural tasks (Table 4). As expected, for the seated rest condition there was no significant difference in tremor power observed between ET participants on DBS and HC. Comparing 8-12 Hz power between ET and HC participants, ET participants with DBS-Off showed greater 8-12 Hz power than HC for head and left hand during all three tasks, as well as the left and right leg during seated postural and standing postural tasks (Table 5). ET participants with DBS-On showed greater 8-12 Hz power for the right leg during the seated postural task, as well as for the left hand, left leg, and right leg during the standing postural task (Table 6).

For sensor cross-correlations, the greatest tremor amplitude was observed in the y-plane (medial-lateral) for all sensors (Figure 3). Thus, all cross-correlations were performed with y-plane sensor data. We observed no significant differences at 0-ms or at -100 to +100 ms latencies for ET participants with DBS-On compared to DBS-Off (all p-values $> .15$), ET participants with DBS-Off compared to HC (all p-values $> .16$), nor ET participants with DBS-On compared to HC (all p-values $> .06$), for any of the five sensor pairs. The largest R value of these cross-correlations was .14 and the smallest was .0002.

For coherence, we calculated the 95% confidence limit (*i.e.*, significance threshold) according to Halliday et al. (1995), which was equal to 0.076. The Head – Chin sensor pair

exceeded this threshold in both HC subjects and ET patients with DBS on and off, for all three conditions. No other sensor pair exceeded this threshold in any group or condition. This was true for both average MSC across 4-12 Hz, as well as MSC at peak tremor frequency. This suggests there was a significant degree of coherence between head and chin sensors, but not for any other sensor pairs (Figure 5). There were no between-group differences in average MSC across 4-12 Hz when comparing HC to ET patients with DBS off (Table 7), HC compared to ET patients with DBS on (Table 8), or in ET patients with DBS off compared to DBS on. There were also no between-group differences in MSC at peak tremor frequency when comparing HC to ET patients with DBS off (Table 9), HC compared to ET patients with DBS on (Table 10), or in ET patients with DBS off compared to DBS on.

4. Discussion

The effectiveness of VIM DBS for reducing tremor in ET patients has been demonstrated through clinical rating scales, but there are far fewer quantitative studies on the effects of DBS, particularly across multiple body parts. In this study, we performed quantitative assessment of tremor using triaxial accelerometers in ET patients on and off VIM DBS, across multiple body areas and during multiple tasks. We also assessed tremor in ET patients on and off DBS across multiple effectors as compared to HC participants.

These results showed that in ET patients DBS reduced tremor power across all measured effectors and tasks in both 4-8 Hz and 8-12 Hz frequency bands, as well as tremor amplitude. There was no significant difference in the magnitude of tremor reduction between sensors or across tasks at either 4-8 Hz or 8-12 Hz, nor for tremor amplitude. TETRAS score was not a significant covariate in the models assessing tremor power or amplitude, indicating that these effects of DBS are not dependent on disease severity. This finding provides new systematic quantitative evidence of DBS tremor reduction in ET for affected areas beyond the upper-limbs, including lower-limbs, and head and chin. This finding was consistent with our hypothesis that DBS would affect tremor across multiple effectors throughout the body. A previous study of functional connectivity showed that a unilateral VIM seed showed significant functional connectivity to upper-limb, lower-limb, and head regions of primary motor cortex in both ET patients and HC subjects (Fang et al., 2016). The behavioral effects of such widespread VIM thalamus connectivity to the primary motor cortex are consistent with and provide a plausible mechanism for the results observed in this study.

One possibility is that there was coupling of tremor across the measured effectors. In order to investigate whether there was coupling of tremor across effectors, we quantified cross-correlations and coherence across pairs of sensors: (1) Left hand – Head, (2) Right hand – Head, (3) Left hand – Left leg, (4) Right hand – Right leg, (5) Head – Chin. At the individual subject level, we cross-correlated the accelerometer signal at a 0-millisecond lag, as well as the largest magnitude correlation within a –100 to +100 millisecond window. Means were calculated for DBS on/off and HC groups. We observed no significant differences in ET participants with DBS-Off compared to DBS-On, nor between ET participants with DBS-Off or DBS-On compared to HC, for any of the cross-correlations. The largest R value among these cross-correlations was .14 and the smallest was .0002.

