Differential Response of Bradykinesia and Hypokinesia to Levodopa in Parkinson's Disease

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Introduction

Although slowness (bradykinesia) and decreased amplitude (hypokinesia) of movements may be associated with differential impairment and disability in Parkinson's disease (PD), clinicians are asked 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.

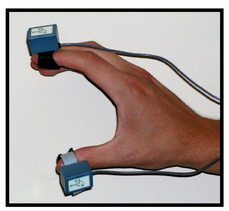
The objective of this study is to evaluate the motor function and response to dopaminergic drugs in patients with PD with various impairments in speed and amplitude of movement. Speed and amplitude are evaluated separately to determine if bradykinesia and hypokinesia should deserve separate clinical assessment.

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) was used to assess separately speed and amplitude during the tasks on a 0 – 4 scale (Table 2). Quantitative variables representing speed (root-mean-square [RMS] angular velocity) and amplitude (RMS excursion angle) were extracted from kinematic data, correlated with clinical MBRS scores, and used to classify patients as hypokinetic, bradykinetic, both, or neither.

Table 1. Patient 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)



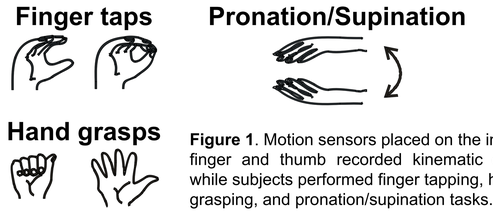


Figure 1. Motion sensors placed on the index finger and thumb recorded kinematic data while subjects performed finger tapping, hand grasping, and pronation/supination tasks.

Table 2. Modified Bradykinesia Rating Scale[1]

Score	Speed	Amplitude
0	Normal	Normal
1	Mild slowing	Mild reduction in amplitude in later performance, most movements close to normal
2	Moderate slowing	Moderate, reduction in amplitude visible early in performance but continues to maintain 50% amplitude through most of the tasks
3	Severe slowing	Severe, less than 50% amplitude through most of the task
4	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

RMS excursion angle and angular velocity were found to be highly correlated with clinician MBRS scores for amplitude and speed, respectively (Figure 2). These quantitative variables were used to classify subjects as bradykinetic only, hypokinetic only, both bradykinetic and hypokinetic, or neither bradykinetic nor hypokinetic. Subjects with average excursion angles worse than that corresponding to an average MBRS amplitude score of 1 were classified as hypokinetic, while subjects with average angular velocities worse than that corresponding to an average MBRS speed score of 1 were classified as bradykinetic.

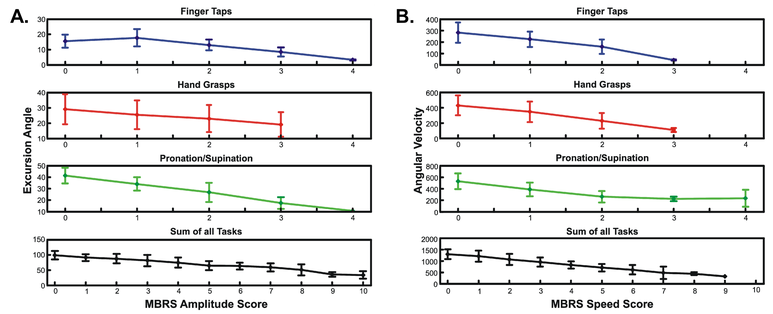


Figure 2. Excursion angle (**A**) and angular velocity (**B**) are plotted versus clinician MBRS amplitude and speed scores, respectively. When summing scores across all tasks, excursion angle was highly correlated with amplitude scores (r = -0.67) and angular velocity was highly correlated with speed scores (r = -0.74).

