# Objective and quantitative assessment of motor function in Parkinson's disease—from the perspective of practical applications

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**Abstract:** Parkinson's disease (PD) is a common neurodegenerative disorder with high morbidity because of the coming aged society. Currently, disease management and the development of new treatment strategies mainly depend on the clinical information derived from rating scales and patients' diaries, which have various limitations with regard to validity, inter-rater variability and continuous monitoring. Recently the prevalence of mobile medical equipment has made it possible to develop an objective, accurate, remote monitoring system for motor function assessment, playing an important role in disease diagnosis, home-monitoring, and severity evaluation. This review discusses the recent development in sensor technology, which may be a promising replacement of the current rating scales in the assessment of motor function of PD.

**Keywords:** Parkinson's disease (PD); motor function; objective measurement; wearable sensors

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## Introduction

Parkinson's disease (PD) is a progressive disorder of the nervous system due to the loss of dopaminergic neurons. Patients need to take long-term medication treatment and are followed up continuously for frequent treatment adjustments, as PD can only be potentially slowed, not halted. Importantly, early diagnosis could help improve a patient's prognosis as more than 50% of nigrostriatal dopaminergic neurons are lost before the appearance of typical motor manifestations (1). Although biomarkers like α-synuclein have been shown to be helpful in the early diagnosis of PD by some studies, there haven't been any large studies. As for PET imaging like DAT, its high price has made it unsuitable for early screening of PD. Another limitation is that patients' visits to the doctor only provide a snapshot of their condition, instead of continuous all-day monitoring, which makes it difficult for the physicians to get the full scope of the patients' disease progression. In clinical practice and clinical research, severity evaluation and treatment adjustments rely too much on clinicians' expertise, leading to limited accuracy and test-retest validity.

Therefore, it is necessary to develop an objective long-term measurement of the motor function in PD patients, with the characteristics of sensitivity, accuracy, portability, and objectivity. Fortunately, the evolution of mobile and computer technology has made this possible with many devices available which could satisfy the above requirements, including wearable sensors (e.g., gyroscopes, accelerometers), balance boards (e.g., pressure sensors such as the Nintendo Wii Balance Board) and optical motion capture systems, to name a few. This review mainly introduces the objective measurement of motor function in PD based on wearable sensors from the perspective of practical applications.

## Diagnosis/early diagnosis

Currently, the diagnosis of PD depends mostly on clinicians' experience, supplemented by imaging tools like PET. Objective measurement based on wearable sensors is expected to become a cost-effective alternative to the current diagnosis tools and techniques. Researchers were able to differentiate between PD patients and healthy controls in a lab environment using gyroscopes attached to different body segments. These subjects were directed to perform standardized motor tasks which reflect the characteristics of certain PD symptoms (2-7). Furthermore, as PD is a multi-symptom disease affecting various body segments and because most of the studies were based on features derived from single body segment, Jens Barth *et al.* managed to combine two different sensor-based systems analyzing hand motor function and gait together (8). The hand motor function analysis was based on a digital pen system called Biometric Smart Pen (BiSP), which was used in six tests consisting of both drawing on paper and movements in the air. Additionally, gait tests were performed with sensors attached on the subjects' shoes. Thirty-two features were selected from over one thousand features and using an AdaBoost classifier, the classification rates between PD group and healthy control group was improved from 89% for hand motor function and 91% for gait analysis, to 97% in combination (8).

Early diagnosis while important still only has limited tools available. Objective measurement based on inertial sensors is a promising cost-effective way to detect early PD patients who have shown minimal motor abnormalities with practically normal Unified Parkinson's Disease Rating Scale (UPDRS). It is generally accepted that mild motor dysfunction has started before the appearance of motor symptoms of PD, therefore inertial sensors can provide an advantage over the naked eye due to its sensitivity. In another study, a single sensor was attached on the lower back of the participant (often L5, near the body center of mass), and participants were asked to maintain an upright standing position with arms crossed on the chest, in both an eyes open (EO) and an eyes closed (EC) state (9,10). A number of features related to postural stability were collected and taken into analysis. Mancini *et al.* found jerk (the derivative of acceleration with respect to time) to be a particularly discriminative measure, exhibiting a high classification rate between subjects of early diagnosed PD and healthy controls (11). It is also worth mentioning that the PD patients did not show more dependence on vision to keep their balance as the researcher had assumed. The EO state was better for differentiating between early PD patients and healthy controls than the EC condition, which may reflect a problem of sensory re-weight in PD patients (11).

