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Short communication

Spiral drawing during self-rated dyskinesia is more impaired than during self-rated off

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ABSTRACT

Objective: The purpose of this study was to examine repeated measures of fine motor function in relation to self-assessed motor conditions in Parkinson's disease (PD).
Methods: One-hundred PD patients, 65 with advanced PD and 35 patients with different disease stages have utilized a test battery in a telemedicine setting. On each test occasion, they initially self-assessed their motor condition (from 'very off' to 'very dyskinetic') and then performed a set of fine motor tests (tapping and spiral drawings).
Results: The motor tests scores were found to be the best during self-rated On. Self-rated dyskinesias caused more impaired spiral drawing performance (mean = 9.8% worse, $P < 0.001$) but at the same time tapping speed was faster (mean = 5.0% increase, $P < 0.001$), compared to scores in self-rated Off.
Conclusions: The fine motor tests of the test battery capture different symptoms; the spiral impairment primarily relates to dyskinesias whereas the tapping speed captures the Off symptoms.

1. Introduction

Assessments of symptoms and follow-up of treatments over time in patients suffering from Parkinson's disease (PD) are primarily done by using clinical rating scales, based on observations and judgments by physicians. During evaluation of treatments and symptoms, both the physician and patient-oriented outcomes offer complementary information [1]. In addition, objective assessments methods for quantifying a patient's motor function can complement both physician and patient perspectives [2].

Telemedicine methods provide means for long-term, frequent and repeated assessments of patients potentially improving the accessibility, quality and efficiency of care and increasing patient compliance. Instances of such methods include electronic diaries, body-attached sensors, and video-based assessment systems, just to name a few. To our knowledge, no systematic analysis of objective measures of motor function in relation to patient-based assessments, to date, has been evaluated in longitudinal studies in PD. Our objective was to investigate the severity of objective assessments of spiral drawing and tapping performance relative to self-assessed motor conditions (On, Off and dyskinesia) in PD patients.

2. Patients and methods

2.1. Patients

This paper is based on data from two clinical studies, both of which were approved by the relevant agencies and written informed consent was given. Sixty-five patients diagnosed with advanced PD were recruited in an open longitudinal 36-months study at nine clinics around Sweden [3]. On inclusion, they were either treated with levodopa/carbidopa gel intestinal infusion, LCIG (Duodopa), or they were candidates for receiving this treatment. In the second study, 35 subjects with a clinical diagnosis of idiopathic PD in Milan, Italy, participated. In the Italian study [4], patients were enrolled in two groups: advanced patients, experiencing on-off fluctuations (F group), and less severe, clinically stable patients (S group). Table 1 shows patient characteristics at baseline. For the Swedish study, information about handedness and the most affected side were also noted.

2.2. Assessments

A test battery, consisting of self-assessments of symptoms and fine motor tests was constructed and implemented in a handheld computer for enabling monitoring of PD [5]. The goal of the test battery is to be used as a tool for repeated status assessments in patients' home environments. Assessments were performed four times per day during test periods of one week in duration. For each test occasion, raw test data were sent in an XML format from the handheld computer over a secure mobile net to a central server for storage and processing [6]. In the Swedish study, the test battery was used quarterly or biannually by patients for up to three years. In total, there were 379 test periods and 10079 test occasions. In the Italian study, patients

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Table 1
Patient characteristics at baseline for the patients from the two studies, presented as median ± interquartile range.

	Swedish study	Italian study (F group)	Italian study (S group)
Patients (*n*, gender)	65 (43 m; 22 f)	15 (13 m; 2 f)	15 (13 m; 2f)
Age (years)	65 ± 11	65 ± 6	65 ± 6
Years with levodopa	13 ± 7	7 ± 8.5	5.5 ± 6
Hoehn and Yahr stage at present	2.5 ± 1[a]	2 ± 0[b]	2 ± 0.5
Total UPDRS	49 ± 20.5[a]	33.5 ± 11.8[b]	26 ± 16.5
Distribution of self-assessment categories[c]	−3 = 153	−3 = 14	−3 = 1
	−2 = 191	−2 = 28	−2 = 14
	−1 = 286	−1 = 97	−1 = 56
	0 = 307	0 = 186	0 = 321
	1 = 351	1 = 43	1 = 11
	2 = 156	2 = 35	2 = 3
	3 = 63	3 = 9	3 = 1

Self-assessment categories: −3, 'very off'; −2, 'moderately off'; −1, 'slightly off'; 0, 'on'; 1, 'slightly dyskinetic'; 2, 'moderately dyskinetic'; 3, 'very dyskinetic'.
[a] Assessments performed in afternoons.
[b] Assessments performed in on-state.
[c] Data are presented as number of observations per self-assessment category during first test periods, using the test battery.

used the test battery for two weeks with a washout week in between. There were 68 test periods and 1633 test occasions; 822 in the F group and 811 in the S group. On test occasions, patients were asked to self-assess their momentary motor condition, just before starting motor tests. They marked their motor condition on a global Treatment Response Scale (TRS) [7] including −3 = 'very off', −2 = 'moderately off', −1 = 'slightly off', 0 = 'on', 1 = 'slightly dyskinetic', 2 = 'moderately dyskinetic' and 3 = 'very dyskinetic'. Motor tests included uncued alternate tapping tests (using first right hand and then left hand) and spiral drawings using dominant hand. The spiral drawing test was repeated three times per test occasion.