For coherence, we observed no differences between HC subjects and ET subjects on or off DBS, for any of the sensor pairs during any of the three tasks. There were no differences in coherence between DBS-Off and DBS-On trials within ET patients, for any of the sensor pairs during any of the three tasks. This was the case for both the average coherence across 4-12 Hz, as well as coherence at peak tremor frequency. The Head – Chin sensor pair was included as a reference point for other sensor pairs, as sensors placed on different segments of the same body part would be expected to have a higher degree of coherence than those on separate limbs (Ben-Pazi et al., 2001). Indeed, the coherence of the Head – Chin sensor pair was always higher than the other sensor pairs, and was the only one which exceeded the 95% significance threshold. It is unclear whether the degree of coherence observed here was mediated by mechanisms in the central nervous system or mechanical coupling of tremor across effectors in the periphery. We did not perform experiments with mechanical dampening of effectors, and thus we cannot conclusively eliminate the possibility of mechanical transmission of tremor across effectors.

Previous quantitative studies regarding the effects of DBS have focused on the upper-limbs (Milosevic et al., 2018; Shah et al., 2017; Wastensson et al., 2013), often in an intraoperative setting. It has been proposed, however, that lower-limb abnormalities such as gait disturbance should be included as part of the features indicating advanced disease progression in ET (Stolze et al., 2001). There is also evidence that DBS can help to normalize abnormalities in gait kinematics in ET patients with long disease duration (Fasano et al., 2012). Our findings extend the lower-limb benefits of DBS beyond gait and show that DBS also improves lower-limb tremor in seated postural and standing postural body positions.

Compared to HC participants, ET patients off DBS showed significantly greater 4-8 Hz tremor power for all measured effectors and tasks, except for the right hand during seated rest. In the 8-12 Hz frequency band, ET patients off DBS showed greater tremor power for the head and left hand during all tasks, as well as both legs during seated postural and standing postural tasks. When ET patients had DBS on, they showed significantly greater power than HC participants in the clinically relevant 4-8 Hz frequency band across all effectors during seated postural tremor and standing postural tremor tasks. In the 8-12 Hz frequency band ET participants with DBS turned on showed greater tremor power for the right leg during the seated postural task, as well as for the left hand, left leg, and right leg during the standing postural task. We did not expect to observe a difference between ET participants and HC during the seated rest tremor task, as resting tremor is less prevalent than postural tremor in ET (Cohen et al., 2003). Although there was no difference between ET and HC groups during the seated rest tremor task when DBS was on, we did observe greater tremor power in ET participants off DBS during seated rest.

These findings warrant further investigation, considering the variability of tremor reduction observed across ET participants and the relative brevity of the evaluative window. The effect of DBS on multiple effectors would also benefit from further investigation during tasks of daily living, which have currently only been studied with measures gathered from a single upper-limb (Heldman et al. 2011). It is also important to note that the current study was

performed after at least a year of receiving DBS and the time-varying and longitudinal effects of DBS on different effector is not known from this study.

5. Conclusions

This work provides the first quantitative assessment of the effects of DBS across multiple body parts that are affected in ET. We found that DBS significantly reduced tremor, and that there was no significant difference in the amount of tremor reduction observed between effectors or across tasks. Additionally, we showed that the relative degree of DBS tremor reduction across ET subjects was not affected by their age, sex, or disease severity.

