Developing a Tool for Remote Digital Assessment of Parkinson's Disease

Panagiotis Kassavetis, MD,[1,2] Tabish A. Saifee, MD,[1] George Roussos, PhD,[3] Loukas Drougkas, MSc,[3] Maja Kojovic, PhD,[1,4] John C. Rothwell, PhD,[1] Mark J. Edwards, PhD,[1] Kailash P. Bhatia, MD[1,*]

Abstract: Background: The natural fluctuation of motor symptoms of Parkinson's disease (PD) makes judgement of any change challenging and the use of clinical scales such as the International Parkinson and Movement Disorder Society (MDS)-UPDRS imperative. Recently developed commodity mobile communication devices, such as smartphones, could possibly be used to assess motor symptoms in PD patients in a convenient way with low cost. We provide the first report on the development and testing of stand-alone software for mobile devices that could be used to assess both tremor and bradykinesia of PD patients.
Methods: We assessed motor symptoms with a custom-made smartphone application in 14 patients and compared the results with their MDS-UPDRS scores.
Results: We found significant correlation between five subscores of MDS-UPDRS (rest tremor, postural tremor, pronation-supination, leg agility, and finger tapping) and eight parameters of the data collected with the smartphone.
Conclusions: These results provide evidence as a proof of principle that smartphones could be a useful tool to objectively assess motor symptoms in PD in clinical and experimental settings.

Patients with Parkinson's disease (PD) commonly experience symptoms that fluctuate in intensity over the course of the day and in relation to their medication dosing. This makes it quite complex to assess symptom burden accurately and judge whether medication changes or other therapeutic interventions might help improve function and reduce disability. Similarly, accurate assessment of benefit in clinical trials of medication and other interventions in patients with PD is made more difficult by the fluctuating nature of the symptoms. Traditionally, assessments are made at clinic visits using objective clinical rating scales, such as the International Parkinson and Movement Disorder Society (MDS)-UPDRS,[1] using patient diaries or other self-completed scales. More-precise objective assessment of tremor, bradykinesia, and gait can be performed using laboratory equipment, for example, accelerometers and gyroscopes. All these methods are useful, but have their disadvantages. Objective clinical rating and laboratory assessment require the presence of the patient and, by its nature, can only realistically be carried out as a "snap-shot" assessment. Patient diaries are well accepted to be complex to fill out, and compliance with such instruments is very poor. They also do not allow objective quantification of symptoms.

During the last few years, a remarkable development of commodity mobile communication devices, such as smartphones, has occurred. They are now commonly equipped with accelerometers and gyroscopes that can provide accuracy comparable to that obtained in the laboratory. They are remarkably powerful and are available at a relatively low cost. These properties have triggered some efforts to utilize them for evaluation of parameters of normal and abnormal movements, but to date solely for assessment of tremor in PD.[2–4] In parallel with the accelerometers and gyroscopes, the touch screens of such smartphones are very sensitive and capable of sampling many different parameters, providing an opportunity for bradykinesia assessment akin to keyboard-based tests that have been used in previous studies.[5,6]

[1]Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, Queen Square, London, United Kingdom; [2]Department of Neurology, Boston University, Boston, Massachusetts, USA; [3]Birkbeck, University of London, London, United Kingdom; [4]Department of Neurology, University Medical Center, Ljubljana, Slovenia

*Correspondence to: Prof. Kailash P. Bhatia, Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, Queen Square, London, WC1N 3BG, United Kingdom; E-mail: kbhatia_editor@movementdisorders.org

In this article, we provide the first report on the development and testing of stand-alone software for mobile devices that could be used to assess their motor symptoms of PD for clinical trials or as part of routine clinical follow-up.

Patients and Methods

Participants

A total number of 14 patients (mean age: 54.7; range, 34–75; 7 women) were consecutively recruited from the movement disorder clinic in the National Hospital for Neurology and Neurosurgery, Queen Square, London (Table 1). All patients fulfilled the UK Queen Square Brain Bank diagnostic criteria[7] and had abnormal dopamine transporter single-photon emission computed tomography scan. All patients were assessed when *off* medication (at least 8 hours after last dose). Written informed consent was obtained from all participants.

