Stimulation rebound in deep brain stimulation for essential tremor

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Introduction

Deep brain stimulation (DBS) is an established treatment for essential tremor (ET) [Baizabal-Carvallo 2014]. Adaptive DBS (aDBS) seeks to mitigate battery drain and side effects of DBS by using feedback from biomarkers to modulate stimulation parameters, generally with a binary, all-or-nothing stimulation control system [Herron 2016, Little 2013]. A recent study identified and quantified a "rebound effect" in patients receiving DBS treatment for ET [Paschen 2019]. This effect manifests when sudden DBS deactivation results in a temporary increase in the severity of motor symptoms before settling to a steady state. ET symptom severity has generally been viewed as largely static in patients; however, the available evidence points to substantial variability due to patient fatigue, as well as factors pertaining to circadian rhythm.

Here is presented a) a clinical assessment- and gyroscope-based analysis of the arc of rebound effect in terms of symptom severity and b) an analysis of the correlation between neural biomarkers and symptom severity, specifically the estimated relative power of the beta band (12-30Hz) from the hand portion of M1. We pay special attention to the role these findings may play in the development of aDBS algorithms.

Methods

- N=3 subjects (0F, 3RH) implanted in left hemisphere with Medtronic Activa PC+S (Fig. 1) combining electrocorticography (ECoG) channel over M1 and DBS stim/recording channel in ventral intermediate nucleus (VIM), each streaming at 200Hz
- Inertial measurement unit (IMU) data recorded using LG G smartwatch streaming at 100Hz
- IMU Symptom severity defined as area under the curve of gyroscope bandpower in 4-12Hz range of frequency domain
- In each session (8-9 per experiment) subject completes Fahn-Tolosa-Marin (FTM) Tremor Rating Scale's drawing section (Fig 2) on tablet-based app

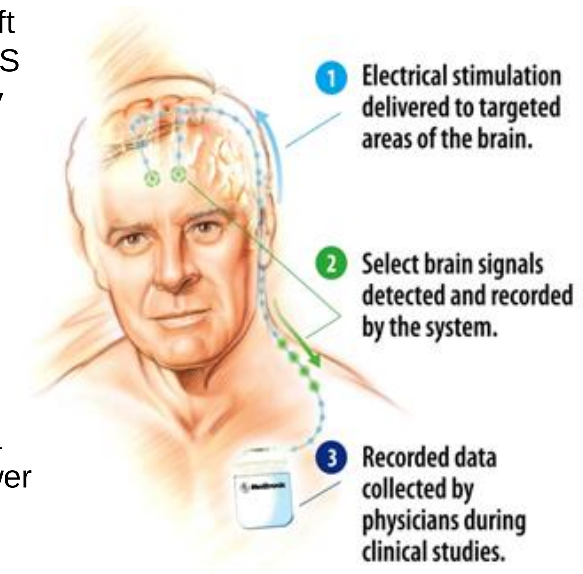

Figure 1: Medtronic Activa™ PC+S device [Medtronic, 2013]

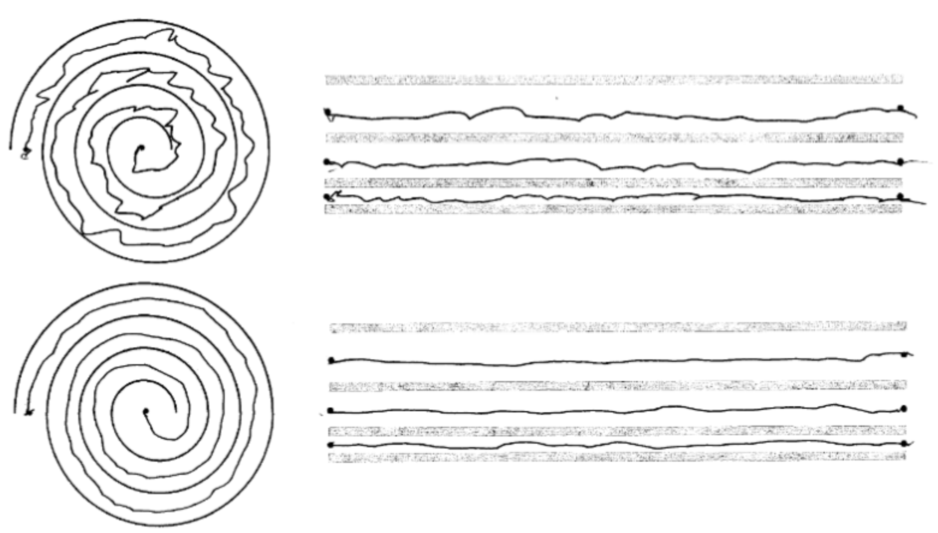

Figure 2: Example spiral and line drawing portion of the FTM test both without stimulation (top) and with adaptive DBS treatment (bottom).