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References

- Barbe MT, Reker P, Hamacher S, Franklin J, Kraus D, Dembek TA, et al. (2018). DBS of the PSA and the VIM in essential tremor: A randomized, double-blind, crossover trial. *Neurology*, 91(6), e543–e550. 10.1212/WNL.0000000000005956 [PubMed: 29970404]
- Ben-Pazi H, Bergman H, Goldberg JA, Giladi N, Hansel D, Reches A, et al. (2001). Synchrony of rest tremor in multiple limbs in Parkinson's disease: evidence for multiple oscillators. *J Neural Transm (Vienna)*, 108(3), 287–96. [PubMed: 11341480]
- Benjamini Y, & Hochberg Y (1995). Controlling the False Discovery Rate: a Practical and Powerful Approach to Multiple Testing. *J.R. Statist. Soc. B*, 57(1), 289–300.
- Chockalingam A, Boggs H, Prusik J, Ramirez-Zamora A, Feustel P, Belasen A, et al. (2017). Evaluation of Quantitative Measurement Techniques for Head Tremor With Thalamic Deep Brain Stimulation. *Neuromodulation*, 20(5), 464–470. 10.1111/ner.12566 [PubMed: 28145626]
- Cohen O, Pullman S, Jurewicz E, Watner D, & Louis ED (2003). Rest tremor in patients with essential tremor: prevalence, clinical correlates, and electrophysiologic characteristics. *Arch Neurol*, 60(3), 405–410. [PubMed: 12633153]
- De Jesus S, Almeida L, Shahgholi L, Martinez-Ramirez D, Roper J, Hass CJ, et al. (2018). Square biphasic pulse deep brain stimulation for essential tremor: The BiP tremor study. *Parkinsonism Relat Disord*, 46, 41–46. 10.1016/j.parkreldis.2017.10.015 [PubMed: 29102253]
- Elble R, Comella C, Fahn S, Hallett M, Jankovic J, Juncos JL, et al. (2012). Reliability of a new scale for essential tremor. *Mov Disord*, 27(12), 1567–1569. 10.1002/mds.25162 [PubMed: 23032792]
- Fang W, Chen H, Wang H, Zhang H, Puneet M, Liu M, et al. (2016). Essential tremor is associated with disruption of functional connectivity in the ventral intermediate Nucleus--Motor Cortex--Cerebellum circuit. *Hum Brain Mapp*, 37(1), 165–178. 10.1002/hbm.23024 [PubMed: 26467643]
- Fasano A, Herzog J, Raethjen J, Rose FEM, Volkmann J, Falk D, & Deuschl G (2012). Lower limb joints kinematics in essential tremor and the effect of thalamic stimulation. *Gait Posture*, 36(2), 187–193. 10.1016/j.gaitpost.2012.02.013 [PubMed: 22555066]
- Halliday DM, Rosenberg JR, Amjad AM, Breeze P, Conway BA, & Farmer SF (1995). A Framework for the Analysis of Mixed Time Series/Point Process Data – Theory and Application to the Study of Physiological Tremor, Single Motor Unit Discharges, and Electromyograms. *Prog. Biophys. Molec Biol*, 64(2-3), 237–278. [PubMed: 8987386]
- Heldman DA, Jankovic J, Vaillancourt DE, Prodoehl J, Elble RJ, & Giuffrida JP (2011). Essential tremor quantification during activities of daily living. *Parkinsonism Relat Disord*, 17(7), 537–542. 10.1016/j.parkreldis.2011.04.017 [PubMed: 21570891]

- Louis ED, & Ottman R (2014). How many people in the USA have essential tremor? Deriving a population estimate based on epidemiological data. *Tremor Other Hyperkinet Mov*, 4, 259 10.7916/D8TT4P4B
- Milosevic L, Kalia SK, Hodaie M, Lozano AM, Popovic MR, & Hutchison WD (2018). Physiological mechanisms of thalamic ventral intermediate nucleus stimulation for tremor suppression. *Brain*, 141(7), 2142–2155. 10.1093/brain/awy139 [PubMed: 29878147]
- Shah A, Coste J, Lemaire J-J, Taub E, Schüpbach WMM, Pollo C, et al. (2017). Intraoperative acceleration measurements to quantify improvement in tremor during deep brain stimulation surgery. *Med Biol Eng Comput*, 55(5), 845–858. 10.1007/s11517-016-1559-9 [PubMed: 27631560]
- Stolze H, Petersen G, Raethjen J, Wenzelburger R, & Deuschl G (2001). The gait disorder of advanced essential tremor. *Brain*, 124, 2278–2286. [PubMed: 11673328]
- Temperli P, Ghika J, Villemure J-G, Burkhard PR, Bogousslavsky J, & Vingerhoets FJG (2003). How do parkinsonian signs return after discontinuation of subthalamic DBS? *Neurology*, 60(1), 78–81. [PubMed: 12525722]
- Vaillancourt DE, Sturman MM, Verhagen Metman L, Bakay RA, & Corcos DM (2003). Deep brain stimulation of the VIM thalamic nucleus modifies several features of essential tremor. *Neurology*, 61(7), 919–925. [PubMed: 14557560]
- Wastensson G, Holmberg B, Johnels B, & Barregard L (2013). Quantitative methods for evaluating the efficacy of thalamic deep brain stimulation in patients with essential tremor. *Tremor Other Hyperkinet Mov*, 3 10.7916/D8VM4B0N

Highlights

- We quantified effects of deep-brain stimulation across multiple body parts in essential tremor.
- Deep-brain stimulation significantly reduced tremor across all tasks and effectors.
- There was no significant difference in the degree of tremor reduction across measured effectors.

Figure 1:
Depiction of sensor placement for measurement of tremor across multiple body parts.