Design

All patients attended a single experimental session where clinical severity of motor symptoms was assessed with the MDS-UPDRS[1] and with the smartphone in random order. Data were collected bilaterally. Patients were given verbal instruction before each of the smartphone tests. The duration of each test was 30 seconds except for the finger tapping, which was 60 seconds. All data collected with the smartphone and was analyzed offline. The experimental session lasted approximately 30 minutes.

Measurements were carried out using an HTC Desire smartphone with a 1-GHz ARMv7 Snapdragon processor running the 2.2 version of the Android operating system. This device carries the high-precision BMA150 digital 3-axis accelerometer, which can sample as a maximum frequency of 1,500 Hz. However, the manufacturer restricts the maximum sampling rate to 50 Hz (obtained by setting the Android Sensor Manager to a sampling rate of SENSOR_DELAY_FASTEST) to achieve

balanced power consumption. All recordings were carried out with this sampling rate set and confirmed by the recorded logs, which were more than adequate for detecting tremor in this context. The HTC Desire also carries a 480×800 pixel S-LCD capacitive panel screen at approximately 252 ppi pixel density that was employed to capture tapping task input.

### Data Collection and Analysis

Tremor

Tremor recordings were made in both hands at rest, at posture, and in action. For rest tremor recordings, patients were asked to relax their hands on their lap in a supine position while the phone was lying in their palm. For the postural tremor recordings, patients were instructed to keep their arm outstretched straight in front of them while holding the phone. For the action tremor recordings, patients were asked to hold the phone and move it between their chest and the totally outstretched position in front of them. For all tremor recordings, the acceleration in x, y, and z axes (m/s^2) and the time (ms) were recorded. The magnitude of the scalar sum acceleration in the three axes $\sqrt{(x^2 + y^2 + z^2)}$ was filtered with a Butterworth high-pass second-order filter at 2 Hz. Fast Fourier transform converted the filtered waveform data into a power spectrum, and the tremor power was calculated as the total power of the frequencies between 2 to 10 Hz. For the signal analysis for all accelerometric data, the software Spike2 v6.15 (Cambridge Electronic Design Ltd., Cambridge, UK) was used.

Bradykinesia

For assessment of bradykinesia, we assessed pronation-supination movements and leg agility with the accelerometers and finger tapping with the touch screen. In the first test, patients were asked to hold the phone and perform alternating pronation-supination movements as fast and as fully as possible. For the leg agility test, the phone was placed on their thigh and they were instructed to hold it lightly with their ipsilateral hand, while raising and stomping the foot on the ground as high and as fast as possible. In the finger-tapping test, two targets were presented in the two edges of the screen and patients were instructed to tap them alternatively as fast and as accurately as possible (Fig. 1). For analysis of the pronation-supination movements and leg agility tests, we removed DC and applied a Butterworth low-pass second-order filter at 4 Hz in order to exclude most of the tremor. The frequency of the movement was derived from the power spectrum. The power of the movement was calculated as the total power between 0 and 4 Hz. For the finger-tapping tests, all tappings within the screen were included in the analysis. In case the subjects were accidentally tapping outside the screen, the trial was restarted. We measured the frequency of the taps (number of taps per second), the mean time that the hand was moving from one target to the next (moving time – ms) and the distance between alternative tapings (number of pixels).

