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Portable objective assessment of upper extremity motor function in Parkinson's disease

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ABSTRACT

Introduction: Objective, portable measures of motor function for out-of-office assessments are needed in Parkinson's Disease (PD). This study had 3 objectives. First, to examine change in objective motor measurements in PD (as assessed with the Objective PD Measurement (OPDM) system). Second, to correlate objective measures with clinical features and putative PD cerebrospinal fluid (CSF) and dopaminergic imaging biomarkers. Third, to assess participant compliance with and perceptions of serial in-home motor assessments.

Methods: De novo PD subjects participating in this pilot study of the Parkinson Progression Markers Initiative (PPMI) completed OPDM assessments at home weekly for 3 months and in the clinic at baseline and 3-, 6-, and 12-months. Tasks included (i)digitography (ii)a repetitive hand tapping task and (iii)timed pegboard task. A global objective motor score (OMS) was derived from the latter three. MDS-UPDRS-III score was obtained at each time point, and CSF and dopamine transporter (DAT) SPECT at baseline.

Results: 27 participants, mean age 62.6 years, 19 male were included. A mean of 10.5 in-home assessments were completed. There was no significant change in in-home OMS over 12 weeks ($p = 0.48$). There was strong correlation between mean baseline OMS and MDS-UPDRS-III scores (spearman's rho = 0.60, $p=<0.0001$). Baseline OMS predicted 6-month MDS-UPDRS-III ($\beta = 0.80$, $p = 0.0002$) but not change in MDS-UPDRS-III score, DAT SPECT, or putative CSF biomarkers.

Conclusions: This study suggests that administration of in-home motor tasks as part of a large multicenter study is feasible and scores derived from these assessments may serve as surrogates of in-person clinician-assessed motor score.

1. Introduction

While standardized scales of motor assessment such as the Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [1] are well validated and have been widely adopted, more objective measures of motor function in Parkinson's disease (PD) are desired. Furthermore, portable measures that can be administered outside of the clinical setting, such as in participants' homes, would be of value in allowing for out-of-office assessments both for clinical care and clinical trials. Several technological advances have great potential in this regard. Some provide massive amounts of data collected over hours to days, such as wearable sensors or telephone applications that measure parameters of motion such as acceleration [2,3]. Other technologies allow for administration of specific tasks at set time points. These may be useful, among other things, for remote assessment of acute and even chronic effects of specific interventions aimed at improving motor function in PD. Their validation against clinically-relevant patient-oriented measures (reflective of patient experiences and

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quality of life), as well as putative biomarkers will be key to their widespread adoption in research and clinical care.

As part of a pilot study aimed at examining feasibility, reliability, and validity of an objective motor measure in de novo PD, a subset of participants in the Parkinsons Progression Markers Initiative (PPMI) were tested with the "Objective Parkinson's Disease Measurement" (OPDM) System. Herein, we report the baseline and longitudinal results. The primary focus of this analysis was to examine how the in-clinic OPDM scored changed over time and how these changes correlated with clinical features and putative PD cerebrospinal fluid and dopaminergic imaging biomarkers. Secondary objectives included assessment of participant compliance with the in-home portion and participant perceptions of it.

2. Methods

The PPMI study is an international multi-site prospective observational study of individuals with PD. Study aims and methodology have been published elsewhere [4]. Inclusion criteria were a diagnosis of PD based on established criteria, dopamine transporter imaging deficit on dopamine transporter SPECT scan, no anticipated need for PD treatment within 6 months of enrollment, and absence of dementia based on the clinical assessment of the site investigator. The PPMI cohort was chosen for OPDM testing for 2 main reasons. First, a cohort de novo at baseline allows for assessment not confounded by treatment effect. Second, the standardized acquisition and processing of imaging and CSF provides a unique opportunity to examine associations between the objective motor measures acquired and putative PD imaging and biofluid biomarkers.