Figure 2: Representative acceleration data during a seated postural tremor trial (20 seconds), from an ET participant with DBS-Off and a HC participant. *Abbreviations: deep brain stimulation (DBS), essential tremor (ET), healthy control (HC).*

Figure 3:

Power spectral density means of ET (DBS-Off and DBS-On) and HC subjects for x, y, and z directions of each sensor during the standing postural task. *Abbreviations: deep brain stimulation (DBS), essential tremor (ET), healthy control (HC).*

Figure 4:

Percent reduction in tremor across effectors for 4-8 Hz power (A-C), 8-12 Hz power (D-F), and the standard deviation of amplitude (G-I). *Abbreviations: forehead (HD), chin (CH), left hand (LH), right hand (RH), left leg (LL), and right leg (RL).*

Figure 5:

Average magnitude squared coherence between 4-12 Hz for ET patients on and off DBS and healthy controls during seated rest tremor, seated postural tremor, and standing postural tremor tasks. Sensor pairs included: (1) left hand and head, (2) right hand and head, (3) left hand and left leg, (4) right hand and right leg, (5) head and chin. The dashed line indicates the 95% confidence interval threshold. *Abbreviations: head (HD), chin (CH), left hand (LH), right hand (RH), left leg (LL), right leg (RL).*

Table 1:

Participant demographic information (± 1 standard deviation), including gender, age, and scores from the following clinical scales: The Montreal Cognitive Assessment (MOCA), Beck Depression Inventory (BECK), the Fahn, Tolosa, Marin Tremor Rating Scale (FTM-TRS) and TRG Essential Tremor Rating Assessment Scale v3.1 (TETRAS).

Group	Gender (M / F)	Age	MOCA	BECK	FTM-TRS (DBS Off)	FTM-TRS (DBS On)	TETRAS (DBS Off)	TETRAS (DBS On)
Essential tremor	12 / 8	70.1 (± 8.1)	26.1 (± 1.6)	5.9 (± 5.9)	48.9 (± 13.9)	26.9 (± 16.2)	52.0 (± 10.8)	27.4 (± 15.2)
Healthy control	11 / 9	71.4 (± 6.4)	27.1 (± 1.8)	2.5 (± 3.3)	2.1 (± 2.1)	-	2.38 (± 2.2)	-

Table 2:

Essential tremor patient scores (DBS off and on) for the Fahn, Tolosa, Marin Tremor Rating Scale (FTM-TRS) and TRG Essential Tremor Rating Assessment Scale v3.1 (TETRAS), as well as deep-brain stimulation (DBS) parameters, including anode and cathode contacts, voltage, pulse width, and frequency. Includes both left and right lateralized DBS settings, where applicable.

ID	FTM-TRS (OFF ON)				TETRAS (OFF ON)				Left VIM				Right VIM			
									lead contacts	voltage (V)	pulse width (µs)	frequency (Hz)	lead contacts	voltage (V)	pulse width (µs)	frequency (Hz)
1	44	15	56.0	16.5	1-2+	2.7	90	185	1-2+	2.7	90	185	1-2+	2.7	90	185
2	55	11	55.0	13.0	2-3+	2.6	120	200	2-3+	3.5	120	200	2-3+	3.5	120	200
3	27	5	43.0	7.0	1-C+	2.1	90	135	1-C+	2.2	90	135	2-C+	2.2	90	135
4	50	34	55.0	35.0	1-C+	2.6	90	145	-	-	-	-	-	-	-	-
5	36	20	43.5	30.0	2-C+	2.0	90	135	2-C+	2.0	90	135	2-C+	2.0	90	135
6	50	20	47.0	20.0	1-C+	2.0	90	135	1-C+	1.8	90	135	1-C+	1.8	90	135
7	51	50	42.0	40.5	1+2	3.3	90	135	-	-	-	-	-	-	-	-
8	67	49	59.5	48.5	0-1-2+	2.2	180	130	-	-	-	-	-	-	-	-
9	36	20	43.0	17.5	2-C+	2.3	90	180	-	-	-	-	-	-	-	-
10	45	8	48.5	11.0	0-1+	2.7	90	135	-	-	-	-	-	-	-	-
11	69	51	69.5	61.0	2-3+	4	117	180	3-1+	1.9	78	130	3-1+	1.9	78	130
12	42	23	35.5	18.0	1-3+	2.2	90	130	-	-	-	-	-	-	-	-
13	54	14	53.5	24.0	-	-	-	-	2-C+	2.7	104	150	2-C+	2.7	104	150
14	75	62	68.0	57.5	-	-	-	-	0-1+2	4.4	180	185	0-1+2	4.4	180	185
15	56	37	63.0	37.5	2-3+	3.3	117	150	-	-	-	-	-	-	-	-
16	16	13	27.5	15.0	1-C+	2.2	90	145	-	-	-	-	-	-	-	-
17	48	14	52.5	15.5	2-C+	2.5	60	180	2-C+	2.6	90	130	2-C+	2.6	90	130
18	51	29	61.0	29.5	1-C+	2.2	120	150	1-C+	3.2	90	135	1-C+	3.2	90	135
19	44	27	53.0	25.0	2-1+	2.7	90	185	2-3+	3.0	90	180	2-3+	3.0	90	180
20	61	36	63.5	25.5	2-3+	5.0	60	180	-	-	-	-	-	-	-	-

Table 3:

Statistical tests (Mann-Whitney U) with false-discovery rate correction comparing 4-8 Hz tremor power between essential tremor (ET) patients with DBS off and healthy controls (HC), for each effector, during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$, **** $p < .0001$.

