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A smartphone-based system to quantify dexterity in Parkinson's disease patients

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ABSTRACT

Objectives: The aim of this paper is to investigate whether a smartphone-based system can be used to quantify dexterity in Parkinson's disease (PD). More specifically, the aim was to develop data-driven methods to quantify and characterize dexterity in PD.

Methods: Nineteen advanced PD patients and 22 healthy controls participated in a clinical trial in Uppsala, Sweden. The subjects were asked to perform tapping and spiral drawing tests using a smartphone. Patients performed the tests before, and at pre-specified time points after they received 150% of their usual levodopa morning dose. Patients were video recorded and their motor symptoms were assessed by three movement disorder specialists using three Unified PD Rating Scale (UPDRS) motor items from part III, the dyskinesia scoring and the treatment response scale (TRS). The raw tapping and spiral data were processed and analyzed with time series analysis techniques to extract 37 spatiotemporal features. For each of the five scales, separate machine learning models were built and tested by using principal components of the features as predictors and mean ratings of the three specialists as target variables.

Results: There were weak to moderate correlations between smartphone-based scores and mean ratings of UPDRS item #23 (0.52; finger tapping), UPDRS #25 (0.47; rapid alternating movements of hands), UPDRS #31 (0.57; body bradykinesia and hypokinesia), sum of the three UPDRS items (0.46), dyskinesia (0.64), and TRS (0.59). When assessing the test-retest reliability of the scores it was found that, in general, the clinical scores had better test-retest reliability than the smartphone-based scores. Only the smartphone-based predicted scores on the TRS and dyskinesia scales had good repeatability with intra-class correlation coefficients of 0.51 and 0.84, respectively. Clinician-based scores had higher effect sizes than smartphone-based scores indicating a better responsiveness in detecting changes in relation to treatment interventions. However, the first principal component of the 37 features was able to capture changes throughout the levodopa cycle and had trends similar to the clinical TRS and dyskinesia scales. Smartphone-based scores differed significantly between patients and healthy controls.

Conclusions: Quantifying PD motor symptoms via instrumented, dexterity tests employed in a smartphone is feasible and data from such tests can also be used for measuring treatment-related changes in patients.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder [36] and is characterized by degeneration of dopaminergic neurons in the substantia nigra. A common treatment for PD is levodopa. Over the course of the disease, levodopa dose and timing of intake have to be adjusted to optimize the therapeutic effect [33]. PD is a multidimensional, progressive disease and patients have different symptom profiles, which makes it difficult for healthcare professionals and patients themselves to assess and manage PD symptoms. From the clinical point of view, it is challenging to remotely and frequently determine the current motor state of the patient to determine whether the patient is under-

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medicated (a state in which the PD motor symptoms such as bradykinesia, tremor, rigidity, and others appear) or over-medicated (the appearance of hyper-kinetic movements related to excessive levels of medication). Therefore, assessing the current motor state of the patient is essential for deriving an optimal treatment strategy.

The current state of the art for assessing PD symptoms in clinical routine and studies is by using clinical rating scales based on observations and judgments of clinicians and medical history. The most commonly used clinical rating scale is the Unified PD Rating Scale (UPDRS) [22], which is used to evaluate the presence, severity and progression of PD symptoms as well as symptom fluctuations. However, clinician-based measurements are not able to capture variations in symptoms on a day-to-day basis since they only reflect one brief point in time. To reveal the full extent of patients' condition and prevent a recall and reporting bias, the motor symptoms need to be captured frequently, before and after medication [16]. Combining the elements of common rating scales with frequent self-assessments and objective tests can also help with covering more aspects of the disease than what can actually be obtained by clinical ratings alone.

Recent advances in information and communication technologies have enabled remote and continuous monitoring of motor symptoms [20]. Previous studies have shown that such technologies provide accurate and valid objective assessment of symptoms. It was previously reported that they may assist in identifying motor functions (On, Off and dyskinesia) [1,7]. The technology-based measures not only generate more valid endpoints for clinical studies but also can be useful in routine clinical care. There is a growing interest in investigating how useful the measures are when providing feedback to patients to increase their symptom and treatment outcome awareness [4].

From the technological point of view, data from different kinds of sensors during standardized tests and passive monitoring of physical activity have been previously analyzed and processed using signal processing and machine learning methods [11,43]. There are different studies with the focus on quantifying various motor symptoms. Some have focused on assessing motor dysfunctions in upper extremities [13,40,41], some on gross motor symptoms like gait [21], while others on combination of both. For instance [39], analyzed data from accelerometers and gyroscopes, which were placed on different parts of patients' bodies with the aim of quantifying drug-induced involuntary movements or dyskinesia, using Fourier transform. A similar approach was employed by Ref. [31] to quantify bradykinesia and tremor. Other studies have focused on analyzing data from upper limbs during standardized tasks like finger tapping [13,35], digital spiral analysis [32] and quantitative digitography [10,38].

