Open-Access Electronic Diary for Motor Fluctuation and Dyskinesia Evaluation in Parkinson Disease: Comparison With Paper Diary

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Objective: To determine the utility of an electronic diary for registering motor fluctuations and dyskinesia in Parkinson disease (PD).

Methods: Free, open-access touch screen software suitable for Android 4.4 or higher, with medication alarms, adjustable intervals, and medication dose settings was developed to evaluate ON-OFF periods and dyskinesia. Prospective evaluation included a first phase conducted to make adjustments concerning motor limitations when using the tablet, as well as for proper motor complication identification, and a second phase of 3 days of use at home with a prior diary training session comparing a modified paper version of Core Assessment Program for Surgical Interventional Therapies in PD and the electronic diary.

Results: All patients correctly identified ON-OFF periods and dyskinesia. Rater/patient matching ON-OFF fluctuations ranged between 94% and 100% for evaluations of different motor states. Dyskinesia matching percentage was 100% for patients with dyskinesia interfering with activities of daily living and 88% for those who reported no-interference. No significant differences between paper and electronic diaries were identified when reporting ON-OFF motor states or in the number of errors when filling the diaries.

Conclusions: This electronic motor diary proved to be reliable for ON-OFF state and dyskinesia identification and classification. However, no advantage to paper diary has been observed in terms of number of erroneous entries. Based on these results, to improve home motor fluctuations, detection efforts should be directed toward the development of automatic wearable devices rather than digital versions of current available ON-OFF diaries.

Key Words: electronic diary, home diary, motor complications, motor fluctuations, dyskinesia

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Motor fluctuations and dyskinesia are frequent complications of dopaminergic treatment of Parkinson disease (PD).[1,2] Although the severity of motor symptoms during OFF state and dyskinesia during ON state are typically estimated using clinical rating scales,[3,4] individual patient diaries are currently the best way to follow up outpatients on a daily basis or during research studies.[5] Physicians obtain information about motor fluctuations and dyskinesia by instructing patients to register motor states at regular intervals throughout the day for a given period. Home diaries are especially useful for understanding symptoms and temporal dynamics, including triggers exacerbating symptoms as well as to understand and rate treatment impact.[6] In PD, disadvantages of ON-OFF paper diaries classically include reduced compliance, recall bias, diary fatigue, low adherence, duplication of data, as well as failed or fraudulent, incomplete or illegible entries, all of which can generate unusable data.[5] They also require time-consuming data postprocessing, are investigator and location dependent, are associated with the limitations of regularly repeated assessments, and lack quantitative outcomes.[7–10]

On the other hand, there is growing interest in objective assessment of health-related outcomes using devices that provide unbiased measurements,[11] quantitative, objective, and easy-to-use technology-based tools and their development to assess PD motor features over long periods, generating clinically relevant and comparable information.[7,12,13]

Our hypothesis is that problems related to paper diaries could be reduced using electronic devices that allow data to be downloaded directly to a database for analysis, reducing entry errors. The aim of this study was to determine the reliability and feasibility of electronic diary use when compared with a paper-based diary.

MATERIALS AND METHODS

The protocol conformed to Helsinki Declaration principles and was approved by the local institutional review board. All participants gave written informed consent before study entry.

A prospective study was conducted between October 2015 and October 2016. It included nondemented PD patients fulfilling United Kingdom Parkinson's Disease Society Brain Bank criteria with documented motor fluctuations and/or dyskinesia according to medical records, scoring at least 1 point on the MDS-UPDRS part IV and 61 points or higher on the Rapid Estimate of Adult Literacy in Medicine Scale.[14] Patients had to be on stable antiparkinsonian medication regimen for at least a month before, as well as during the 2 weeks of study duration. The study was divided in 2 phases. In the first phase patients were initially trained and familiarized with the electronic motor diary in the context of acute levodopa challenge, as previously reported,[15] testing patients recognized the ON or OFF states and the presence of dyskinesia. Dyskinesia was registered and classified as those causing or not causing interference with activities of daily living (ADL).