Task	Sensor	ET (DBS-off) group mean ± StDev	HC group mean ± StDev	Mann- Whitney U	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Head	.0513 ± .0848	.00565 ± .00283	79	.001	***.001
	Chin	.0760 ± .113	.00673 ± .00405	88	.002	***.003
	Left hand	.0493 ± .101	.00631 ± .0115	86	.002	***.002
	Right hand	.0465 ± .0774	.0117 ± .0186	144	.130	.130
	Left leg	1.28 ± 5.67	.00255 ± .00179	102	.008	***.008
	Right leg	.0460 ± .145	.00251 ± .00184	85	.002	***.002
<i>Seated Postural Tremor</i>	Head	.330 ± .817	.00716 ± .00312	40	1.51×10^{-5}	*** 3.39×10^{-5}
	Chin	.178 ± .386	.00935 ± .00889	62	1.89×10^{-4}	*** 3.10×10^{-4}
	Left hand	8.12 ± 24.6	.0159 ± .0113	40	1.51×10^{-5}	*** 3.39×10^{-5}
	Right hand	.830 ± 2.83	.00885 ± .00708	68	2.60×10^{-4}	*** 3.91×10^{-4}
	Left leg	1.17 ± 5.03	.00186 ± .000438	28	3.27×10^{-6}	*** 1.18×10^{-5}
	Right leg	.202 ± .532	.00203 ± .000359	14	4.90×10^{-7}	*** 8.82×10^{-6}
<i>Standing Postural Tremor</i>	Head	.539 ± .957	.0124 ± .00601	24	1.93×10^{-6}	*** 1.16×10^{-5}
	Chin	.289 ± .508	.0227 ± .0495	43	2.20×10^{-5}	*** 4.40×10^{-5}
	Left hand	10.2 ± 6.36	.0266 ± .0167	27	2.87×10^{-6}	*** 1.18×10^{-5}
	Right hand	.523 ± 1.61	.0135 ± .0106	57	1.10×10^{-4}	*** 1.97×10^{-4}
	Left leg	.529 ± 2.18	.00288 ± .00147	31	4.84×10^{-6}	*** 1.45×10^{-5}
	Right leg	.0751 ± .182	.00325 ± .00169	34	1.93×10^{-6}	*** 1.16×10^{-5}

Table 4:

Statistical tests (Mann-Whitney U) with false-discovery rate correction comparing 4-8 Hz tremor power between essential tremor (ET) patients on DBS and healthy controls (HC), for each effector, during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor	ET (DBS-On) group mean ± StDev	HC group mean ± StDev	Mann- Whitney U	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Head	.00860 ± .00686	.00565 ± .00283	132	.068	.087
	Chin	.0128 ± .0115	.00673 ± .00405	131	.063	.087
	Left hand	.00572 ± .00522	.00631 ± .0115	157	.253	.285
	Right hand	.00957 ± .0116	.0117 ± .0186	216	.678	.718
	Left leg	.00454 ± .0103	.00255 ± .00179	202	.968	.968
	Right leg	.00554 ± .0133	.00251 ± .00184	140	.108	.130
<i>Seated Postural Tremor</i>	Head	.0994 ± .223	.00716 ± .00312	71	2.92×10^{-4}	$*** 5.84 \times 10^{-4}$
	Chin	.0572 ± .113	.00935 ± .00889	84	.001	$** .002$
	Left hand	2.26 ± 6.85	.0159 ± .0113	66	1.55×10^{-4}	$*** 4.65 \times 10^{-4}$
	Right hand	.336 ± 1.40	.00885 ± .00708	114	.02	$* .03$
	Left leg	.0304 ± .0690	.00186 ± .000438	62	9.11×10^{-5}	$*** 3.28 \times 10^{-4}$
	Right leg	.0192 ± .0434	.00203 ± .000359	71	2.92×10^{-4}	$*** 5.84 \times 10^{-4}$
<i>Standing Postural Tremor</i>	Head	.200 ± .391	.0124 ± .00601	59	6.00×10^{-5}	$*** 3.11 \times 10^{-4}$
	Chin	.111 ± .191	.0227 ± .0495	71	2.92×10^{-4}	$*** 5.84 \times 10^{-4}$
	Left hand	3.29 ± 6.92	.0266 ± .0167	60	6.91×10^{-5}	$*** 3.11 \times 10^{-4}$
	Right hand	.669 ± 2.74	.0135 ± .0106	112	.017	$* .028$
	Left leg	.0118 ± .00976	.00288 ± .00147	50	1.57×10^{-5}	$*** 2.82 \times 10^{-4}$
	Right leg	.0105 ± .00935	.00325 ± .00169	55	3.36×10^{-5}	$*** 3.03 \times 10^{-4}$