Clinical Results

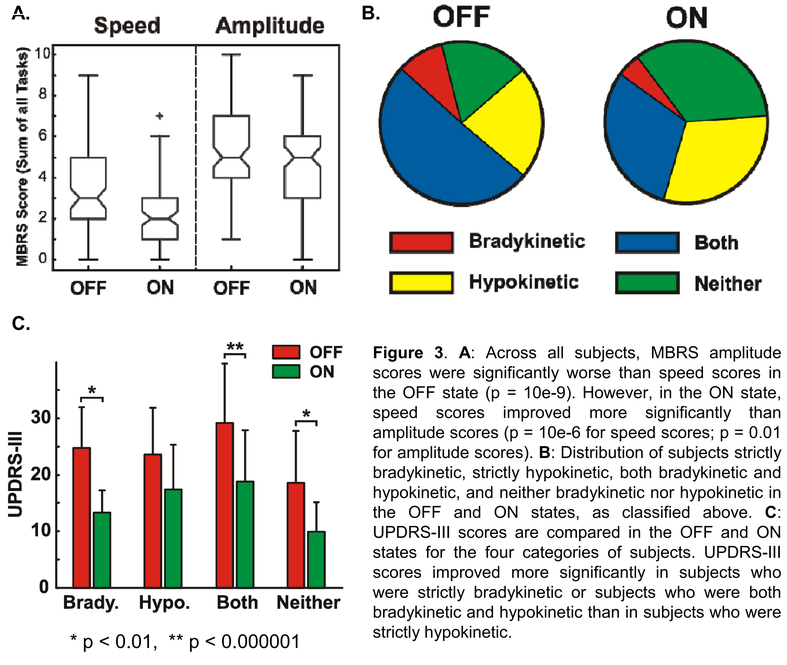


Figure 3. **A**: Across all subjects, MBRS amplitude scores were significantly worse than speed scores in the OFF state (p = 10e-9). However, in the ON state, speed scores improved more significantly than amplitude scores (p = 10e-6 for speed scores; p = 0.01 for amplitude scores). **B**: Distribution of subjects strictly bradykinetic, strictly hypokinetic, both bradykinetic and hypokinetic, and neither bradykinetic nor hypokinetic in the OFF and ON states, as classified above. **C**: UPDRS-III scores are compared in the OFF and ON states for the four categories of subjects. 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.

Quantitative Comparison

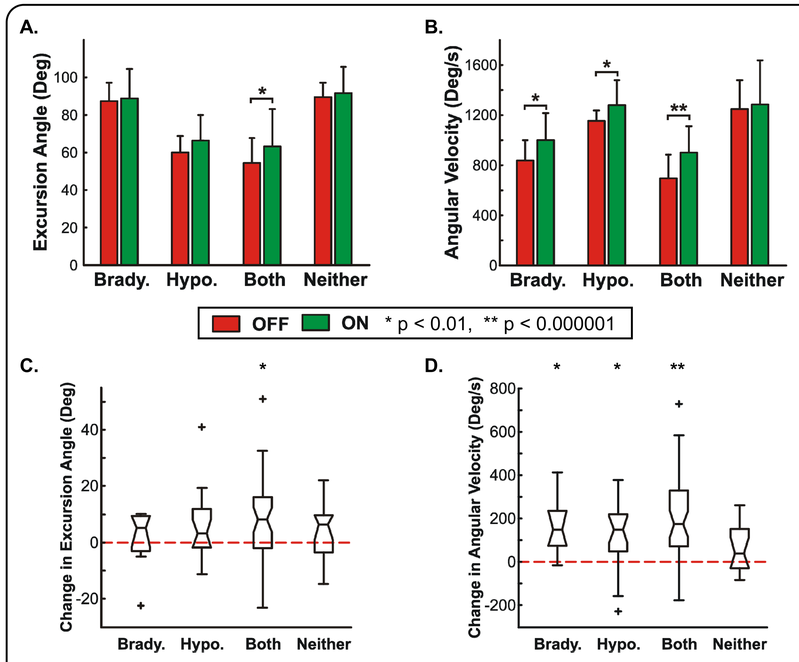


Figure 4. Excursion angle (**A**) and angular velocity (**B**), representing amplitude and speed, respectively, are compared on the OFF and ON states. The changes in excursion angle (**C**) and angular velocity (**D**) from the OFF to the ON state are compared to zero (dashed red line). Excursion angle only improved significantly in subjects both bradykinetic and hypokinetic, while angular velocity improved in all affected groups.

Conclusions

While hypokinesia was more common and more pronounced than bradykinesia, our data suggest that dopaminergic drugs normalize bradykinesia more significantly than hypokinesia. Quantitative variables extracted from the kinematic data recorded using the motion sensors provided a high degree of sensitivity for examining separately speed and amplitude. Speed deficits were improved in all affected subgroups, while amplitude deficits were only significantly improved in subjects with speed deficits in addition to amplitude deficits. Speed and amplitude of movement are differentially associated with motor impairment in PD and deserve separate measurement in research studies.

Acknowledgements

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