PARKINSON DISEASE

Digital assessment at home — mPower against Parkinson disease

Walter Maetzler and Andrea Pilotto

Results of a new study have shown the enormous potential of smartphone-collected, real-world data for the differentiation of patients with Parkinson disease from controls. This study spearheads a new phase for the evaluation of symptoms associated with Parkinson disease that is patient-centred, digital, objective, continuous and relevant to everyday life.

Refers to: Omberg, L. et al. Remote smartphone monitoring of Parkinson's disease and individual response to therapy. *Nat. Biotechnol.* https://doi.org/10.1038/s41587-021-00974-9 (2021).

Increasingly, digital devices are being used for collection of real-world data to remotely evaluate symptoms and function in neurological diseases. These devices enable remote tracking not only of disease-relevant parameters, but also of treatment responses, and could even shape therapies by acting as a closed-loop system. In this way, remote collection of real-world data in clinical management could improve care and empower patients while reducing health-care costs[1,2]. In a recent observational study published in *Nature Biotechnology*, Omberg et al.[3] demonstrate the use of remote data collection to monitor Parkinson disease (PD) in the mPower study. The results were promising, but also raise unresolved questions.

According to the FDA[4], real-world data relate to patient health status and/or the delivery of health care and include data from electronic health records, patient-generated data and data collected with mobile devices. Collection of real-world data can be active, whereby individuals manually enter data or perform a specified task with a digital device, or passive, when no intervention by the device wearer is needed (for example, with wearable sensors or devices placed in the home). The mPower study involved active collection of real-world data — participants with and without PD were asked to perform tapping, walking, balancing and voice tasks using a smartphone application three times per day. The study was US-based and conducted entirely remotely.

The remote recruitment strategy produced encouraging results, as >12,700 people participated, including >1,400 people with a self-reported diagnosis of PD. However, the design did not allow for clinical confirmation of the diagnosis, and less than 78% of participants self-reported whether they did or did not have a diagnosis of PD. Furthermore, the baseline characteristics of participants with PD differed from those without PD — among those with PD, the average age was older, the level of education was higher and a higher proportion were female than among controls without PD, making the statistical comparisons difficult. In addition, ~25% of participants wore the smartphone incorrectly or not at all during some tasks[3]. Consequently, the quality of the data collected must be viewed with caution.

Careful and nuanced data analysis was also needed. Use of initial diagnostic classifiers that were based on a machine learning training–test approach suggested that these classifiers provided excellent discrimination between people with PD and people without, but this discriminatory power was driven by confounders, such as age, sex, education, repetitive patterns of longitudinal measures, and specific environmental factors. Deeper analysis was needed to avoid these biases, and this analysis determined that the two groups could be separated with an area under the curve of 0.8 on the basis of the tapping task, whereas the performance on the walking, voice, balance and cognitive tasks were similar between the groups. These results demonstrate how constitutional parameters and general behavioural patterns in real-world data can feign disease-associated differences. In light of these findings, we must ask ourselves whether a prospective cross-sectional study based on remotely collected real-world data can successfully differentiate people with disease from people who are healthy, or whether this approach is better suited to intraindividual, longitudinal observations. For example, real-world data might generate particularly powerful outcome parameters in double-blind, cross-over study designs in which each person receives active drug and placebo at different times[5].

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Another limitation of the mPower study, and a common limitation of remotely conducted studies, is the low retention rate. In mPower, participants with PD stayed in the study for a median of only 15 days, and participants without PD stayed for a median of only 1 day[3]. How retention rates of such studies can be substantially improved is not yet clear. Early involvement of patients in the development of study designs is widely thought to be in important factor because the parameters chosen for assessment in this scenario are more likely to be meaningful for patients. Recently published frameworks for the development and validation of digital measures support involvement of patients in study design[6,7]. Similarly, the FDA recently rejected a proposal to use the Verily Study Watch for active assessment of PD motor symptom severity on the basis that the applicants could not convincingly demonstrate how measures such as finger tapping represent “meaningful change in patient function”[8].

The question also arises as to whether passive collection of real-world data might result in a higher level of adherence and fewer missing data, simply because less effort is required

Table 1 | **Requirements for successful collection and validation of real-world data**

Requirement	Example aim	Example study design
Establish the wearability, usability and acceptability of the device to be used for measurement of a digital parameter	Ascertain that operation of the device is possible even with disease-related disabilities	Focus groups and qualitative interviews with participants who have used the device over sufficient time. Suggested *n* 10–20
Establish whether the digital parameter can be measured with accuracy in comparison with an existing gold standard	Determine whether a wearable device on the lower back can accurately measure walking speed, as defined by a stationary optical system	Cross-sectional observational study. Suggested *n* 20–100
Establish whether the digital parameter tests what it is intended to test by comparing measurements with other tests (clinical and/or patient-reported outcome)	Demonstrate that real-world walking speed deteriorates with increasing disease severity	Longitudinal observational studies in the target population. Suggested *n* 100–1,000
Establish the sensitivity of the digital parameter to change, such as disease progression or treatment response	Demonstrate that step time variability measured with a device on the lower back improves with cholinergic treatment	Longitudinal observational studies or inclusion as an exploratory parameter in clinical trials
Establish the smallest change in the digital parameter that a patient and/or medical professional would consider clinically relevant	The target population and/or the treating medical team rate (for example, on a Likert scale) whether a meaningful change of gait disability (for example, from moderate to severe) occurred during the observation period	Longitudinal observational studies or inclusion as an exploratory parameter in clinical trials

from the participant. Currently available technology enables collection of data for a week or longer without the need to recharge devices. Moreover, stationary systems can be set up in the home to collect high-quality digital measures over long periods of time[9]. An additional advantage is that passively collected real-world data represents everyday behaviour more realistically than actively collected real-world data, as the participants simply continue their usual life throughout data acquisition.

The mPower study also demonstrates that we need new approaches to the validation of real-world data (TABLE 1). We need a clear understanding of which aspect of a disease (for example, state, trait, treatment response, disease progression or prodromal marker)

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should be measured, which symptom or function is to be measured, whether this symptom or function is measurable with the proposed method, and whether the outcome is relevant for patients. Such novel validation concepts are already being investigated in PD and other diseases in large public–private partnership projects in the European Union, such as IDEA-FAST (for fatigue and sleep assessment) and Mobilise-D (for mobility assessment). The results of the mPower study[3] strongly suggest that for rapid development and validation of real-world data in clinical and medical research contexts, we need to think big, patient-focused, transdisciplinary and collaborative.

Walter Maetzler[1]✉ *and Andrea Pilotto*[2,3]

[1]*Department of Neurology, University Hospital Schleswig-Holstein, Campus Kiel, Kiel University, Kiel, Germany.*

[2]*Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy.*

[3]*Parkinson's disease rehabilitation Centre, FERB Onlus, S. Isidoro Hospital Trescore Balneario, Bergamo, Italy.*

✉*e-mail: w.maetzler@neurologie.uni-kiel.de*

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Competing interests
The authors declare no competing interests.

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