The OPDM pilot sub-study of PPMI recruited patients participating in PPMI at 3 sites: Institute of Neurodegeneration, Oregon Health and Science University, and University of Pennsylvania. Institutional review board (IRB) approval and written informed consent were obtained at each site.

2.1. Clinical and biomarker assessments

Given the exploratory nature of this study, data from all potentially relevant motor and non-motor assessments that occurred at baseline, and all in-clinic motor assessments during the first year of the PPMI study were included in this analysis.

- Clinical motor assessments: (i) The MDS-UPDRS (including Hoehn and Yahr staging) was administered at baseline and at the 3-, 6-, and 12-month visits. As mentioned, all patients were de novo at baseline. None had initiated medications at the 6-month assessment, and 12 were on dopaminergic medications at 12-months, all of whom performed the 12-month assessment in the ON medication state. Measures of interest derived from the MDS-UPDRS score included total OFF MDS-UPRS part III motor score (MDS-UPDRSIII), MDS-UPDRS item 3.4 (finger tapping) as well as the rigidity, and tremor subscores (as defined in the supplement).
- Cognitive assessment: at screening and at the annual visit, participants were administered the Montreal Cognitive Assessment (MOCA) [5].
- Function/activities of daily living (ADL) were measured with the Schwab and England scale.
- Biofluid and imaging biomarker collection: (i) cerebrospinal fluid was collected via lumbar puncture at the baseline visit and processed as described [6] (ii) dopamine transporter (DAT) SPECT scan was conducted at the screening visit as described [4] (screening and baseline visits occurred within 45 days of each other in 85% of participants).

2.2. Objective motor assessment (OPDM measurements)

The OPDM device, manufactured by the Kinetics foundation, resembles a laptop. Its measures 10 × 6.5 × 2 inches and weighs 10.2 pounds. Participants underwent in-clinic OPDM assessments at baseline and at the 3-, 6-, and 12-month visits. In-clinic assessments occurred with each hand separately. In addition, participants took the OPDM device home and were instructed to self-administer the OPDM tasks weekly, on the same day of the week and at approximately the same time of day, for 3 months. At the end of that period, a questionnaire designed for this pilot study was administered to assess participants' experience with the device and the in-home testing.

Three tests were administered with the OPDM. Participants were instructed to perform each task as fast as possible.

(i) In the digitography task, the participant taps on a two-key keyboard with the index and 3rd digit. Key movement is detected by an optical encoder in the device. For each action, the time stamp, key side, and direction of the key movement (up or down) is recorded. A full downstroke produces 20 detections by the optical encoder corresponding to 21 unique positions for each key. Using the sequence of these actions, each key location relative to these 21 positions is tracked through time. The downstroke velocity is calculated by the OPDM as the distance traveled divided by the time elapsed in the movement of a key from the 3rd position down through the 18th position.

(ii) For the repetitive hand tapping task, the participant taps on one of two buttons placed 173 mm apart. The device records when either button is released or depressed and the time this occurs. Transition duration is recorded by the device as the time elapsed between the release of a button and the depression of the opposite button. Dwell duration is the time elapsed between the depression of a button and the release of that button. Cycle duration is the sum of dwell duration and the following transition duration.

(iii) During the eight peg pegboard test, the participant removes a peg from a hole and inserts it into a hole corresponding to the same position on the opposite side of the keyboard. The OPDM device tracks peg insertion or removal and timing of each. Transition duration is measured by the device as the time elapsed between removal of a peg and insertion of the peg on the opposite side. Dwell duration is the time elapsed between insertion of a peg and removal of the next peg. Cycle duration is the sum of a dwell duration and the following transition duration.

The primary outcome utilized in this study was the objective motor score (OMS), a score derived as follows [7]:

$$OMS = -13.45X1 + 16.87X2 + 5.485X3 + 82.2$$

Where

X1 = Log of the average of the downstroke velocities from both keys during the keyboard test.
X2 = Log of the average of the cycle duration during the pegboard test.
X3 = Log of the average of the transition durations during the keyboard test.

3. Analysis

All data included in this study were downloaded from the PPMI

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