Objective Measurement of Upper Extremity Motor Function in de novo Parkinson's Disease

Lama Chahine MD[1], Liz Uribe MS[2], Penelope Hogarth MD[3], Danna Jennings MD[4], and The Parkinson's Progression Markers Initiative*

[1]Department of Neurology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA; [2]Department of Biostatistics, University of Iowa, Iowa City, Iowa; [3] Department of Neurology, Oregon Health Sciences University; [4]Institute For Neurodegeneration, New Haven, Connecticut

Background/Objectives

Objective measures of motor function in Parkinson's disease (PD) are needed. Portable measures would allow for out-of-office assessments, useful in clinical care and trials

Validation of objective tests against clinical measures and putative biomarkers are key

The "Objective Parkinson's Disease Measurement" (OPDM) System was piloted among de novo PD patients participating in the PPMI study. We aimed to examine the association between OPDM measures and clinical features

Methods

PPMI inclusion criteria (i) diagnosis of PD based on established criteria (ii) a dopamine transporter imaging deficit on dopamine transporter SPECT scan (iii) no treatment for PD (iv) absence of dementia based on the clinical assessment of the site investigator

Clinical assessments: MDS-UPDRS and Hoehn and Yahr at 3 month, 6 month, 9 month, and 1 year visits. MOCA and screening and 1 year

Biomarker: DATscan and CSF collected at screening/baseline

OPDM measures (figure 1): (i) digitography task (ii) repetitive hand (iii) eight peg pegboard test

OMS = -13:45X1 + 16:87X2 + 5:485X3 + 82:2

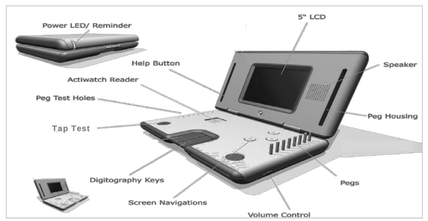
Where

X1 Log of the mean of the downstroke velocities from both keys, right and left hands combined by mean value from the keyboard test

X2 Log of the mean of the cycle duration, right and left hands combined by mean value from the pegboard test

X3 Log of the mean of the transition durations, right and left hands combined by mean impairment value from the keyboard test

Figure 1. Illustration of Objective Parkinson's Disease Measurement" (OPDM) System



(i) Digitography task: participant taps on keys with index and 3rd digit. Key movement detected by optical encoder. For each action, the time stamp, key side, and direction of the key movement is recorded and downstroke velocity is calculated

(ii) Repetitive hand tapping task: participant taps on buttons placed 173 mm apart. Device records when button released or depressed and time this occurs. Transition duration=time elapsed between release of a button and depression of opposite button. Dwell duration=time elapsed between depression of a button and release of that button. Cycle duration=sum of dwell duration and following transition duration.

(iii) Eight peg pegboard test: participant removes peg from hole and inserts it into hole corresponding to same position on opposite side of keyboard. Device tracks peg insertion or removal and timing of each. Transition duration=time elapsed between removal of peg and insertion of peg on opposite side. Dwell duration=time elapsed between insertion of a peg and removal of next peg. Cycle duration=sum of dwell duration and following transition duration.

Results

Table 1. Baseline demographic and disease characteristics

TAP-PD Demographics Table Variable	Enrolled TAP-PD Subjects N = 27
Mean age in years (SD, range)	62.6 (10.3, 37-85)
Males: Females	19:8
Education (n, %) <13 years 13-23 years	 4 (14.81) 23 (85.19)
Mean disease duration in months (SD, range)	6.1 (4.28, 1-17)
Side most affected (n, %) Right Left Symmetric	 11 (40.74) 16 (59.26) 0
Handedness (n, %) Right Left Mixed	 24 (88.89) 2 (7.41) 1 (3.70)
Mean OFF MDS-UPDRS part III score (SD, range)	21.0 (7.67; 7-36)
Mean OFF MDS-UPDRS part III bradykinesia subscore (SD, range)	6.6 (3.84; 2-17)
Hoehn & Yahr (n, %) Stage 1 Stage 2	 12 (44.44%) 15 (55.56%)
Mean MOCA Total Score (SD, range)	26.5 (1.99; 21-30)
Mean Modified Schwab & England (SD, range)	92.4 (4.68; 80-100)

Table 3. Association between baseline OMS score and disease characteristics at the baseline, 3 month, 6 month, and 1 year assessments, adjusting for age, gender, and disease duration

	Baseline (n=27)		3 months (n=26)		6 months(n=25)		1 year (n=24)	
Variable	Parameter Estimate (β, 95% CI)	p-value	Parameter Estimate (β, 95% CI)	p-value	Parameter Estimate (β, 95% CI)	p-value	Parameter Estimate (β, 95% CI)	p-value
MDS-UPDRS III (Motor Score)	0.66 (0.3767, 0.9384)	0.0001	0.6993 (0.3232, 1.0755)	0.0009	0.6531 (0.2034, 1.1028)	0.0064	0.5630 (0.2177, 0.9084)	0.0027
Total Bradykinesia Subscore	0.2839 (0.1246, 0.4431)	0.0013	0.3126 (0.1197, 0.5055)	0.0029	0.2683 (0.0673, 0.4693)	0.0112	0.1792 (-0.0298, 0.3881)	0.0891
Hoehn & Yahr	0.0326 (0.0095, 0.0557)	0.0077	0.0240 (-0.0004, 0.0484)	0.0539	0.0354 (0.0120, 0.0588)	0.0047	0.0265 (-0.0026, 0.0557)	0.0721
MoCA	-0.2158 (-0.4348, 0.0032)	0.0531	not collected		not collected		-0.2205 (-0.4950, 0.0540)	0.1099
Modified Schwab & England Activities of Daily Living	-0.0001 (-0.1023, 0.1021)	0.9985	-0.1289 (-0.4973, 0.2395)	0.4750	-0.4296 (-0.8050, -0.0542)	0.0268	-0.0136 (-0.1413, 0.1141)	0.8273

Results

27 PD patients participated in baseline visit, and 24 in 12 month visit

Baseline OMS score not significantly associated with demographic/ clinical variables (table 2)

Baseline OMS correlated with baseline OFF MDS-UPRS III scores and at each follow-up visit after adjusting for age, gender, and disease duration (table 3) but not with MoCA or S&E

OMS not significantly different at 6 month (p=0.07) or 1 year (p=0.10) assessment compared to baseline (baseline to 1 year difference: 2.22 (SE 1.32, range -0.45 to 4.88) points)

Mean change in OFF medication MDS-UPDRS from baseline to 6 months was 3.39 and from baseline to 1-year was 4.61 (p=0.020). Baseline OMS was not significantly associated with change in OFF MDS-UPDRS part III score from baseline to 6 months (p=0.98) or baseline to 1 year (p=0.64)

No association between baseline OMS scores and baseline CSF total tau, total/phospho tau ratio, synuclein, or amyloid

No association between OMS score and baseline or 1-year striatal binding ratios on DATscan SPECT

Discussion/Conclusions

OMS is likely a valid surrogate measure of motor function in early/de novo PD

OMS did not have prognostic value in predicting rate of change in MDS-UPDRS and was not significantly associated with CSF biomarkers nor dopamine transporter binding

Based on this preliminary data, the OPDM device is a useful tool to objectively assess motor function. Its utility for remote motor testing in clinical trials warrants study

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