TABLE 1 Patients' demographic and clinical characteristics

Subject No.	Gender	Age (Years)	Disease Duration (Months)	Dopaminergic Treatment
1	F	61	72	Levodopa
2	F	52	42	Levodopa
3	M	71	28	Not treated
4	M	64	24	Not treated
5	F	52	46	Levodopa
6	M	75	70	Levodopa
7	F	40	84	Pramipexole, rasagiline
8	F	34	28	Ropinirole
9	M	50	48	Not treated
10	F	56	8	Ropinirole
11	M	66	9	Rasagiline
12	M	49	24	Rasagiline
13	M	55	80	Not treated
14	F	41	60	Pramipexole, rasagiline
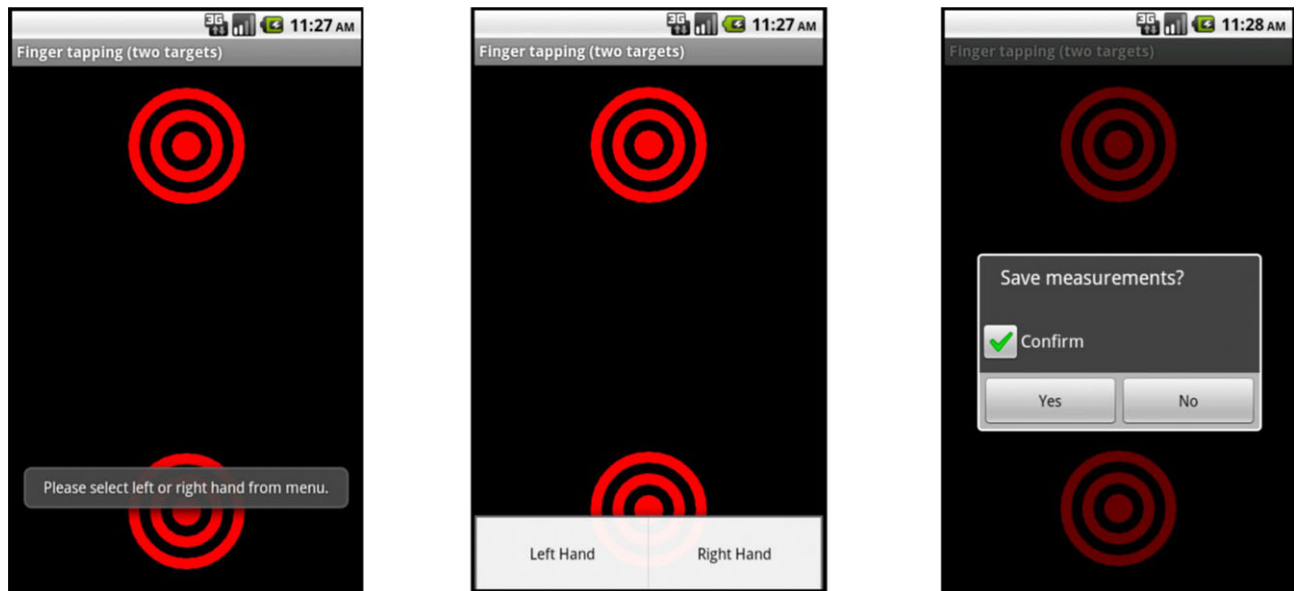
Figure 1 Screen shots of the smartphone during the finger-tapping task.

Statistical Analysis

In order to explore the agreement between the MDS-UPDRS scores and the assessed symptoms with the smartphone, we performed bivariate correlation analysis of the variables as they are shown in Table 2. Assumptions of parametric data were tested and data were found to be nonparametric. Spearman's rho test was used for bivariate correlations. IBM SPSS software (IBM Corp, Armonk, NY) was used for statistical analysis.

Results

Tremor

Mean frequency of the rest tremor was found to be 4.33 Hz (standard deviation [SD] = 1.36). The power of rest tremor as

TABLE 2 MDS-UPDRS subscores and smartphone variables for tremor and bradykinesia

	Smartphone Recordings	MDS-UPDRS
Tremor	Rest tremor (**amplitude**)	3.17 (rest tremor amplitude)
	Postural tremor (**amplitude**)	3.15 (postural tremor of the hands)
	Action tremor (amplitude)	3.16 (kinetic tremor of the hands)
Bradykinesia	Pronation-supination movements (**amplitude and frequency**)	3.6 (pronation-supination movements of hands)
	Leg agility (**amplitude** and frequency)	3.8 (leg agility)
	Finger tapping (**frequency, mean moving time, mean distance between taps**)	3.4 (finger tapping)