As an alternative to wearable sensors-based systems, some research groups have focused on assessing dexterity performance of PD patients by analyzing upper limb motor data collected by means of touch screen devices [12,17,32]. The touch screens of the smartphones record physical properties of movements that can be produced either by a pen tip or finger with great spatial and temporal precision. Such smartphone measurements were previously used for assessing different fine motor dysfunctions like tremor [12], dyskinesia [17], drawing impairments [40,41] and global tapping performance [24]. Quantitative measures during alternating tapping tests and digital spiral analysis have been previously used as measures of bradykinesia [10] and severity of PD symptoms [32]. To our knowledge, there is no study reporting an approach where tapping and spiral drawing test data were combined in data-driven manner and related to objective measures such as various clinical ratings and actual treatment.

The purpose of this paper was to investigate whether a smartphone-based system, which consists of tapping and spiral drawing tests, can be used for quantifying dexterity in advanced PD. The paper reports clinimetric properties of smartphone-based measures of dexterity including correlations to clinical rating scales, test-retest reliability, sensitivity to treatment interventions, and ability to differentiate between tests performed by patients and healthy controls.

2. Materials and methods

2.1. Participants

Nineteen advanced PD patients and 22 healthy controls were recruited in a single center, open label, single dose clinical trial in Uppsala, Sweden (Table 1, [34]. Written informed consent was given after approval by the regional ethical review board (in Uppsala, Sweden).

2.2. Data collection

The trial included a single levodopa-carbidopa dose experiment for the PD patients, where both patients and healthy controls were asked to perform dexterity tests (tapping and spiral drawing) using a smartphone before and at specific time intervals after a dose was given [34,40,41]. For the patients, the dose administered was 150% of their individual levodopa equivalent morning dose to follow transitions between Off, On, and On with dyskinesia motor states. Up to 15 samples per PD patient were collected, one measurement at baseline (20 min prior to dosing), one at the time of dose administration (0 min) and thereafter follow-up measurements at 20, 40, 80, 110, 140, 170, 200, 230, 260, 290, 320, and 360 min after dose administration. The healthy controls were asked to perform the tests, 8 times each, at time point 0 (first test) and then at 20, 40, 60, 80, 110, 140, and 170 min, without receiving any medication.

On each test occasion, subjects performed upper limb motor tests (tapping and spiral drawings), using a smartphone (Fig. 1). The smartphone had a 4" (86 × 53 mm) touch screen with a 480 × 800 pixels and recorded both position (x and y coordinates) and time-stamps (in milliseconds) of the pen tip. The subjects were instructed to be seated on a chair and perform the tests using an ergonomic pen stylus with the device that was placed on a table and supporting neither hand nor arm. During tapping tests, they were asked to alternately tap two fields, as shown on the screen of the device, as fast and accurate as possible, using first right hand and then left hand. The time to complete a tapping test was 20 s. During the spiral tests, the subjects were instructed to trace a pre-drawn Archimedes spiral as fast (within 10 s) and accurately as possible, from the center out, using the dominant hand. The test was repeated three times per test occasion. The total number of measurements with the smartphone for PD patients was 285, and for healthy controls was 176.

2.3. Clinical assessments of motor symptoms

Along with smartphone-based measurements, patients were video recorded while performing standardized motor tasks according to UPDRS at the above-mentioned time points.

The recorded videos were presented in a randomized order to three movement disorder specialists, so that the ratings were blinded with respect to time from dose administration. The specialists rated three UPDRS-part III (motor examination) items including UPDRS item #23 (finger tapping), UPDRS #25 (rapid alternating movements of hands), and UPDRS #31 (bradykinesia), according to the definitions of the motor examination part of the UPDRS [6]. For items #23 and #25 the specialists were asked to assign a single score per time point without reference to any hand. The specialists also rated dyskinesia on a severity scale from 0 to 4 [8] and overall mobility according to Treatment Response Scale (TRS) [28], ranging from −3 (very Off) to 0 (On) to +3 (very dyskinetic). For every scale, mean scores per time point for the three specialists were calculated and used in subsequent analysis.

2.4. Data processing and analysis

2.4.1. Feature extraction

The raw dexterity data were processed with time series analysis methods to calculate 37 spatiotemporal features, which represent the severity of symptoms. Different kinematic quantities, including time, distance, speed, and velocity were used as primary signals to be