Impact of Unilateral and Bilateral DBS on The Essential Tremor Rating Assessment Scale

Peter M. Grund[1], Leonardo Brito de Almeida[1], Erin Holker[2], Scott Cooper[1]
[1]Department of Neurology, [2]Department of Rehabilitative Medicine

BACKGROUND

- **Essential tremor** (ET) is the most common movement disorder.[1]
- It is estimated that 30–50% of ET patients are refractory to medication and require more advanced surgical therapies such as **deep brain stimulation** (DBS).[2]
- Despite DBS being a well-established therapy modality, not enough has been done to **measure its impact** on commonly used clinical measures of motor performance and quality of life indices in ET.[3]
- The purpose of this chart review is to **quantify if ET DBS patients improve** on the The Essential Tremor Rating Assessment Scale (TETRAS) following surgery, if so, **how much**, and **if there are other important predictors** of improvement.
- We **hypothesized** that:
  1. relative to pre-surgery scores, TETRAS evaluations on unilateral or bilateral DBS would have reduced performance (TETRAS-P) and activities of daily living (TETRAS-ADL) scores
  2. bilateral patients would have reduced performance and ADL scores relative to unilateral patients post-surgery
  3. improvement in TETRAS performance scores would be *positively* correlated with improvement in ADL scores
  4. pre-surgery depression would be negatively correlated with improvement in TETRAS-ADL scores, but show no correlation with improvement in TETRAS performance scores

METHODS

Measures

- **TETRAS-P (performance):** 9-item, physician-administered subscale quantifying action tremor
- **TETRAS-ADL (activities of daily living):** 12-item patient-reported functional impact of tremor on common daily activities such as eating, drinking, and dressing
- **Demographic variables**: Lead manufacturer, lead laterality, age at ET symptom onset, age at surgery date, sex
- **Neuropsychological variables**: Dementia Rating Scale, Montreal Cognitive Assessment, Beck's Depression Inventory–2 (BDI–2), apathy score

Data processing

- Extracted data from EPIC flowsheets for all ET patients who had surgery or DBS programming at the University of Minnesota/M Health Fairview since 1 Jan 2020 – present.
- Processed data using R (readr, lubridate, lme4, emmeans) for cleaning, transformation, and analysis.
- We defined "surgery date":
  1. for **unilateral patients** as the date of the lead implantation surgery
  2. for **bilateral staged patients** as date of the *second* lead surgery if it occurs within 60 days of the first
  3. for **bilateral patients** who had two lead surgeries **more than 60 days apart** as the date of the *first* surgery

Statistical approach

- To visualize each patient's TETRAS-P and ADL score trajectories over time, we normalized the y-axis to each patient's recent pre-surgery score and added **LOESS curve smooths** (figures 1 and 2).
- Two separate **linear mixed effect models** were used to predict performance and ADL score by DBS status and random effect of individual (figures 3 and 4).
- Other potential **predictors** of performance and ADL scores were tested (tables 2 and 3).
- For each patient, we computed a **change in performance score** and **change in ADL score**, defined as the difference between their most recent *post-surgery* score and their most recent *pre-surgery* score. We then correlated change in performance with change in ADL (figure 5).
- Linear regressions then analyzed the relationship between **pre-surgery depression** and **improvement on performance** and **ADL scores**.

Patient demographics

Table 1.

Variable	Bilateral N = 50[1]	Unilateral N = 16[1]	Overall N = 66[1]
Sex			
Male	32 (64%)	12 (75%)	44 (67%)
Female	18 (36%)	4 (25%)	22 (33%)
Age at onset	36.3 (18.7)	42.6 (20.9)	37.8 (19.3)
Handedness			
Right	44 (88%)	15 (94%)	59 (89%)
Left	6 (12%)	1 (6.3%)	7 (11%)
Race/ethnicity			
White	47 (94%)	16 (100%)	63 (95%)
Other	3 (6.0%)	0 (0%)	3 (4.5%)
Manufacturer			
Boston	21 (42%)	7 (44%)	28 (42%)
Medtronic	17 (34%)	4 (25%)	21 (32%)
Abbott	12 (24%)	5 (31%)	17 (26%)

[1] n (%); Mean (SD)

Demographic predictors tested

Table 2.