3. Statistical analysis

Three self-assessed (SA) motor states were derived after the self-assessment answers were pooled as following: SA:Off (including −3 and −2), SA:On (including −1, 0 and 1), and SA:Dys (including 2 and 3). The traced spirals were automatically processed by a computer method which used discrete wavelet transform and principal component analysis and generated a 'spiral score' representing PD-related drawing impairments. A detailed description of the computer method can be found elsewhere [8]. The scorings provided by the computer method were evaluated against the averaged scorings of two trained neurologists and the results showed that there were strong correlations among them. The scale of the score was based on a modified version of Bain & Findley scale ranging from 0 = 'no impairment' to 5 = 'moderate impairment' to 10 = 'extremely severe impairment'. For the spiral tests, a 'test occasion spiral score' (TOSS) was defined as the mean of the scores of the three spirals per test occasion. For the tapping tests, mean speed (number of taps per 20 s) and accuracy (percentage of correct taps) for the right hand were calculated and used in the subsequent analysis. The rationale for not including results of tapping test with the left hand in the analysis was that majority of Swedish patients (62/65) were right-handed.

Differences in mean values of motor test results among the motor self-assessments were analyzed using linear mixed-effects (LME) models [9]. LME models are designed to be used with repeated measures and include a special term called a random effect which represents subject-specific effects or the influence of a particular subject in his/her measurements which is not directly captured by fixed effects (or population effects). In our analysis, we regard the patient variable as a random effect and self-assessments as fixed effects. The dependent variables were the motor test results: mean tapping speed and accuracy, and TOSS. The analysis was performed in R statistical software.

4. Results

For the Swedish study, the mean TOSS score differed significantly across the three self-assessed motor states ($P < 0.001$, ANOVA) with a mean value (for all states combined) of 4.46 [Wald-type approximate 95% CI; 4.14, 4.77]. The worst mean TOSS score was found in SA:Dys with 0.43 [0.35, 0.51] units higher than the SA:Off ($P < 0.001$). The mean TOSS score did not differ significantly between SA:On and SA:Off ($P = 0.16$). Both tapping speed and accuracy scores were found to be the highest in the SA:On. The tapping speed was 2.24 [1.30, 3.18] units (#taps/20 s) higher in the SA:Dys than in the SA:Off ($P < 0.001$). In contrast, tapping accuracy was better in the SA:Off than in the SA:Dys with 1.79 [0.39, 3.20] units (percent accurate taps) difference ($P < 0.05$). In the Italian study, patients in the F group had similar trends of motor test results over SA motor states as the Swedish patients. However, there were no significant differences between the three SA motor states. Fig. 1 shows the fixed effects coefficients representing mean motor scores for each individual self-assessment category for the two studies.

5. Discussion

The main finding of the present study is that dyskinesias impair spiral drawing performance and tapping accuracy, whereas tapping speed is improved, compared to performance in self-rated Off state in patients with advanced PD. It was expected that motor disability in the Off state would be identified by the tests, and it is an additional strength of the method that On state and On with dyskinesias were separated. The result suggests that objective fine motor tests are useful in determining the state of patients in the complication phase of PD.

The rationale behind including the Italian study in the analysis was to have data from more early PD patients along with the advanced PD patients from the Swedish study. The curves of TOSS and tapping speed were similar in the most advanced (Swedish) patient group and the fluctuating group (Italian F), only at different levels. The stable patients (Italian S) were, as expected, more stable, but with a tendency of best performance in the TRS 0. Tapping accuracy was fairly stable in the less disabled patients, but poor in the extreme motor states −3 and +3 in the advanced patients. In contrast to the tapping speed, the tapping accuracy was not different between stable and fluctuating groups in the Italian study. This finding could possibly reflect earlier deterioration of tapping speed than of tapping accuracy. If this assumption holds, worsening of the alternating tapping accuracy could become a marker for considering advanced PD treatments. Preliminary results of a longitudinal analysis of symptom data, collected by the test battery, during the Swedish study indicate that the tapping accuracy deteriorated throughout the 36-months study period whereas tapping speeds remained stable after the initial LCIG-related improvement. Trends were similar to those for UPDRS and PD quality of life questionnaire 39 (PDQ-39). A detailed analysis of study outcomes is planned to be published separately.

The effect of handedness in right-handed Swedish patients (95% of the patients) was more prominent than the effect of the side in which PD symptoms started i.e. they had better tapping scores (both speed and accuracy) during tapping test with the right hand than during tapping test with the left hand. In general, patients from the two clinical studies presented in this paper did not have action tremor. As previously described [8], the two neurologists rated firstly the spiral drawing impairment and secondly they rated