



Actigraphy monitoring of symptoms in patients with Parkinson's disease



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HIGHLIGHTS

- Little is known about activity-related disease symptoms in patients with Parkinson's disease (PD).
- We examined the relationships between physical activity and severity in PD symptoms.
- We conducted maxima values of power-law exponent of physical activity during awake-time.
- Change in physical activity was related to increased severity in disease symptoms.
- Actigraphy may be used to monitor daily severity of activity-related PD symptoms.

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ABSTRACT

Although the Unified Parkinson's Disease Rating Scale (UPDRS) is the “gold-standard” tool in assessing the severity of symptoms in patients with Parkinson's disease (PD), not all activity-related disease symptoms can be accurately captured by the well-established clinical rating scale. Using an alternative approach, this study examined the level of physical activity measured by actigraphy over time and whether change in physical activity was associated with disease severity assessed by UPDRS.

We used a longitudinal design in which physical activity and disease severity were assessed repeatedly during a 4-month interval, over a 3-year observational period, in a sample of 61 patients with idiopathic PD and a control group of 32 neurologically intact individuals. Physical activity data during awake-time were analyzed using the power-law exponent (PLE) method. Correlational relationships between changes in maxima values of PLE and scores of total UPDRS, UPDRS—part II (Activities of Daily Living), and UPDRS—part III (Motor Examination) in patients with PD were examined. Results show an increase in maxima values of PLE and the UPDRS total score in PD patients and that there is a positive association between changes in maxima values and total UPDRS score ($r = 0.746$, $p = 0.032$), UPDRS—part II score ($r = 0.687$, $p = 0.027$), and UPDRS—part III score ($r = 0.893$, $p = 0.018$). There was no significant change in the level of physical activity over time for the controls.

Findings from this study indicate that change in physical activity, as captured by actigraphy, is associated with increased severity in patients' clinical symptoms of PD over time. Thus, these data suggest that, when used in conjunction with the conventional UPDRS measure, an actigraphic measure of physical activity may provide clinicians an adjunct measurement approach to monitor patients' activity-based disease progression or responses to treatment in outpatient clinic settings.

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1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease that affects millions of people worldwide. Patients with PD experience various movement-related abnormalities that significantly impact their independence and quality of life. Currently, the Unified Parkinson's Disease Rating Scale (UPDRS) [1] is considered a “gold standard” reference scale in assessing various dimensions of disease severity in patients with PD. However, daily fluctuation in disease symptoms may

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not be fully captured or understood via the sole use of this clinical rating scale. Patients' symptoms of disease may well be masked by their dopaminergic medications and/or disease stages/severity [2]. In the treatment of patients with PD, the severity of symptoms is conventionally assessed using the UPDRS based on neurological examination, the patient's diary, or the caregiver's reports. These methods, however, lack quantitative aspects, thereby making them inadequate for the precise assessment of drug efficacy [3]. However, none of these studies have been successful in developing reliable analytical methods that quantitatively represent the disease progression in patients with PD [4–6]. Therefore, from a clinical standpoint, additional adjunct clinical tools that can provide an objective yet concomitant evaluation of activity-related disease symptoms manifested in daily life and during disease progression are warranted.

Research has shown that actigraphy-based observations can be useful and effective in objectively assessing activity-related disease symptoms such as tremor and motor fluctuations in patients with PD [3–7]. In our own previous work, we have shown that, by analyzing the power-law exponent (PLE; α) for local maxima and minima of severities in the activity time series [5,8,9], variation in physical activity captured by actigraphy was significantly correlated with the progression of PD symptoms. Our work suggests that actigraphic data, when analyzed by the PLE method, may provide clinically useful and objective information regarding PD patients' disease severity.

There have been, however, limited accelerometer-based studies that examine patterns of daily physical activity among independently living adults and how variation in movement-related activities may be correlated with change in clinically identified symptoms of severity over time. Addressing these issues could be clinically important in providing a comprehensive evaluation of patients' disease status on a range of symptoms. Their severity information can be subsequently used by clinicians in aiding their clinical decisions about patients' treatment options and/or evaluation of their responses to intervention modalities.

The purpose of this study, therefore, was to examine whether daily physical activity among independently living adults' physical activity would be associated with clinically rated symptoms over time in patients with PD. On the basis of our prior work [5,8–11], we hypothesized that variation in actigraphic recordings of patients' kinematics of movement disorder symptoms during awake-time would be correlated with PD symptoms assessed by UPDRS over time.