Variable	Perform. change score	ADL change score
Lead laterality (bilateral vs. unilateral)	<.001	0.041
Lead manufacturer	0.3435	0.453
Age at surgery	0.1142	0.9595
Age at ET symptom onset	0.2572	0.3102
Sex[1]	**0.0270**	0.4219

[1] Female sex predicted greater motor change score

Pre-surgery neuropsychology predictors tested

Table 3.

Variable	Perform. change score	ADL change score
Dementia Rating Scale	0.2716	0.9032
Montreal Cognitive Assessment	0.3745	0.7089
BDI–2[1]	0.2624	**0.0035**
Apathy score	0.7426	0.0776

[1] Higher pre-surgery BDI–2 predicted higher ADL change score

RESULTS

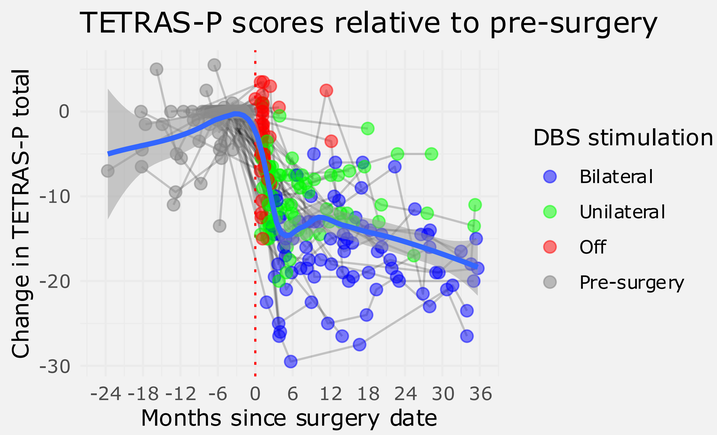


Figure 1:
Longitudinal plot of TETRAS-P score changes relative to most recent pre-surgery scores by patient (y=0), colored by DBS status, with an overlayed LOESS trend line and surgery date marked

DBS status	*EMM*	*CL*
pre	26.6	24.5–28.7
off (post-op)	24.4	22.1–26.8
unilateral	17.1	15.0–19.3
bilateral	11.4	9.3–13.5

Note: **Bonferroni-adjusted**

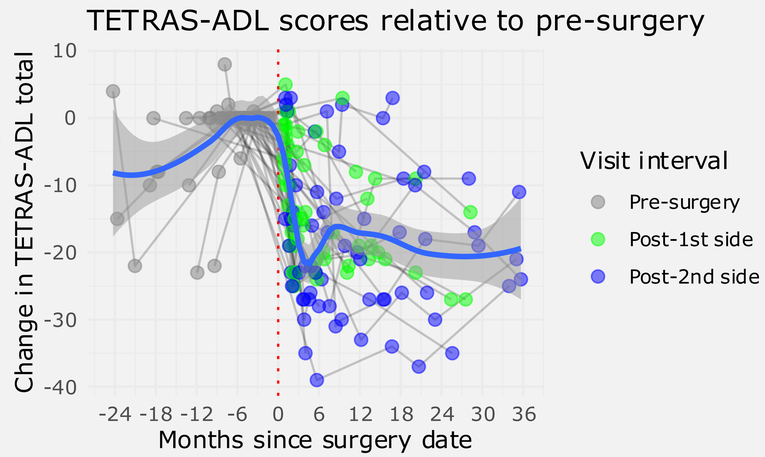
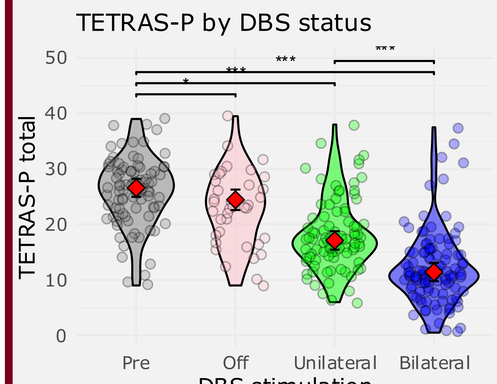


