Home-based Motion Sensor Monitoring for Parkinson's Disease Clinical Trials

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Introduction

Clinical trials of new symptomatic and neuroprotective treatments for Parkinson's disease (PD) often involve dozens of sites and thousands of participants. These clinical trials typically rely on subjective rating scales, which can suffer from bias, placebo effects, limited resolution, and poor intra- and inter-rater reliability. Additionally, symptoms that tend to fluctuate throughout the day cannot be monitored in a single visit. To compensate for this lack of temporal resolution, study participants are often asked to complete daily diaries; however, these diaries yield suboptimal data due to poor compliance, recall bias, and inaccurate self-assessment. The objective of this study is to determine the reliability of a home-based motion sensor system compared to traditional measures for gauging PD motor symptom and side-effect severities.

Experimental Methods

Eighteen patients with PD (13 males; mean age 63.1±8.4 years, range: 44-76) and treated with subthalamic deep brain stimulation (DBS) performed tasks evaluating tremor and bradykinesia while wearing a wireless motion sensor unit (Kinesia™, Great Lakes NeuroTechnologies, Cleveland, OH) on the index finger (Figure 1). Kinesia, which outputs motor scores on a 0-4 scale with 0.1 resolution, has been previously described and validated for assessing tremor, bradykinesia, and dyskinesia associated with PD.

Figure 1. Kinesia includes a wireless finger-worn motion-sensor unit (**A**) and a touch screen tablet PC with inductive charge (**B**). The automated motor assessment included three 15-second tasks (**C**). The first two tasks were assessments of rest and postural tremor, while the third task involved repetitive finger tapping to evaluate bradykinesia (speed), hypokinesia (amplitude), and dysrhythmia (rhythm).

The sequence of three tasks was performed three separate times with DBS turned off and on at 10 separate stimulation amplitudes, as DBS provides a unique opportunity slowly modulate symptom severity (Figure 2). This study paradigm provided a wide range of symptom severities with relatively few subjects. It also simulated subtle motor symptom progressions in individual subjects in a manner that otherwise might take years to observe. Each task was digitally videoed for subsequent blinded rating by two clinicians according to Unified Parkinson's Disease Rating Scale (UPDRS) and Modified Bradykinesia Rating Scale (MBRS) criteria. Test-retest reliability was calculated as intraclass correlation (ICC).

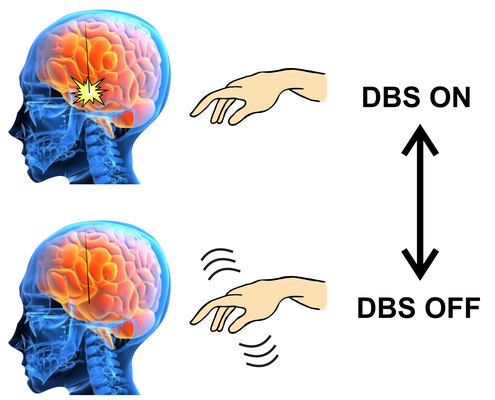

Figure 2. DBS voltage output amplitude was slowly adjusted to modulate the severity of parkinsonism during testing sessions.

In a separate study, patients with PD used Kinesia in the home once per hour for two consecutive days during each of two weeks to evaluate tremor, bradykinesia, and dyskinesia along with the traditional dyskinesia diary, which asks study participants to indicate their predominant status every half hour as OFF, ON without dyskinesia, ON with non-troublesome dyskinesia, or ON with troublesome dyskinesia.

Test-Retest Reliabilty

	Clinician ICC	Kinesia ICC	Percent fewer subjects	Number of subjects based on Clinicians	Number of subjects based on Kinesia
Rest Tremor	0.63	0.68	7.5	100	93
Postural Tremor	0.68	0.71	3.9	100	96
Speed	0.62	0.94**	34.6	100	65
Amplitude	0.72	0.94**	23.3	100	77
Rhythm	0.45	0.63*	28.3	100	72

*p<0.05, **p<0.0001

Table 1. Based on ICC differences, Kinesia would reduce the number of participants required for a clinical trial by up to 35% compared to trials using clinician scores (numbers in the right-most column assume 100 study participants would be required if clinician scores were used).

Diary Comparison

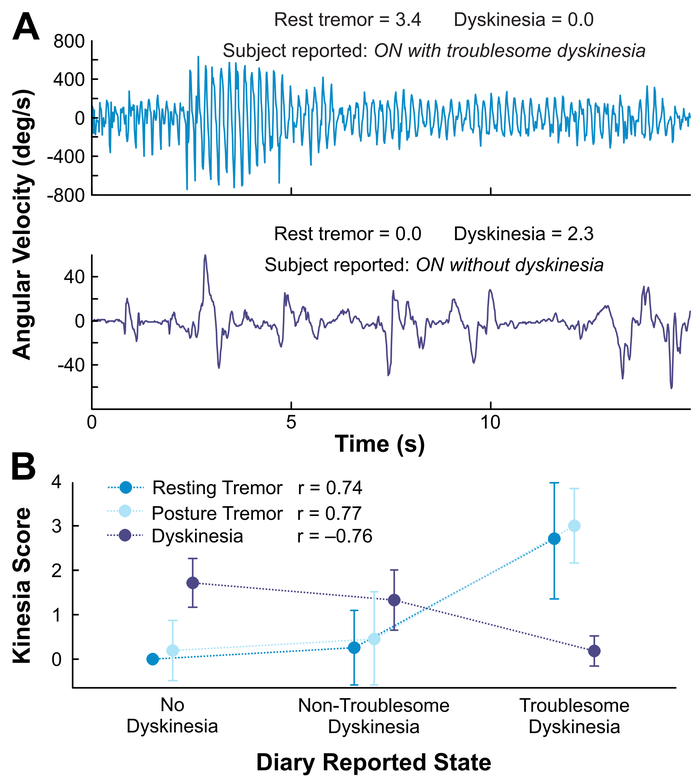

Figure 3. A) Angular velocities recorded from one of the gyroscopes in the motion sensor unit are plotted during two home-based assessments of resting tremor and dyskinesia performed by a single participant. The top plot shows oscillatory movement indicating tremor while the bottom plot shows low-amplitude, irregular movements indicating dyskinesias. However, based on her dyskinesia diary responses, the participant inaccurately marked tremor as dyskinesia and did not notice when dyskinesia occurred. **B)** Average tremor and dyskinesia scores are plotted for each state marked in the dyskinesia diary (this participant did mark any time as OFF). The correlations between Kinesia scores and diary-reported state indicate this participant consistently inaccurately identified her states.

Conclusions

- Motion sensors can provide increased test-retest reliability over clinical assessments.
- The increased reliability afforded by motion sensors over clinical assessments **can decrease the number of subjects, shorten the duration, and lower the costs** required detect significant outcomes in clinical trials.
- Home-based motion sensor monitoring can improve temporal resolution and reduce variability due to inaccurate self-assessment.

This work was supported by NIH/NINDS 1R43NS074627-01A1.

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