Smartphones variables that significantly correlate with MDS-UPDRS are presented in bold.

recorded with the phone was correlated significantly with the 3.17 (rest tremor) MDS-UPDRS score (r = 0.60; $P < 0.001$). Mean dominant frequency for the postural tremor was 4.91 Hz (SD = 1.84), and its power also correlated significantly with the 3.15 (postural tremor of the hands) MDS-UPDRS score (r = 0.65; $P < 0.001$). The power of the kinetic tremor did not correlate significantly with the MDS-UPDRS scores (r = −0.17; $P = 0.420$; Figs. 2 and 3).

Bradykinesia

The 3.6 (pronation supination movements) MDS-UPDRS score correlated significantly with both the movement power (r = −0.72; $P < 0.001$) and frequency (r = −0.55; $P = 0.003$). Similarly, the 3.8 (leg agility) MDS-UPDRS scores correlated significantly with the leg movement power as measured by the phone (r = −0.5; $P = 0.015$), but not with the frequency (r = −0.31; $P = 0.162$). Finally, the 3.4 (finger tapping) MDS-UPDRS score correlated significantly with the tapping frequency on the phone (r = −0.75; $P = 0.001$), the mean moving time (r = 0.65; $P = 0.001$), and the distance between taps (r = −0.61; $P = 0.003$; Figs. 2 and 3).

Discussion

Our data presented in this article indicate that mobile communication devices such as smartphones could be used to objectively assess motor symptoms in patients with PD. We found significant correlation of five subscores of the MDS-UPDRS (rest tremor, postural tremor, pronation–supination, leg agility, and finger tapping) and eight smartphone variables. This is the first time that a smartphone has been used to holistically assess motor symptoms in PD patients including tremor and bradykinesia.
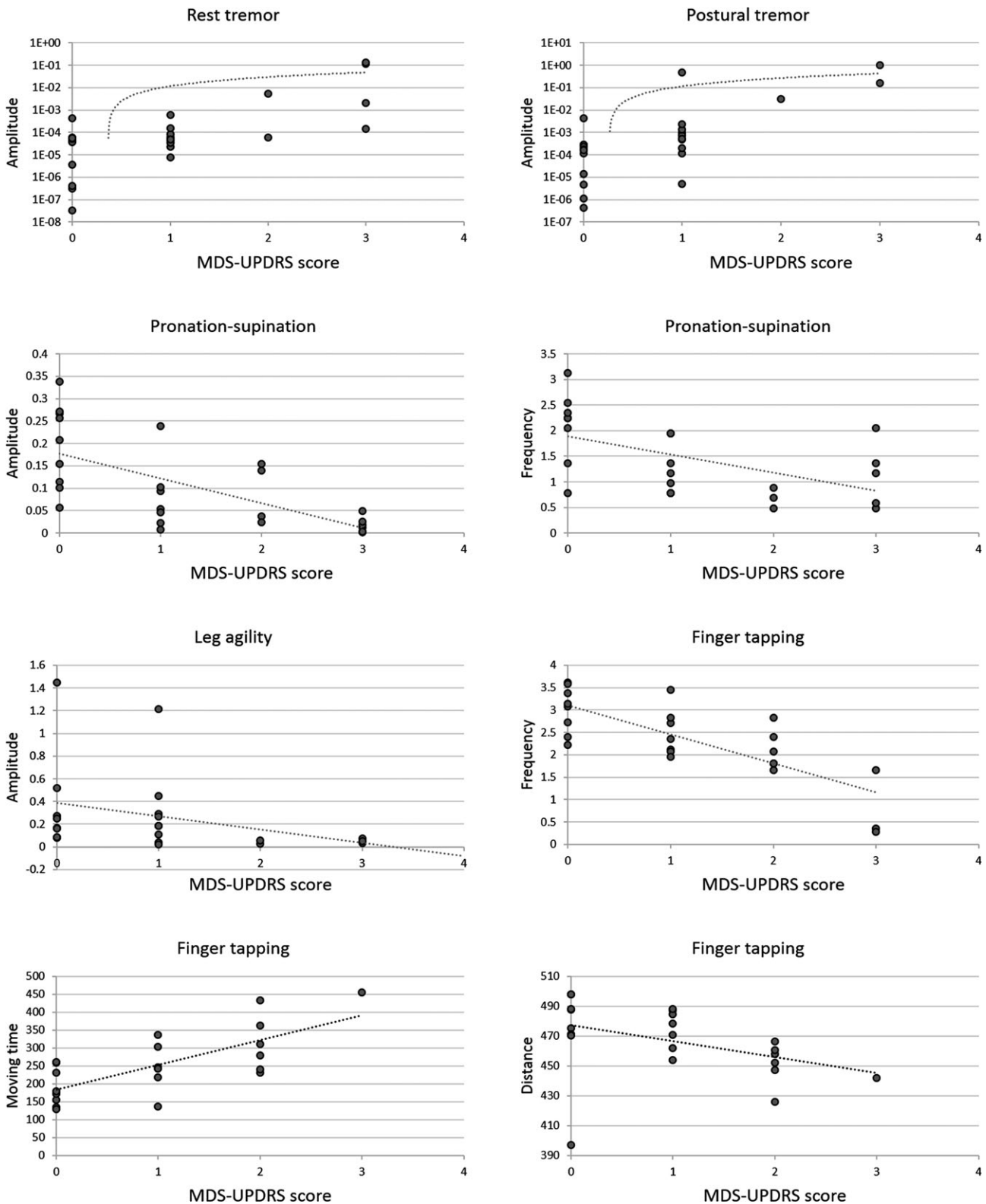
Figure 2 Significant correlations between MDS-UPDRS scores and smartphone tests. Vertical axes in rest tremor and postural tremor graphs are logarithmic. Power units arbitrary.