A second phase was completed with a different group of participants selected in consecutive fashion who underwent a diary training session on use of a modified paper version of Core Assessment Program for Surgical Interventional Therapies in PD (CAPSIT-PD) and for the electronic diary. During the training session, patients were coached regarding definitions used for different functional states and on how to complete the diaries. This involved ticking off options from the checklist on the paper diary, or clicking on the screen during a 3-second period for the electronic diary. The user-friendly touch screen application was designed for tablet-like devices which included reminders to register motor state (ON-OFF and dyskinesia) and for medication intake. Once activated, the application allowed

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patient to enter information using buttons: the *ON-state button* option allowed patients to record presence or absence of dyskinesia, and if present, whether or not they interfered with ADL. The *OFF-state button* offered 2 possible results: presence of *complete* or of *partial OFF-state*, similar to the Core Assessment Program for Surgical Interventional Therapies in PD (CAPSIT-PD) paper diary. Every 30 minutes, participants had to select 1 of 4 possible states recommended for registry of motor fluctuations by CAPSIT-PD[16] These were: (1) *ON* defined as able to move or the best motor state; 2) *ON with dyskinesia*, defined as able to move but limited by involuntary or unintentional movements; 3) *complete OFF*, defined as not able to move or worst state; (4) *partial OFF*, defined as able to move slowly but without reaching the worst state. Dyskinesia was classified according to severity into 2 categories: interfering or not interfering with ADL. Independently displayed alarms were previously set up by the programmer, for time intervals and medication dose adjustments. Special considerations concerning tremor, bradykinesia, and rigidity were included. For example, a 3-second delay gave patients time for proper feedback or to correct data entries. Symbols were assigned to each alarm for easy comprehension. Patients were asked not to turn the device off, and to specify sleep and awake cycles. During sleep periods, motor-state reminders were deactivated. The application was displayed on full-screen mode and could not be closed. All other tablet functions were disabled. During the second phase, 3 extra optional motor states were added including falls, episodes of freezing of gait, and OFF-related dystonia (for download and software instructions, movan@fleni.org.ar).

During sleep, the paper diary was completed on awakening, as was the electronic version (using the "sleep" button option on the tablet). Participants were randomly assigned to start with one or other method, and completed a 24-hour motor fluctuation registry, during 3 consecutive days for 2 weeks (on the same days of each week). Every 30 minutes, participants chose 1 of 4 possible states recommended by CAPSIT-PD for motor fluctuations registry.[16] All diary data were included for analysis. Errors were considered when there was no response (considered missing data: absence of registry in paper diary and ON-OFF not entered in electronic diary) and compared. More than 1 response (considered duplication) was not included in the global evaluation of errors because they were not comparable between the 2 diaries (not allowed in the electronic application). MDS-UDyRS (historical section part 1: On-Dyskinesia and part 2 Off-Dystonia) was recorded after each diary (paper or electronic) was completed.[17]

Statistical Analysis

Data were tested for normal distribution and results presented as mean±SD. Differences in demographic and clinical features between groups were evaluated using a *t* test for quantitative variables. Categorical data were compared by means of a χ^2 test using the Fisher correction as needed. For the second phase, a power analysis was performed to rule out differences of more than 20% between diaries (power=0.8, alpha=0.5). Minimal sample size was calculated as 14 participants. Two-sided *t* test was performed to test the null hypothesis of no difference between paper and electronic diaries, and significance level was set at *P* value of 0.05 or less. All analyses were performed using Stata v13.0.

RESULTS

First Phase

A total of 17 consecutive PD participants with motor fluctuations were evaluated, of which 11 (64%) showed dyskinesia. Demographic data are depicted in Table 1. All patients correctly identified ON-OFF periods and dyskinesia during acute levodopa challenge. Degree of rater/patient ON-OFF fluctuation agreement ranged between 94% and 100% for different motor states. Dyskinesia match percentage was 100% for patients with dyskinesia interfering with ADL, and 88% for those without interference.

TABLE 1. Patient Demographics and Clinical Characteristics

First phase (n=17)	
Age (mean±SD)	59 ± 9.6
Males, n (%)	13 (76%)
Disease duration (mean±SD)	12 ± 5.3
Second phase (n=16)	
Age (mean±SD)	64 ± 7.1
Males, n (%)	9 (56%)
Disease duration (mean±SD)	12.3 ± 5.9
Education level (mean±SD)	12.5 ± 3.5
LEDD (mean±SD)	1149.5 ± 632
MoCA score (mean±SD)	25.2 ± 2.4

SD indicates standard deviation; LEDD, levodopa equivalent daily dosage; MoCA, Montreal Cognitive Assessment.[18]