Table 5:

Statistical tests (Mann-Whitney U) with false-discovery rate correction comparing 8-12 Hz tremor power between essential tremor (ET) patients with DBS off and healthy controls (HC), for each effector, during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor	ET (DBS-Off) group mean ± StDev	HC group mean ± StDev	Mann- Whitney U	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Head	.00336 ± .00285	.00158 ± 4.98×10^{-4}	104	.009	*,021
	Chin	.0172 ± .0220	.00694 ± .00401	174	.482	.482
	Left hand	.0103 ± .0141	.00462 ± .00805	104	.009	*,021
	Right hand	.0180 ± .0274	.00972 ± .0101	173	.465	.482
	Left leg	.470 ± 2.09	.00146 ± 5.13×10^{-4}	161	.291	.328
	Right leg	.0219 ± .0802	.00152 ± 4.96×10^{-4}	145	.137	.189
<i>Seated Postural Tremor</i>	Head	.0192 ± .0631	.00242 ± .00106	114	.020	*,039
	Chin	.0490 ± .119	.0115 ± .00816	136	.083	.125
	Left hand	.807 ± 2.21	.0108 ± .0112	76	7.96×10^{-4}	**,005
	Right hand	.0680 ± .164	.0149 ± .0110	158	.256	.307
	Left leg	.202 ± .891	.00121 ± 2.90×10^{-4}	87	.002	**,006
	Right leg	.0193 ± .0712	.00138 ± 2.53×10^{-4}	87	.002	**,006
<i>Standing Postural Tremor</i>	Head	.0153 ± .0300	.00364 ± .00205	115	.021	*,039
	Chin	.0737 ± .121	.00819 ± .0266	122	.035	.057
	Left hand	1.12 ± 2.38	.0140 ± .0105	86	.002	**,007
	Right hand	.0838 ± .174	.0201 ± .0116	158	.256	.307
	Left leg	.181 ± .772	.00230 ± 8.93×10^{-4}	75	7.22×10^{-4}	**,005
	Right leg	.0137 ± .0317	.00272 ± 9.31×10^{-4}	67	3.21×10^{-4}	**,005

Table 6:

Statistical tests (Mann-Whitney U) with false-discovery rate correction comparing 8-12 Hz tremor power between essential tremor (ET) patients on DBS and healthy controls (HC), for each effector, during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor	ET (DBS-On) group mean ± StDev	HC group mean ± StDev	Mann- Whitney U	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Head	.00177 ± 6.30 × 10 ⁻⁴	.00158 ± 4.98 × 10 ⁻⁴	167	.383	.575
	Chin	.00706 ± .00429	.00694 ± .00401	194	.883	.989
	Left hand	.00369 ± .00333	.00462 ± .00805	145	.134	.345
	Right hand	.00632 ± .00454	.00972 ± .0101	228	.461	.615
	Left leg	.00144 ± .00124	.00146 ± 5.13 × 10 ⁻⁴	244	.242	.484
	Right leg	.00177 ± .00124	.00152 ± 4.96 × 10 ⁻⁴	182	.640	.768
<i>Seated Postural Tremor</i>	Head	.00523 ± .00868	.00242 ± .00106	173	.478	.615
	Chin	.0157 ± .0142	.0115 ± .00816	165	.355	.575
	Left hand	.265 ± .832	.0108 ± .0112	134	.076	.228
	Right hand	.0687 ± .235	.0149 ± .0110	199	.989	.989
	Left leg	.00535 ± .0145	.00121 ± 2.90 × 10 ⁻⁴	119	.028	.101
	Right leg	.00225 ± .00132	.00138 ± 2.53 × 10 ⁻⁴	83	.001	***.006
<i>Standing Postural Tremor</i>	Head	.00784 ± .00967	.00364 ± .00205	161	.301	.542
	Chin	.0296 ± .0258	.00819 ± .0266	156	.242	.484
	Left hand	.654 ± 1.61	.0140 ± .0105	106	.010	*.045
	Right hand	.142 ± .523	.0201 ± .0116	203	.947	.989
	Left leg	.00700 ± .00876	.00230 ± 8.93 × 10 ⁻⁴	77	6.00 × 10 ⁻⁴	***.006
	Right leg	2.53 × 10 ⁻⁴ ± .00385	.00272 ± 9.31 × 10 ⁻⁴	78	6.70 × 10 ⁻⁴	***.006