In a similar attempt to characterize tremor in PD LeMoyne et al.[3] used a smartphone attached to the hand with a custom-made glove. Daneault et al. also used a smartphone to assess patients with various types of tremor.[4] Our study extend these finding by reporting data from a group of 14 participants and provide correlations with the gold-standard tool for rating
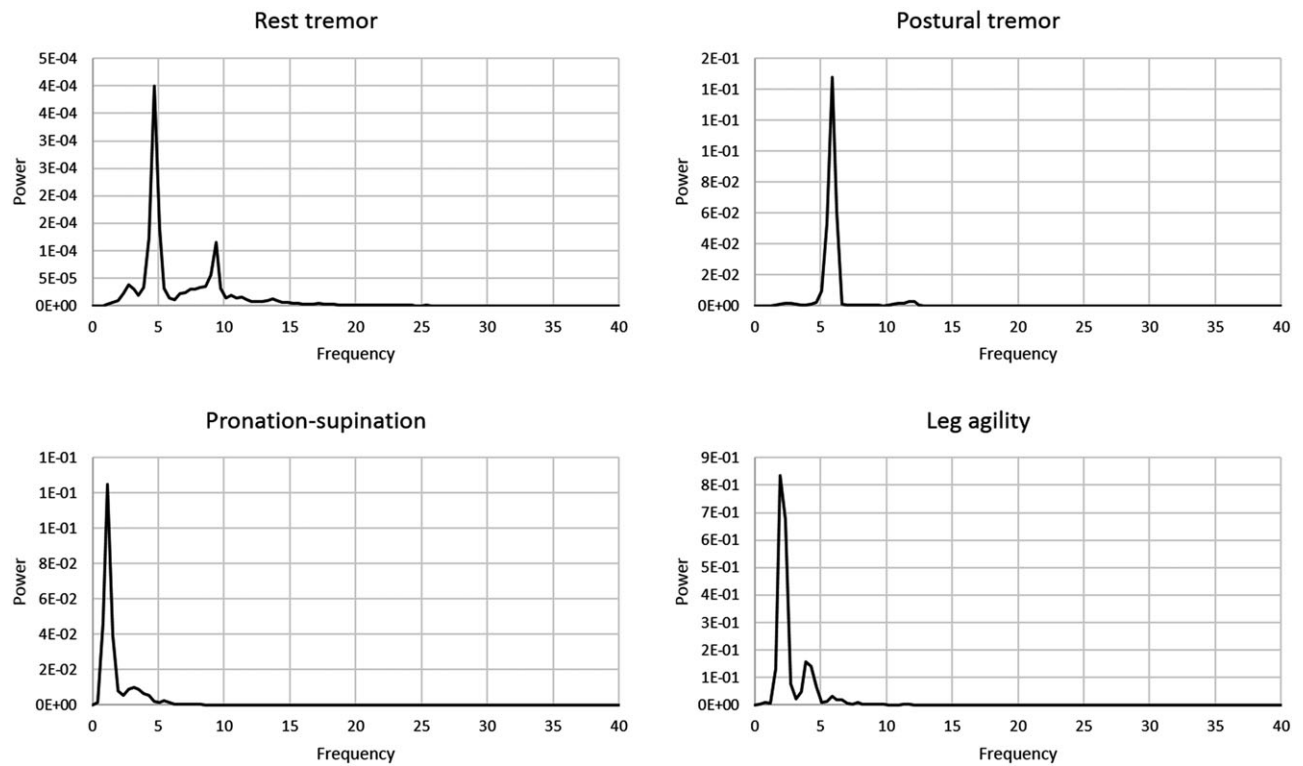
Figure 3 Examples of power spectra of four variables measured with the smartphone. Power units arbitrary.

