Quantitative Keyboard Tapping Measurement Correlates with Electrophysiological Changes in STN LFPs of PD Patients Treated with Dopaminergic Medication Better Than UPDRS Subscores

Musa Ozturk1, Aviva Absch2, David Francis1, Jianping Wu3, Joohi Jimenez-Shahed4, Nuri Firat Ince4

1University of Houston, Houston, TX; 2University of Colorado, Aurora, CO; 3Medtronic, Minneapolis, MN; 4Baylor College of Medicine, Houston, TX
Contact: nince@uh.edu

Motivation
- The correlation of the symptom measures with neural patterns is important for the development of novel closed-loop therapies
- There is a need for reliable and objective assessments of the motor symptoms of patients with Parkinson’s disease

Introduction
- The inter rater reliability of UPDRS was reported to be sufficient for cardinal symptoms but its intra-rater reliability was shown to be low to moderate1
- Previous studies with computer-assisted tasks primarily focused on correlating UPDRS scores with the task measurements2
- We employed a computerized keyboard task alongside UPDRS subscores, in order to quantify the bradykinesia severity
- NOVELTY: we tested these two modalities against the pharmacological modulations of LFP subbands.

Methods
- STN-LFP recordings from nine PD patient
- Three LEDD intake cycles: ~24 hours
- Real-time UPDRS and keyboard task testing in every OFF and ON state
- UPDRS sub-items 22 (rigidity), 23-26 (bradykinesia) used for testing
- Keyboard task based on alternating finger-tapping for 30 seconds, repeated twice
- Investigated LFP subband powers: theta-alpha (4-12Hz), low-beta (13-21Hz), high-beta (21-30Hz), gamma (70-90Hz) and HFOs (200-400Hz)
- The HFO change was represented as the ratio of slow (200-300Hz) and fast (300-400Hz) HFOs since they were mutually exclusive in each state.
- Due to repeated samples, a mixed model approach was used to find the correlations

Results
- Figure 2: (i) Illustrations of some of UPDRS bradykinesia tasks: a-fingertapping, b-supination/pronation. (ii) Patient performing UPDRS fingertapping task. (iii) Patient performing computerized keyboard tapping task.

Figure 3: Raw LFP traces and accelerometer data from OFF and ON motor states of a representative patient. Alongside the dramatic suppression in accelerometer recordings, there is a clear change in the LFP oscillations as well.

Figure 4: (i) Time evolving spectra of a representative patient with data from 30 minutes before the levodopa intake and 120 minutes after the verbal ON confirmation. (ii) The distribution of power changes in individual bands. There was a significant change in all bands except high-beta and HFO (p<0.05).

Figure 5: (i) The keyboard and bradykinesia score difference between states (ON score - OFF score) for individual patients and trials. The red line marks the no change level. Bradykinesia score always indicates improvement, whereas some trials have worse keyboard score in the ON state. (ii) The scatter plot of bradykinesia vs keyboard scores correlates and forms OFF and ON clusters.

Table 1: The correlations between symptom measures (columns) and neural modulations (rows). Correlations with p value less than 0.01 are marked bold. Keyboard improvement is represented as the ratio of OFF and ON scores in order to obtain a comparable metric among patients.

| Correlation between symptom improvement and the LFP subband power changes |
|-----------------|-----------------|-----------------|
|                  | Keyboard task    | Bradykinesia    |
|                  | Thet-alpha power | Low-beta power  | High-beta power |
| r=0.43           | p=0.04           | r=0.34          | p=0.1           |
| r=0.51           | p=0.01           | r=0.28          | p=0.19          |
| r=0.39           | p=0.05           | r=0.32          | p=0.55          |
| r=0.68           | p=0.04           | r=0.24          | p=0.04          |
| Gamma power      |                  |                 |
| r=0.62           | p=0.002          | r=0.43          | p=0.04          |

Abbreviations
- HFO: High frequency oscillations
- LEDD: Levodopa equivalent daily dose
- OFF: state without medication effect
- ON: medicated motor state
- PD: Parkinson’s disease
- STN: Subthalamic nucleus
- UPDRS: Unified Parkinson’s Disease Rating Scale

References
3- Tavares T. et al. (2005), Quantitative measurements of alternating finger tapping in Parkinson’s disease correlate with UPDRS motor disability and reveal the improvement in fine motor control from medication and deep brain stimulation. Mov. Disord., 20: 1286–1298. doi:10.1002/mds.20556

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Conclusion
- Moderate correlation between keyboard task and bradykinesia score implies that they do not agree completely
- Overall, improvement in keyboard task explained the changes in the neural data better, perhaps thanks to lack of rater bias
- It is fair to admit that keyboard tapping is not a comprehensive measure of bradykinesia, so, new task designs which incorporate more information can provide a better estimate of the symptom severity3
- In short, the superior correlations obtained from keyboard scores indicate that a well-designed computerized assessment task can help determining the symptom severity in a more reliable and standardized fashion

Figure 4:
- (i) Illustrations of some of UPDRS bradykinesia tasks: a-fingertapping, b-supination/pronation. (ii) Patient performing UPDRS fingertapping task. (iii) Patient performing computerized keyboard tapping task.

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