A mobile-based system can assess Parkinson’s disease symptoms from home environments of patients

Treatment of Parkinson’s disease (PD) patients involves major challenges like the large within- and between-patient variability in symptom profiles and the emergence of motor complications. As PD progresses, the symptoms develop slowly and they represent a significant source of disability in advanced patients. During evaluation of treatments and symptoms, both the physician- and patient-oriented outcomes offer complementary information. In addition, quantitative assessments of symptoms using sensing technologies can potentially complement and enhance both patient and clinician perspectives. At Högskolan Dalarna, the Lecturer Mevludin Memedi has developed a telemetry system that assesses symptoms via analysis of self-assessments and motor tests to objectively measure disease-related outcomes and to improve the management of PD.
clinics around Sweden. On inclusion, 35 of the patients were treated with levodopa-carbidopa intestinal gel (LCIG, hereafter denoted as LCIG-non-naïve) and 30 patients were candidates for switching from oral treatment to LCIG (hereafter denoted as LCIG-naïve). Thirty patients in Milan, Italy, who had a clinical diagnosis of idiopathic PD participated in a second study.

Both patients and HE subjects performed repeated, time-stamped and remote assessments of their subjective and objective health indicators using a telemetry test battery implemented on a touch screen handheld device. On each test occasion, patients were first asked to answer seven PD-related questions and then to perform a set of upper limb motor tests including tapping and tracing spirals on the screen of the device (Figure 1). The subjects were instructed to place the device on a table, be seated in a chair and use an ergonomic stylus to perform the tests. Measurements with the test battery were performed four times per day during week-long test periods in the homes of patients.

One aim of the work was to develop methods for quantifying the severity of PD-related impairments during alternating tapping and spirography tests. Initially, the digitized movement data, consisting of stylus position and timestamps, were processed using time series analysis techniques. This step was essential for deriving a number of quantitative measures, useful for representing relevant symptom information. Numerous measures comprising spatial displacements and time-dependent effects of movements were calculated including low- and high-frequency components, statistical moments, trend components, irregularity components and similarity measures. The tapping data was summarized into scores for speed, accuracy, fatigue, arrhythmia and a global tapping severity. Secondly, different machine learning methods were used to map the quantitative measures to clinician-based measures, which were derived through visual inspection of tapping graphs and images of static spirals. Va-
Methods for assessing the severity of symptoms and treatment-related complications are crucial for effective clinical management of PD.

RESULTS

The method for scoring the drawing impairment in spirals correlated well with the visual ratings of spirals given by two neurologists with a Spearman rank correlation coefficient of 0.89 (p<0.001). In addition, the method had good test-retest reliability indicating a good stability of its scores over time. The method for automatic assessment of alternating tapping performance of patients had good validity, internal consistency and sensitivity to treatment changes. In addition, the method was able to discriminate between patients in different stages of PD and HE subjects and its scores significantly differed among categories of the UPDRS motor scale measuring upper limb motor performance (Figure 2).

The objective measures of upper limb motor function could discriminate between motor conditions among patients; tapping speed was related to Off symptoms whereas spatial irregularity during spirography was related to dyskinesias.

The six symptom dimensions of the test battery had a good internal consistency with a Cronbach’s alpha coefficient of 0.81. The OTS correlated well with total UPDRS and total PDQ-39 scores with a coefficient of 0.59 (p<0.001). In the case of LCIG-naïve patients, the mean OTS improved to the first test period on LCIG treatment and this improvement remained significant until month 24 (Figure 3). The maximum improvement was seen at month 3 with 0.15 units (32%, p<0.001) higher than at baseline.

In the case of evaluation of the web-based system, eleven of the 14 neurologists had a positive impression, 1 had a neutral impression and 2 had a negative impression. The responses of the nurses can be summarized in a qualitative manner as follows: the web-based system is very useful, the results during the test periods showed agreement with qualitative observations of the patient e.g. “one patient was in a bad condition at baseline, he improved after starting LCIG, then he became better again, 24-h infusion started and the patient became better again; we can clearly follow this change in the system, comparisons between patients are possible, that is one patient is in better/worse condition than another”. Responses to the questionnaire were mixed; a majority of the nurses were quite satisfied with the usability although a sizeable minority was not.

