Differential Response of Speed, Amplitude, and Rhythm to Dopaminergic Medications in Parkinson's Disease

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Introduction

Although slowness (bradykinesia), decreased amplitude (hypokinesia), and dysrhythmia of movements may be associated with differential impairment and disability in Parkinson's disease (PD), clinicians are instructed to rate rapid alternating movements into a combined 0-4 severity scale through the Unified Parkinson's Disease Rating Scale motor subscale (UPDRS-III). Clinical raters consider multiple aspects of movement including speed, amplitude, hesitations, fatiguing, and arrests in movement. Previous research has shown that individual clinicians weigh individual components of bradykinesia differently, thus creating a considerable degree of variability across clinicians. The objective of this study is to evaluate motor function and response to dopaminergic medication in patients with PD with various impairments in speed, amplitude, and rhythm of movement.

Methods

Eighty-five PD patients (Table 1) performed UPDRS-directed finger tapping, hand grasping, and pronation/supination tasks in the OFF (12-15 hours after dopaminergic drug withdrawal) and ON states while wearing wireless six-degree-of-freedom motion sensors (KinetiSense™, CleveMed) on the index finger and thumb (Figure 1). Each motion sensor contains three orthogonal accelerometers for measuring linear acceleration and three orthogonal gyroscopes for measuring angular velocity. A Modified Bradykinesia Rating Scale (MBRS) separately assessed speed, amplitude, and rhythm during the tasks on a 0 4 scale (Table 2). Quantitative variables representing speed (root-mean-square [RMS] angular velocity), amplitude (RMS excursion angle), and rhythm (coefficient-of-variation) were extracted from kinematic data, correlated with clinical MBRS scores, and used to classify patients as hypokinetic, bradykinetic, dysrhythmic, or a combination of the three. Additionally, fatigue was measured as decreases in speed and/or amplitude during the last five seconds compared to the first five seconds of movement.

Table 1. Subject Demographics

Age (yr) (mean ± SD [range])	64.6 ± 9.1 (46-85)
Gender	56 men, 29 women
Disease Duration (yr) (mean ± SD [range])	9.5 ± 5.6 (2-31)
UPDRS-III OFF (0-108; high: worse) (mean ± SD [range])	25.7 ± 11.1 (4.5-66)
UPDRS-III ON (0-108; high: worse) (mean ± SD [range])	16.7 ± 9.9 (1-60.5)
Hoehn and Yahr OFF (0-5; high: worse) (mean ± SD [range])	2.4 ± 0.6 (1-5)
Hoehn and Yahr ON (0-5; high: worse) (mean ± SD [range])	2.2 ± 0.5 (1-4)

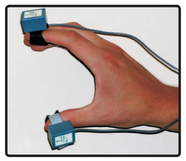


Figure 1. Motion sensors placed on the index finger and thumb recorded kinematic data while subjects performed finger tapping, hand grasping, and pronation/supination tasks.

Table 2. Modified Bradykinesia Rating Scale[1]

Score	Speed	Amplitude	Rhythm
0	Normal	Normal	Regular, no arrests or pauses in ongoing movement
1	Mild slowing	Mild reduction in amplitude in later performance, most movements close to normal	Mild impairment, up to two brief arrests in 10 seconds, none lasting > 1 second
2	Moderate slowing	Moderate, reduction in amplitude visible early in performance but continues to maintain 50% amplitude through most of the tasks	Moderate, 3 to 4 arrests in 10 seconds; 1 or 2 lasting > 1 second
3	Severe slowing	Severe, less than 50% amplitude through most of the task	Severe, 5 or more arrests/10 seconds; more than 2 lasting > 1 second
4	Can barely perform the task	Can barely perform the task	Can barely perform the task

[1]A. Kishore, A.J. Espay, C. Marras, T. Al-Khairalla, T. Arenovich, A. Asante, J. Miyasaki, and A.E. Lang, "Unilateral versus bilateral tasks in early asymmetric Parkinson's disease: Differential effects on bradykinesia," Movement Disorders, vol. 22, 2007, pp. 328-333.

Subgroup Classification

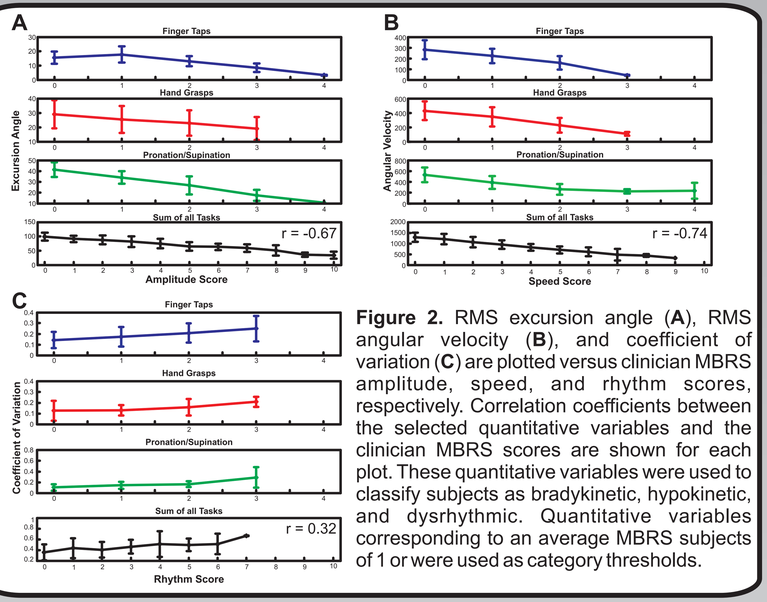


Figure 2. RMS excursion angle (**A**), RMS angular velocity (**B**), and coefficient of variation (**C**) are plotted versus clinician MBRS amplitude, speed, and rhythm scores, respectively. Correlation coefficients between the selected quantitative variables and the clinician MBRS scores are shown for each plot. These quantitative variables were used to classify subjects as bradykinetic, hypokinetic, and dysrhythmic. Quantitative variables corresponding to an average MBRS subjects of 1 or were used as category thresholds.