Results

- Rebound effect was present in all patients by both clinical and IMU measurements, albeit in highly variable manifestations (Fig. 3 & 4)
- Mean time-to-peak by *clinical* measurements **T_{cp}=10 min (SD=5.7)**; mean gap between peak severity and steady state severity in FTM point scale, range=[0,4], **Δs_c = 0.83 (SD=0.24)**
- Mean time-to-peak by *gyroscope* measurements **T_{gp}=6.65 min (SD=0.80)**; mean percent gap between peak severity and steady state severity **Δs_g = 94% (SD=26%)**
- Percent increase in cortical beta bandpower from peak symptom severity relative to steady state **$\Delta\beta$ = 61%**

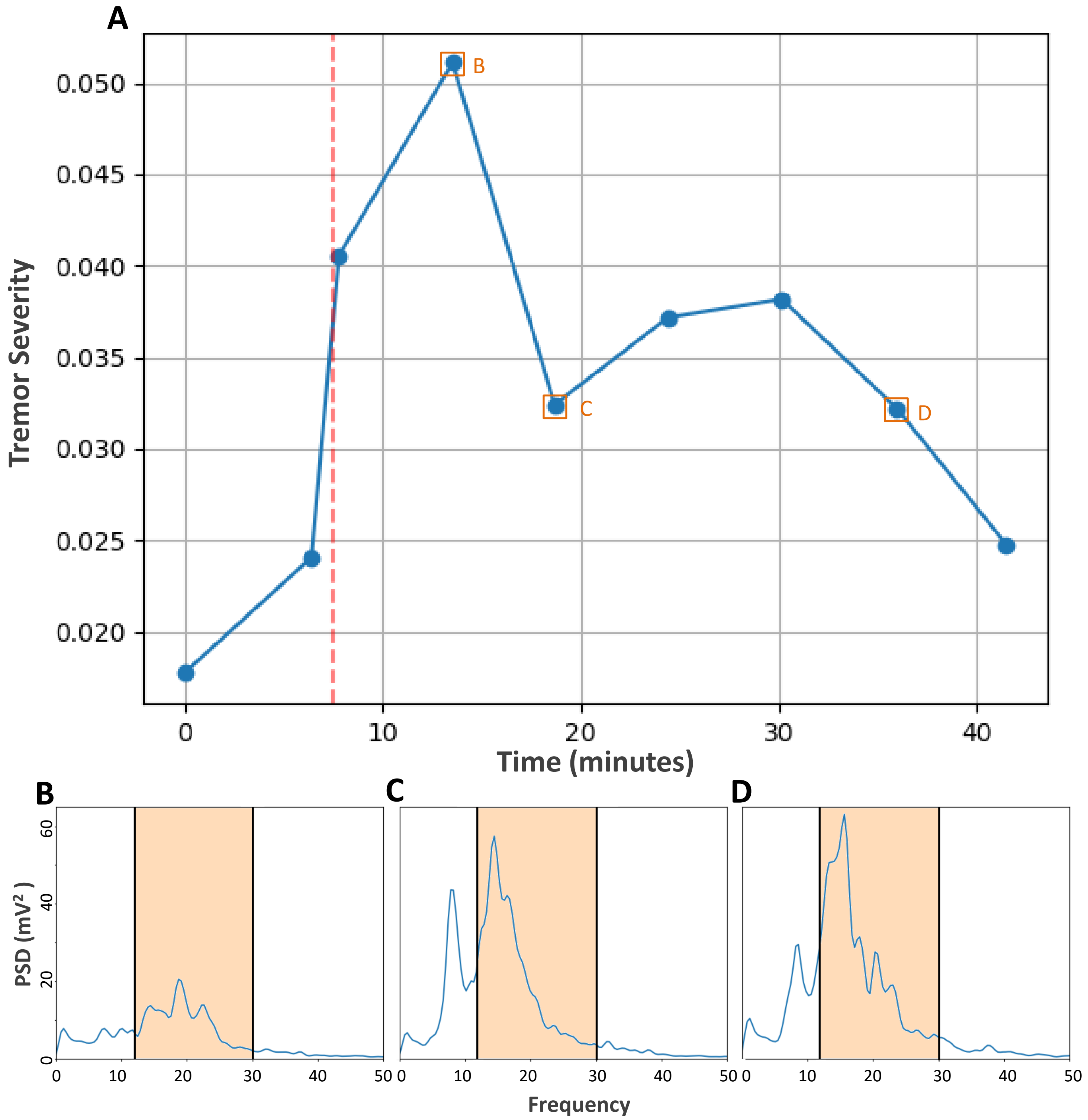

Figure 3: Rebound experiment in subject 1 with both IMU and cortical recordings from a subset of sessions. A) Tremor severity measured by IMU over course of experiment. Red dotted line indicates cessation of stimulation. Orange boxes and letters correspond to cortical recordings shown below. B-D) Cortical recordings while patient completed the drawing portion of the FTM. Beta band (12-30 Hz), which has been found to inversely correlate with "level of activity" in M1 [Kondylis 2016], in orange.

Results (cont.)

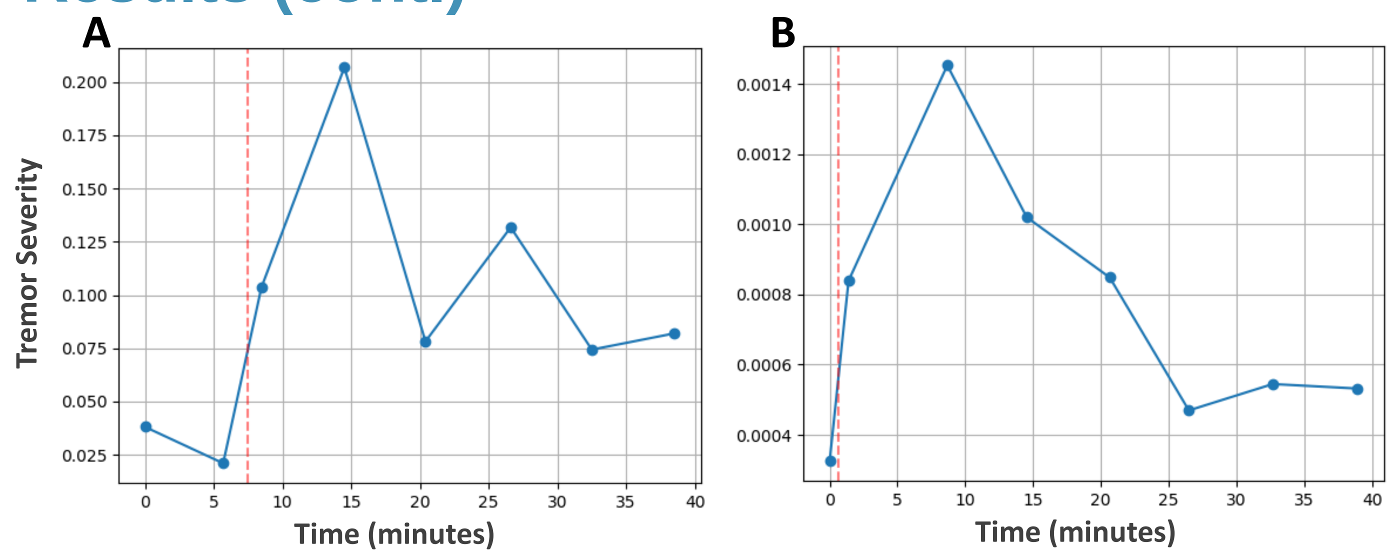

Figure 4: Severity of tremor from gyroscope data over experiment in remaining two subjects. Red dotted line indicates cessation of stimulation. A) was taken as subject 2 completed both the spiral-drawing and line-drawing components of the FTM. B) was taken while subject 3 completed only the line-drawing portion of the FTM.

Discussion

- Unlike in previous works, rebound effect was seen in all patients examined, albeit not during identical tasks; this is in line with the heterogeneity between patients typical of ET
- Also diverging from previous works, in which symptom severity peaked almost immediately after treatment was disabled, our findings indicate that there is a "ramp-down" period immediately following the cessation of stimulation
- The correlation between cortical beta bandpower and tremor severity appears to be inverse, but this relatively coarse method of assessment may be missing more nuanced, and potentially reliable, correlating neural features [Priori 2013]
- We hypothesize that beta bandpower may relate to effort required to complete a task, thus decreasing while the patient completes more difficult tasks

Conclusion

- Subsequent experiments will be focused on determining whether the decrease in beta bandpower is itself a function of the presence of tremor or a byproduct of increased effort required to accomplish a task while tremoring
- Additional investigation into which neural features are most relevant to tremor, indirectly or directly, will also be conducted
- Rebound has clear ramifications for aDBS control systems, implying that binary control may inadvertently worsen tremor substantially when disabled and as such is an undereffective means of treatment

References

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