2. Materials and methods

2.1. Study design

We used a longitudinal design in which study participants were contacted and assessed with the planned study outcome measures every 4th month over a period of 3 years.

2.2. Participants

A total of 61 outpatients with idiopathic PD and 32 control participants were recruited from the department of Neurology of Shuguang Hospital Affiliated with Shanghai University of TCM. Eligibility criteria for patients with PD included individuals who were (a) at least 40 years of age, (b) diagnosed on two of the cardinal symptoms (bradykinesia, tremor, rigidity, or postural instability) assessed by the UPDRS [1], (c) on dopaminergic medications (i.e., levodopa), (d) showing no sign of mental deficit (e.g., dementia) and major depressive disorder, and (e) not affected by unstable cardiovascular disease or extrapyramidal syndromes due to other central nervous diseases identified by the investigators. Inclusion criteria for the control participants included neurologically intact and healthy community-dwelling adults. The study protocol was approved by the Ethics Committee of Shuguang Hospital Affiliated with Shanghai University

of TCM according to the principles outlined in the Declaration of Helsinki. An informed consent was obtained from each participant.

2.3. Control of medications

Patients' anti-Parkinson drugs were administered per the international medication guidelines [12] and monitored throughout the study period. Patients were instructed to adjust their medications for at least 14 days (mean \pm SD, 30.6 \pm 15.7) until their symptoms of PD approached a steady state.

2.4. Outcome assessment

The study included two outcome measures: (a) the UPDRS [1] and (b) actigraphy. Each is detailed below. Measures were taken at 4-month intervals across a 3-year period.

The UPDRS with two subsections (part II—Activities of Daily Living [ADL] and part III—Motor Examination [Motor]) was used. Items contained in UPDRS were rated on a 5-point (0–4) scale, with higher scores indicating severity of the disease. The UPDRS assessment for patients with PD was made during an “on” medication status by a neurologist. All assessments were conducted before actigraphy recordings (described below).

Patients with PD and the controls were given an actigraphy (MicroMini-Motionlogger®, Ambulatory Monitoring, Inc.) in which they were instructed to wear the device on their dominant wrist for 24 h per day during a 7-day period. Zero-crossing activity counts [11,12] were recorded every minute to register and quantify participants' physical activity.

Once the actigraphy was returned, the wrist activity data recorded during awake-time were then transmitted to the program software provided by the manufacturer, and the data were aggregated into 1-minute epochs for analysis using the Action-W (version 2, Ambulatory Monitors Inc.). The power-law (scaling) exponent (α), obtained as the slope of a straight line fit in the double-logarithmic plot of time scales vs. magnitudes of fluctuation, was used to emphasize the level of such correlation [9]. As Ohashi et al. [9] demonstrated, physical activity data have different power-law exponents in periods with higher and lower activity levels, corresponding to qualitatively different physiological states. The actual procedures we used are as follows: First, a daytime physical activity time series was integrated, as in DFA, and wavelets with different time scales (S) were slid along the time series and correlated with the data to obtain the wavelet coefficients ($W(S)$) at each point. We used the third derivative of the Gaussian function as the so-called “mother wavelet”:

$$\psi(t) = t(3-t^2)e^{-0.5t^2}$$

where t is time. This is equivalent to using the Gaussian second derivative (so-called “Mexican hat”) wavelet to examine the raw signals, though the integration approach automatically removes the local

Table 1
Demographic and clinical profiles of the study population at baseline.

	Baseline	3-Year follow-up
Age (years)	61.2 \pm 7.9	
Sex (male/female)	32/24	
Duration (years)	6.8 \pm 5.7	
Hoehn & Yahr	2.8 \pm 1.4	3.3 \pm 1.2
Levodopa/DCI (mg/day)	416.8 \pm 209.7	482.4 \pm 174.6
Pramipexole (mg/day)	1.63 \pm 0.78	2.35 \pm 1.17
Entacapone (mg/day)	169.74 \pm 76.68	185.73 \pm 56.35
Selegiline hydrochloride (mg/day)	8.22 \pm 3.53	11.98 \pm 6.87
Adamantanamine (mg/day)	57.31 \pm 36.7	79.66 \pm 34.86
Artane hydrochloride (mg/day)	2.86 \pm 2.37	3.93 \pm 2.61

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