motor symptoms in PD patients, the MDS–UPDRS. In addition, for the first time, we report on measures of bradykinesia, which is an essential criterion for the clinical diagnosis of PD according to the UK PD society Brain Bank clinical diagnostic criteria,[8] in contrast to tremor.[9]

Although most of the correlations described above are statistically significant ($P < 0.05$), the coefficients of determination show that the smartphone scores only account for a small amount of variance in the MDS–UPDRS scores. This is mainly because MDS–UPDRS is a nonlinear scale and therefore a linear regression model cannot predict variability with great accuracy. In addition, the MDS–UPDRS carries intrinsic variability, which cannot be predicted by the smartphone scores. For example, a patient with rest tremor amplitude of 1 cm can be rated either as 1 or as 2 in the MDS–UPDRS scale, but will always have the same score in the smartphone measurement (provided that the measuring technique is the same). The only test that did not correlate significantly between MDS–UPDRS and the smartphone assessment was the kinetic tremor. Our cohort of patients happened to have only minimal kinetic tremor given that they scored either 0 or 1 in the MDS–UPDRS. With such a narrow spectrum of symptoms, the validity of the smartphone assessment of kinetic tremor remains unclear. Regarding the assessment of postural tremor, the action of holding the phone may have affected the quality of the measured tremor. The kinematics of holding an object compared to simply hold the arms against gravity do not differ significantly (both are isometric muscle contractions, although of different intensity), but the

weight of the phone itself can affect the measurement by dumping the tremor. This is a limitation for all tremor measurements that use a nonweightless device to assess tremor.

The use of smartphones for the objective assessment of motor symptoms in patients with PD is expected to substantially lower the cost and increase objectivity, repeatability, accessibility, and convenience of rating. The opportunity to objectively assess the symptoms multiple times during the day would be valuable in assessing treatment efficacy and progression of the disease in the context of clinical trials and in clinical practice as an adjacent tool to the MDS–UPDRS. Notably, assessment of motor symptoms with wearable devices has increasingly become popular and is expected to generate very promising results in the near future.[10,11]

With this study, we provide evidence as a proof of principle that mobile communication devices such as smartphones could be used to objectively assess motor symptoms at comparatively low cost in patients with PD. In future versions of the software, we include gait analysis and a server side for storage and automated analysis of the data. Further development of the software will surely provide a tool for remote, objective, and continued assessment of PD motor symptoms in clinical and experimental settings.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution,

Disclosures

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