CHARACTERISTICS OF THE PARTICIPANTS IN THE TWO CLINICAL STUDIES

<table>
<thead>
<tr>
<th></th>
<th>Swedish study</th>
<th>Italian study (F group)</th>
<th>Italian study (S group)</th>
<th>Healthy elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n, gender)</td>
<td>65 (43m; 22f)</td>
<td>15 (13m; 2f)</td>
<td>15 (13m; 2f)</td>
<td>10 (5m; 5f)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 ± 11</td>
<td>65 ± 6</td>
<td>65 ± 6</td>
<td>61 ± 7</td>
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<tr>
<td>Years with levodopa</td>
<td>13 ± 7</td>
<td>7 ± 8.5</td>
<td>5.5 ± 6</td>
<td>NA</td>
</tr>
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<td>Hoehn and Yahr stage at present</td>
<td>2.5 ± 1*</td>
<td>2 ± 0**</td>
<td>2 ± 0.5</td>
<td>NA</td>
</tr>
<tr>
<td>Total UPDRS</td>
<td>49 ± 20.5*</td>
<td>33.5 ± 11.8**</td>
<td>26 ± 16.5</td>
<td>NA</td>
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</tbody>
</table>

Table 1. Characteristics of PD patients and of healthy elderly participants, presented as median ± interquartile range.
* Assessments performed in the afternoon. ** Assessments performed in the On state. Abbreviation: NA, not applicable.
Discussion

Methods for assessing the severity of symptoms and treatment-related complications are crucial for effective clinical management of PD. Relevant telemedicine approaches to remote monitoring of PD motor symptoms and complications include e-diaries, wearable inertia sensor systems, various testing tools and video-based monitoring systems. The objective methods for quantifying the symptom severity can potentially complement and enhance both clinician and patient perspectives. Objective assessments may better help to capture symptom severity and fluctuations as compared to using conventional clinical rating scales which are subject to clinical judgment and bias. In this article the use of IT-based methods was explored in order to develop a system architecture, consisting of computer-based methods for quantitative assessment of symptoms and the software around this platform, for providing an effective alternative to management of PD.

The methods for assessing the severity of upper limb motor impairments during alternating tapping and spirography were evaluated as being feasible approaches for quantitative and objective assessment of symptoms. The methods were designed and tailored for long-term telemetering of symptoms as well as had good level of clinical interpretability. Both the methods provided
means for deriving objective measures of symptom severity, which in turn can be used as valid outcomes in clinical trials for remote evaluation of upper limb motor function of patients.

The OTS and the six symptom dimensions of the test battery were evaluated as being feasible outcome measures for long-term and remote monitoring of PD symptoms. The internal consistency among the dimensions was good indicating that they measure the same construct of symptom severity. In addition, the OTS correlated well with total UPDRS and total PDQ-39 scores as well as was sensitive to treatment changes and could reflect the natural PD progression over time in advanced Swedish patients. In general, using an OTS may facilitate the patient screening process and help avoiding sub-optimization of treatments. The OTS could also be beneficial for deciding if a treatment change leads to an improvement of a patient's general condition or not.

The results from the usability evaluation of the web-based system showed that the information presented was comparable to qualitative clinical observations of the nurses who had experience using the telemetry device during the Swedish study. In addition, from the demonstration of its functionalities to the neurologists it was concluded that using the system assists in identifying patients who are not doing well and facilitates follow-up optimization of an individual patient's treatment. The system was seen as most important for fluctuating patients and for regional patients, i.e., patients living in regions far away from a clinic and can be considered as a tool that will assist in the management of patients.

Although the methods presented in this article were good at reflecting the severity of symptoms, they could not detect and measure symptoms which are typical for movement patterns exhibited during under- and over-medications. Another interesting issue that may be investigated is how dosing information will be related to the symptoms and how to develop a method for an individualized optimal dosing.

In summary, despite the efficacy of the currently available telemedicine systems, their effectiveness in routine clinical practice has yet to be established and should be widely adopted. Many aspects including validity, reliability, security, privacy, usability and acceptability must be considered before they can be applied in routine clinical care.

MEVLUDIN MEMEDI
Lecturer, Högskolan Dalarna, Borlänge
mimi@du.se

REFERENCES