Table 7:

Statistical tests (t-test) with false-discovery rate correction comparing average magnitude squared coherence between 4-12 Hz for essential tremor (ET) patients with DBS off and healthy controls (HC). Sensor pairs included (1) Left hand – Head, (2) Right hand – Head, (3) Left hand – Left leg, (4), Right hand – Right leg, (5) Head – Chin. Each sensor pair was compared during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor Pair	ET (DBS-Off) group mean ± StDev	HC group mean ± StDev	t-score	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Left hand – Head	.0370 ± .0168	.0430 ± .0130	1.26	.216	.646
	Right hand – Head	.0400 ± .0127	.0417 ± .0105	.504	.617	.842
	Left hand – Left leg	.0549 ± .0660	.0431 ± .0150	.780	.440	.842
	Right hand – Right leg	.0472 ± .0389	.0442 ± .0198	.308	.760	.876
	Head – Chin	.102 ± .0353	.0993 ± .0223	.310	.758	.876
<i>Seated Postural Tremor</i>	Left hand – Head	.0538 ± .0300	.0486 ± .0254	.589	.559	.842
	Right hand – Head	.0470 ± .0168	.0411 ± .0147	1.17	.249	.646
	Left hand – Left leg	.0384 ± .0228	.0322 ± .00687	1.15	.258	.646
	Right hand – Right leg	.0363 ± .0116	.0323 ± .00541	1.38	.177	.646
	Head – Chin	.134 ± .0578	.100 ± .0360	2.22	.032	.248
<i>Standing Postural Tremor</i>	Left hand – Head	.0510 ± .0253	.0473 ± .0152	.563	.577	.842
	Right hand – Head	.0464 ± .00931	.0463 ± .0164	.0224	.982	.982
	Left hand – Left leg	.0395 ± .0227	.0354 ± .0100	.751	.457	.842
	Right hand – Right leg	.0345 ± .0113	.0349 ± .0105	.114	.910	.974
	Head – Chin	.148 ± .0629	.113 ± .0326	2.21	.033	.247

Table 8:

Statistical tests (t-test) with false-discovery rate correction comparing average magnitude squared coherence between 4-12 Hz for essential tremor (ET) patients on DBS and healthy controls (HC). Sensor pairs included (1) Left hand – Head, (2) Right hand – Head, (3) Left hand – Left leg, (4), Right hand – Right leg, (5) Head – Chin. Each sensor pair was compared during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor Pair	ET (DBS-On) group mean $\pm$ StDev	HC group mean $\pm$ StDev	t-score	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Left hand – Head	.0354 $\pm$.00541	.0430 $\pm$.0130	2.41	.021	.269
	Right hand – Head	.0365 $\pm$.00680	.0417 $\pm$.0105	1.87	.070	.311
	Left hand – Left leg	.0356 $\pm$.0114	.0431 $\pm$.0150	1.78	.083	.311
	Right hand – Right leg	.0333 $\pm$.0105	.0442 $\pm$.0198	2.18	.036	.269
	Head – Chin	.102 $\pm$.0657	.0993 $\pm$.0223	.171	.865	.944
<i>Seated Postural Tremor</i>	Left hand – Head	.0493 $\pm$.0304	.0486 $\pm$.0254	.070	.944	.944
	Right hand – Head	.0454 $\pm$.0215	.0411 $\pm$.0147	.733	.468	.735
	Left hand – Left leg	.0341 $\pm$.0180	.0322 $\pm$.00687	.422	.676	.890
	Right hand – Right leg	.0328 $\pm$.0137	.0323 $\pm$.00541	.133	.895	.944
	Head – Chin	.121 $\pm$.0669	.100 $\pm$.0360	1.24	.222	.557
<i>Standing Postural Tremor</i>	Left hand – Head	.0538 $\pm$.0299	.0473 $\pm$.0152	.871	.389	.735
	Right hand – Head	.0490 $\pm$.0271	.0463 $\pm$.0164	.372	.712	.890
	Left hand – Left leg	.0390 $\pm$.0180	.0354 $\pm$.0100	.795	.432	.735
	Right hand – Right leg	.0381 $\pm$.0175	.0349 $\pm$.0105	.700	.490	.735
	Head – Chin	.139 $\pm$.0635	.113 $\pm$.0326	1.63	.112	.337