Clinical Results

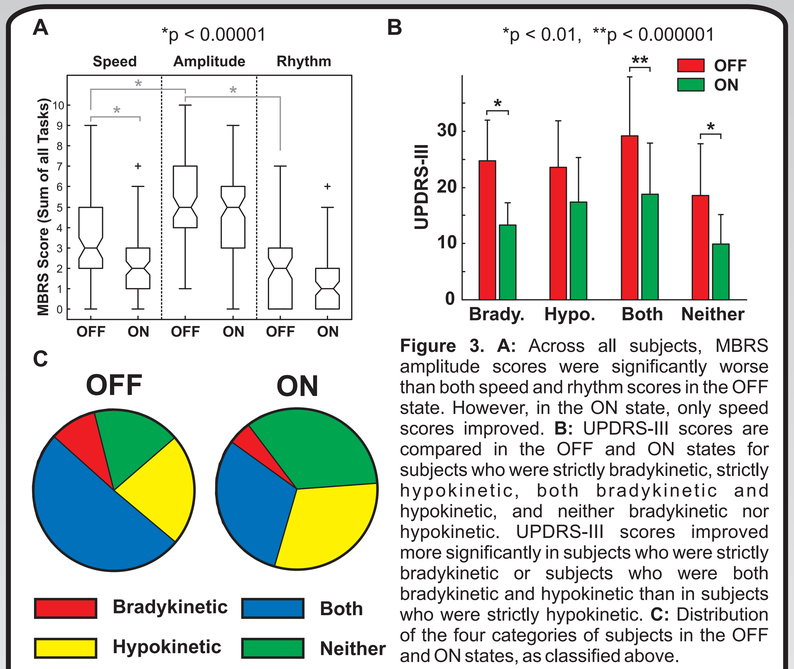
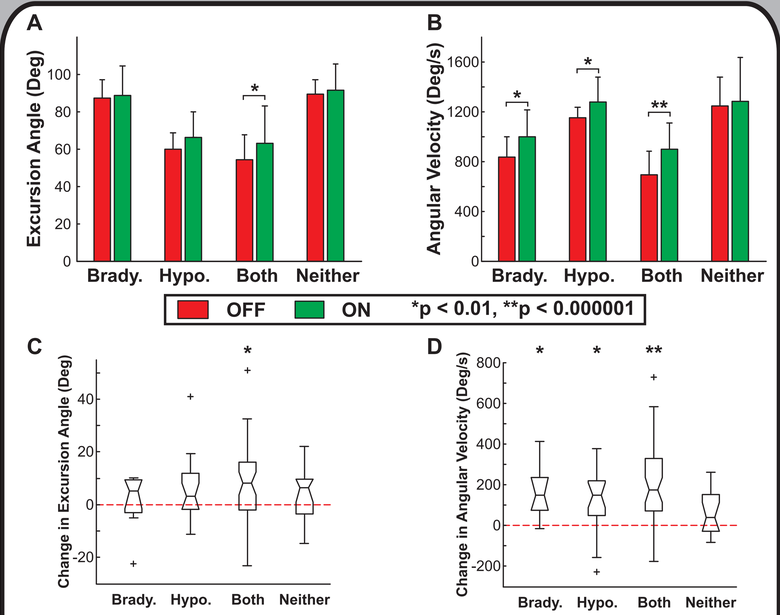


Figure 3. A: Across all subjects, MBRS amplitude scores were significantly worse than both speed and rhythm scores in the OFF state. However, in the ON state, only speed scores improved. **B:** UPDRS-III scores are compared in the OFF and ON states for subjects who were strictly bradykinetic, strictly hypokinetic, both bradykinetic and hypokinetic, and neither bradykinetic nor hypokinetic. UPDRS-III scores improved more significantly in subjects who were strictly bradykinetic or subjects who were both bradykinetic and hypokinetic than in subjects who were strictly hypokinetic. **C:** Distribution of the four categories of subjects in the OFF and ON states, as classified above.

Quantitative Comparison



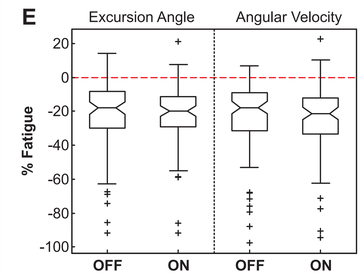


Figure 4. Excursion angle (**A**) and angular velocity (**B**), representing amplitude and speed, respectively, are compared in the OFF and ON states. The changes in excursion angle (**C**) and angular velocity (**D**) from the OFF to the ON state are compared to zero (dashed red line). Excursion angle only improved significantly in subjects both bradykinetic and hypokinetic, while angular velocity improved in all affected groups. Fatigue in both amplitude and speed was not improved in the ON state (**E**). The coefficient of variation (rhythm) did not improve significantly in the ON state for dysrhythmic subjects (not shown).

Conclusions

Our data suggest that although amplitude is the most affected manifestation of movement impairment, dopaminergic medications improve speed to a greater extent than amplitude, fatigue, or dysrhythmia. Quantitative variables extracted from the kinematic data recorded using the motion sensors provided a high degree of sensitivity for examining separately speed, amplitude, and rhythm. These movement components are differentially associated with motor impairment in PD and deserve separate measurement in research studies.

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