Second Phase

Sixteen consecutive participants were recruited, and all completed the second phase of the study. Patient demographics are shown in Table 1. Total values corresponding to 3-day registry were calculated both for paper and electronic diaries and are summarized in Table 2. No differences were found between either type of diary with respect to: total OFF time, partial OFF time, total ON time, total dyskinesia time, total freezing, dystonic, and falling episodes. Differences were found only for total sleep time category (*P*=0.04). Patients reported longer sleep duration on electronic diary days (mean, 25.8; 95% confidence interval [95% CI], 23.1–28.6 vs mean, 20.9; 95% CI, 16.5–25.3 hours; *P*=0.04). There were no significant differences on the mean of errors by missing data between paper diary and the electronic diary (mean, 18.6; 95% CI, 7.1–30.1 vs mean, 11.1; 95% CI, 6.7–15.6 errors; *P*=0.23). Mean number of duplications in paper diary was 9 (95% CI, 0.18–17.8).

DISCUSSION

The main finding of the present study was that the use of an electronic diary application was reliable and viable for ON-OFF state and dyskinesia identification and classification. However, no advantage to paper diary has been observed in terms of number of erroneous entries which was the main hypothesis for an electronic diary construction.

We designed an easy and user-friendly software application for portable electronic devices, allowing even patients with reduced mobility to register their motor state (severe OFF state), generating adequate, standardized and readily interpretable data. Electronic devices offer all the benefits of virtual data communication systems, as well as registering ON-OFF sleep states and dyskinesia, they allow the use of programmed alarms (sound, vibration, or light) to remind patients to take medication, confirming medication was taken and need for an ON-OFF self-evaluation entry, they have a 30-day minimum data storage, remote Wi-Fi connection, and a reduced size for easy transportation.

Use of these devices by an elderly population with different degrees of motor impairment, hardware/software failures (regular data backup, control of battery life, device charging, that is, contact

TABLE 2. Comparison Between Clinical Categories for Paper and Electronic Diaries

Categories	Electronic Diary Mean (95% CI)	Paper Diary Mean (95% CI)	*P*
UDysRS score	7.1 (4.3–9.8)	7.6 (4.9–10.3)	0.54
Total ON time, h	26.3 (21.4–31.1)	27.4 (19.9–34.9)	0.65
Total OFF time, h	4.3 (1.9–6.7)	5.1 (2.3–7.9)	0.28
Total partial OFF time, h	10.3 (6.4–14.3)	7.7 (4.5–10.9)	0.41
Total dyskinesia time, h	3. 9 (1.4–6,6)	5.8 (1.9–9.7)	0.42
Total sleep time, h	25.8 (23.1–28.6)	20.9 (16.5–25.2)	**0.04**
Falling episodes	0.2 (−0.1–0.5)	0 (0)	0.19
Freezing episodes	5.7 (1.2–10.2)	6.5 (0.7–12.3)	0.71
Dystonic episodes	3.2 (0.2–6.1)	1 (−0.1–2.1)	0.08
Missing data (error)	11.1 (6.7–15.6)	18.6 (7.1–30.1)	0.23
Duplications	NA	9 ± (0.18–17.81)	NA

UDysRS indicates Unified Dyskinesia Rating Scale; NA, not applicable.

with support teams), data extraction/management and cultural, educational, and socioeconomic factors may play a negative role, limiting electronic diary yield.[9] Our software took these problems into consideration and included particular issues concerning tremor, bradykinesia, and rigidity; for example, 3-second intervals for clicking options give time for proper feedback and to correct data entries, or using symbols to represent each alarm for easier recognition by patients. However, it was not good enough to show the advantages of registered motor fluctuations free of errors. This could be possibly related with the fact that in the paper diary, patients could correct their errors retrospectively, whereas that was not an option in the electronic application.

Strengths of the current study include the development of a tool for global evaluation of PD motor fluctuations contemplating patients motor limitations; falls, dystonia, and freezing episodes can also be reported, such that the type of data collected is similar to that recorded using paper. Also, the impossibility of making errors by duplication is one of the main advantages of this software.

In conclusion, use of this electronic motor diary proved to be reliable for ON-OFF state and dyskinesia identification and classification (depending on impact on ADLs) when compared with the paper diary but limitations related to the control of the errors in completing both diaries are still a shortcoming to reach the effectiveness of a home logger of use in the home. Considering this, we think that to improve at home motor fluctuations detection efforts should be directed to toward the development of automatic wearable devices rather than digital versions of current available ON-OFF diaries.

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