Table 9:

Statistical tests (t-test) with false-discovery rate correction comparing peak frequency magnitude squared coherence for essential tremor (ET) patients with DBS off and healthy controls (HC). Sensor pairs included (1) Left hand – Head, (2) Right hand – Head, (3) Left hand – Left leg, (4) Right hand – Right leg, (5) Head – Chin. Each sensor pair was compared during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor Pair	ET (DBS-Off) group mean ± StDev	HC group mean ± StDev	t-score	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Left hand – Head	.0464 ± .0287	.0590 ± .0390	1.17	.250	.417
	Right hand – Head	.0814 ± .112	.0421 ± .0266	1.53	.134	.304
	Left hand – Left leg	.0862 ± .103	.0490 ± .0576	1.41	.165	.310
	Right hand – Right leg	.103 ± .126	.0523 ± .0403	1.70	.098	.304
	Head – Chin	.179 ± .161	.115 ± .0803	1.59	.119	.304
<i>Seated Postural Tremor</i>	Left hand – Head	.0848 ± .0640	.0665 ± .0509	1.00	.323	.484
	Right hand – Head	.0770 ± .0612	.0490 ± .0258	1.88	.068	.304
	Left hand – Left leg	.0570 ± .0512	.0362 ± .0216	1.68	.101	.304
	Right hand – Right leg	.0397 ± .0298	.0447 ± .0226	.603	.550	.688
	Head – Chin	.200 ± .138	.0944 ± .108	2.70	.010	.153
<i>Standing Postural Tremor</i>	Left hand – Head	.0794 ± .100	.0674 ± .0762	.427	.672	.720
	Right hand – Head	.0534 ± .0470	.0565 ± .0682	.169	.867	.867
	Left hand – Left leg	.0597 ± .0691	.0412 ± .0700	.847	.402	.549
	Right hand – Right leg	.0471 ± .0253	.0550 ± .0662	.496	.623	.719
	Head – Chin	.197 ± .169	.125 ± .132	1.50	.142	.304

Table 10:

Statistical tests (t-test) with false-discovery rate correction comparing peak frequency magnitude squared coherence for essential tremor (ET) patients on DBS and healthy controls (HC). Sensor pairs included (1) Left hand – Head, (2) Right hand – Head, (3) Left hand – Left leg, (4) Right hand – Right leg, (5) Head – Chin. Each sensor pair was compared during seated rest tremor, seated postural tremor, and standing postural tremor conditions. Significance indicated by: * $p < .05$, ** $p < .01$, *** $p < .001$.

Task	Sensor Pair	ET (DBS-On) group mean ± StDev	HC group mean ± StDev	t-score	p-value	FDR adjusted p-value
<i>Seated Rest Tremor</i>	Left hand – Head	.0514 ± .0481	.0590 ± .0390	.551	.585	.798
	Right hand – Head	.0465 ± .0444	.0421 ± .0266	.377	.708	.817
	Left hand – Left leg	.0610 ± .0390	.0490 ± .0576	.776	.443	.785
	Right hand – Right leg	.0756 ± .0765	.0523 ± .0403	1.21	.235	.745
	Head – Chin	.132 ± .111	.115 ± .0803	.580	.566	.798
<i>Seated Postural Tremor</i>	Left hand – Head	.0558 ± .0414	.0665 ± .0509	.728	.471	.785
	Right hand – Head	.0790 ± .0519	.0490 ± .0258	2.31	.026	.197
	Left hand – Left leg	.0355 ± .0199	.0362 ± .0216	.105	.917	.968
	Right hand – Right leg	.0568 ± .0399	.0447 ± .0226	1.17	.248	.745
	Head – Chin	.196 ± .150	.0944 ± .108	2.48	.018	.197
<i>Standing Postural Tremor</i>	Left hand – Head	.0684 ± .0803	.0674 ± .0762	.040	.968	.968
	Right hand – Head	.105 ± .127	.0565 ± .0682	1.52	.136	.682
	Left hand – Left leg	.0343 ± .0203	.0412 ± .0700	.422	.675	.817
	Right hand – Right leg	.0776 ± .114	.0550 ± .0662	.770	.446	.785
	Head – Chin	.167 ± .140	.125 ± .132	.982	.332	.785