Short-Timescale Assessment of Motor Symptomatology in Parkinson's Disease and Essential Tremor

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Introduction

Parkinson's disease (PD) affects over 4 million people worldwide, making it the second-most prevalent neurodegenerative disease behind Alzheimer's disease. Cardinal motor symptoms of PD include resting tremor, bradykinesia, rigidity, and postural or gait-related instability. Current therapies, including dopamine replacement and deep brain stimulation of the subthalamic nucleus (STN) or internal globus pallidus (GPi), aim to alleviate these hallmark motor symptoms: as such, clinical evaluation focuses on assessing their severity. Currently, clinicians use the Unified Parkinson's Disease Rating Scale (UPDRS) to quantify symptomatology in PD patients. While this scale has been validated, its subjectivity, susceptibility to inter-rater variability, and its inability to capture short-timescale fluctuations in symptomatology make it an imperfect tool.

PD researchers, clinicians, and patients have begun to harness the rise of ubiquitous mobile computing to assess symptomatology. The mPower app, which allowed patients to complete tasks designed to evaluate cognition, gait, vocal tremor, and speed/dexterity, became available on Apple's app store in 2015. Within the first year, over 1,000 participants with a confirmed diagnosis of PD enrolled in the study, indicating the promise of such an approach.

Methods

19 PD patients, 11 essential tremor (ET) patients, and 20 control subjects completed 15 short trials of the task, in which the subject must track the movement of a point around the screen with a stylus. This software was developed by James Yu, MD '19.

Using the positional data gathered through subject testing, seven metrics were calculated for 3-second epochs throughout each trial. Using a support vector machine (SVM) learning algorithm, a seven-dimensional hyperplane was generated for each patient. This hyperplane was used to derive a "symptom score," and the relative contributions of each metric to this score were collected ("metric weights"). These data were compared to same-day UPDRS motor subsection scores from corresponding PD patients using a simple linear regression model.

PD patient data were compared to pooled ET patient data using another individualized SVM classifier. This cross-comparison was chosen due to the observed heterogeneity of PD symptomatology compared to that of ET.

Results

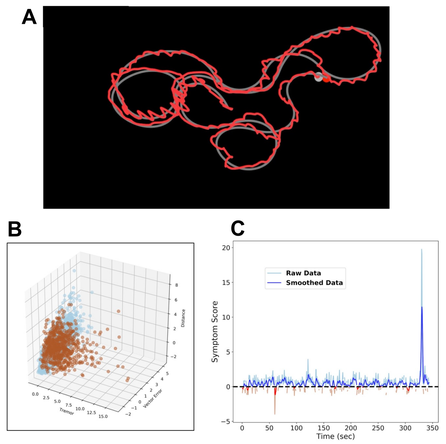

Figure 1: Multi-dimensional motor metrics approach to assessing short-timescale symptomatology. Panel (A) shows the trace the patient (red) and the target (grey) over the course of a single trial (approximately 40s in duration). In panel (B), the single-epoch scores from the same patient (brown) and a randomly-selected pool of control patient epochs (blue) for three of the seven total motor metrics used (tremor, vector error, and distance) suggests the location of a hyperplane classifier that might differentiate between these two groups of data (B). In panel (C), the symptom scores generated by a seven-dimensional SVM analysis for each epoch from this patient are plotted chronologically.

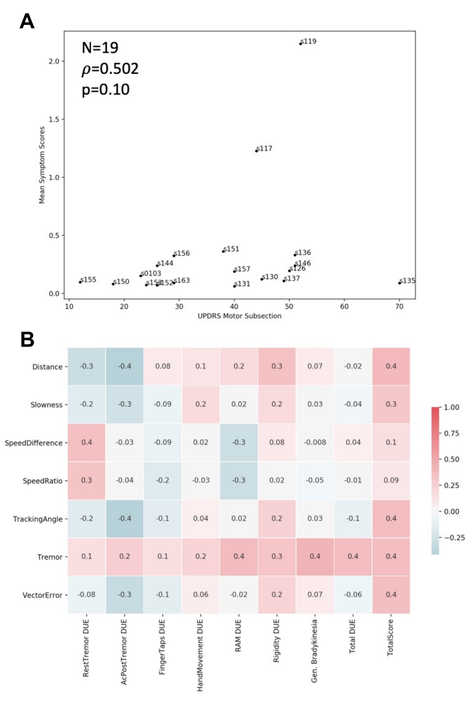

Figure 2: Correlations between motor metrics and UPDRS clinical assessments. Panel (A) shows the individual UPDRS motor subsection score on the horizontal axis and the corresponding SVM-calculated symptom score on the vertical axis of 19 PD patients. Linear regression analysis indicated a correlation between the clinical scores and the mean calculated symptom scores (Spearman's rho = 0.502, p=0.10). Panel (B) further explores this relationship by examining the correlations between individual components of the UPDRS motor subsection and our seven calculated motor metrics. A Spearman's rank correlation analysis was used to compare the mean raw score generated by each metric to each sub-component of the UPDRS motor subsection. Notable correlations include a strong positive relationship between the metric 'Tremor' and all UPDRS sub-scores The 'Tremor' metric also correlated most strongly with the total UPDRS score (ρ=0.4). The total score also correlated strongly with calculated metrics for 'Distance,' 'Slowness,' 'Tracking Angle,' 'Tremor,' and 'Vector Error.'

Results

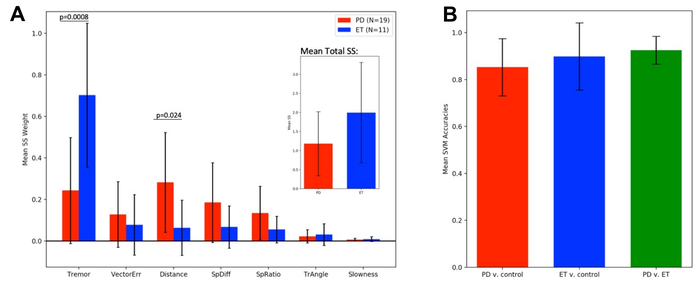

Figure 3: Multi-dimensional motor metric analysis can differentiate between PD and ET with high accuracy. Panel (A) shows mean SVM-derived calculated SS weights for PD (red) and ET patients (blue), and inset shows mean overall SS compared to controls. Panel B shows mean SVM classification accuracies for individual PD and ET patients compared to controls (left, center) and PD patients compared to polled ET patients (right). In both panels, error bars represent standard deviation and p-values are derived from two-tailed parametric T-tests.

Conclusions

- A short timescale, multi-dimensional motor metrics-based quantification of PD symptomatology provides detailed temporal information about symptom fluctuations in patients
- When averaged over a longer time course, this quantification correlates with the UPDRS motor subsection, a validated clinical scale of PD symptomatology
- The metrics calculated to assess different domains of PD motor symptomatology are also effective at differentiating between PD and a non-PD movement disorder, ET

Funding

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Selected References

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