Figure 2:
Longitudinal plot of TETRAS-ADL score changes relative most recent pre-surgery scores by patient (y=0), colored by visit interval, with an overlayed LOESS trend line and surgery date marked

Visit interval	*EMM*	*CL*
pre	29.0	26.1–31.9
post-op (1st side)	19.1	15.7–22.5
post-op (2nd side)	11.8	8.9–14.7

Note: **Bonferroni-adjusted**

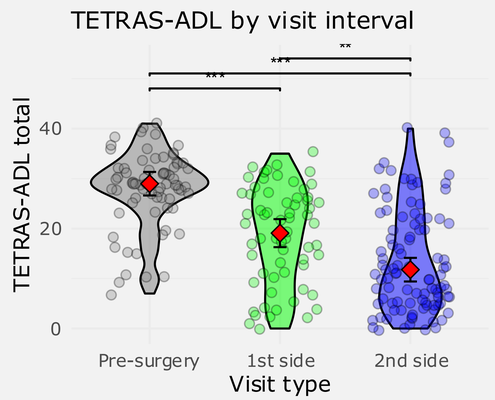


Red diamonds with error bars show estimated marginal means (EMMs) with standard error

Figure 3:
Violin plot showing the distribution of TETRAS-P scores across DBS status.

Contrast	*Estimate*	*p*
pre vs. off	2.15	**0.0165**
pre vs. unilateral	9.47	**<0.001**
pre vs. bilateral	15.17	**<0.001**
off vs. unilateral	7.32	**<0.001**
off vs. bilateral	13.02	**<0.001**
unilateral vs. bilateral	5.70	**<0.001**

Degrees-of-freedom method: kenward-roger; P value adjustment: **Bonferroni** method for 6 tests



Red diamonds with error bars show estimated marginal means (EMMs) with standard error

Figure 4:
Violin plot showing the distribution of TETRAS-ADL scores across surgery status.

Contrast	*Estimate*	*p*
pre vs. post (1st)	9.89	**<0.001**
pre vs. post (2nd)	17.20	**<0.001**
post (1st) vs. post (2nd)	7.31	**<0.001**

Degrees-of-freedom method: kenward-roger; P value adjustment: **Bonferroni** method for 3 tests

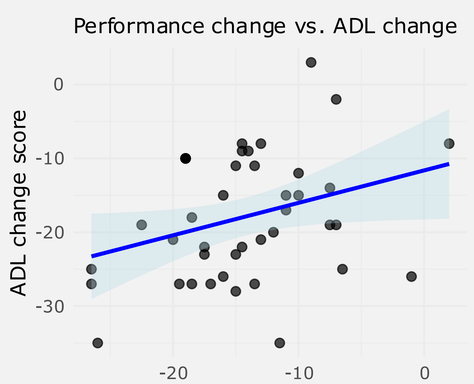


Figure 5:
Scatterplot showing correlation between performance change and ADL change scores.

Statistic	*Value*
p	**0.044**
r	0.3130

DISCUSSION

- In this retrospective chart review project, we found that bilateral DBS stimulation significantly reduced scores on the TETRAS-P and TETRAS-ADL relative to pre-surgery scores.
- Bilateral DBS stimulation resulted in significantly better improvement on both subscales compared to unilateral DBS stimulation.
- Performance and ADL improvement appeared to persist 36 months post-surgery.
- Performance and ADL change scores were only modestly positively correlated with one another.
- As expected, depression did not predict performance change score. However, contrary to our hypothesis, higher depressive symptom scores were predictive of *greater* improvement on the ADLs.

REFERENCES

1. Flora et. al (2010). Deep brain stimulation for essential tremor: a systematic review. DOI: 10.1002/mds.23195
2. Zesiewicz et. al (2011). Evidence-based guideline update: Treatment of essential tremor. DOI: 10.1212/WNL.0b013e318236f0fd
3. Ondo et. al (2017). Comparison of the Fahn-Tolosa-Marin Clinical Rating Scale and The Essential Tremor Rating Assessment Scale (TETRAS). DOI: 10.1002/mdc3.12560

This work was supported by (1) the MnDRIVE DBS Core and
(2) 5R01NS124814 Extramural Research Programs in the Neurosciences and Neurological Disorders