In many studies regarding early diagnosis, it is hard to select a single feature that is discriminative enough, but several combined features have shown some differentiation ability. A classifier could take all of the selected features altogether into an analysis and discriminate early PD patients from controls. In the study carried out by Tien *et al.*, they mounted an inertial measuring system on the subject's foot, providing numerical measures of gait performance (12). With the help of classifiers, the objective measuring system was able to discriminate early-stage PD from control group with a sensitivity of 80% and a specificity of 86% (12).

The iTUG is a technological evolution of the traditional time up and go (TUG) test, which is a widely used and well-established test of mobility (13). In three (out of the four) components of iTUG, significant differences were shown in cadence, angular velocity of arm-swing, turning duration and time to perform turn-to-sits between early PD and control groups (13). PD patients performed normally in sit-to-stand, though they had especially slow turning, arm swing, cadence, and trunk rotation during straight walk walking (13). As an improved TUG test, iTUG (based on inertial sensors) also revealed a distinct difference between early PD patients whose Postural Instability Gait Disorder (PIGD subscore of UPDRS III,clinical measure of mobility and balance) score was nearly normal and the control group by analysing 180° turns (14). The Salarian *et al.*'s study showed that duration of turning was the most sensitive measure with the highest test-retest reliability, meanwhile, was the only metric that revealed the progression of PD during 18 months (14). This feature could be used to monitor progression and evaluate therapy.

In fact, many typical motor function disorders of PD such as tremor, postural instability, gait deficits, and dyskinesia tend to appear in the later course of disease, making them unsuitable for early diagnosis (15,16). Therefore some studies have been focused on atypical motions, like drawing ability (17) and movement symmetry (18,19), which may become a supplementary basis for the early diagnosis of PD. A recent study suggested that a digital pen implanted with the Manus Platform (a novel sensor system) could discriminate early PD patients from control subjects who did not have PD but did have other impairments or PD-like symptoms (such as essential tremor) (17). The promising result made it possible to be a low-cost alternative to DATSCAN (17). Also, early PD patients may exhibit very subtle asymmetrical gait and hand movements (19), which are hard to be observed and evaluated by naked eyes. Therefore, a novel symbol based symmetry index referred to as "$SI_{symb}$", which was derived from inertial sensor data, was developed to differentiate between early-to-mid-stage PD patients and healthy controls (18). This novel continuous symbolic symmetry index, $SI_{symb}$, presented high sensitivity and specificity. This index showed that the asymmetry of upper limb movements is considerably greater than that of lower limb movements (18), a result that agrees with the clinical fact that reduced arm swing is often one of the earliest motor symptoms of PD (20).

## Home-based monitoring

Currently, assessing the impact of medication and changes in a patients' condition depends a lot on the patients' diaries and memory, which is neither objective nor reliable. A study suggested that the subjective complaints of PD patients do not necessarily match the findings of quantitative objective assessment (21) in reflecting motor fluctuation of PD. An ideal home-based monitoring device should have following functions: record and store movement data continuously over the long-term; portable enough to avoid interfering with the daily activities of the patients; able to test subjects in a home-based and unsupervised environment; reveal the real condition of the patients (work as a remote UPDRS assessment); with the ability to capture the occurrence of motor fluctuation and patients' compliance.

### *Continuous monitoring in daily activities*

Monitoring motor function of PD patients during real life activities could provide physicians with an assessment of specific motor symptoms, predict fall risk, evaluate medication compliance and provide information for early diagnosis.

Unlike guided and standardized motor tasks, motor assessment in unsupervised environment allows subjects to moving in daily activities, which means that two subjects can walk with different motion parameters not because of disease itself but due to individual differences (22). A fully charged measuring device such as portable gait rhythmogram (PGR) could achieve 40 consecutive hours of recording (23). With this PGR attached to the limbs, different motor fluctuations were observed according to the alterations in gait rhythm: if a subject was noted with a shift to a faster gait cycle, he/she may suffer from short-step walking, festination or freezing of gait (FOG); on the other hand, if a subject was found to exhibited a shift to a slower gait cycle, there was high possibility that he/she had bradykinesia or instability (24). On the other hand, some researchers thought that parameters regarding the gait performance were not representative enough and the utilization of alternative measures like entropy or the measure of the arm swing might be a better choice (22). In presenting variation in ON and OFF states, arm swing and entropy showed better performance compared to step frequency, stride length and speed (22).

When it comes to specific motor symptoms, tremor (25) is a candidate for home monitoring. To assess tremor in daily activities, a measuring system should not only discriminate tremor from other Parkinsonian motor symptoms, but also quantify tremor severity. With the help of a kinesis motion capture device consisting of a finger-worn motion sensor, and a wrist-worn command module for data acquisition and wireless data transmission, motor variation was presented in an straight and easy-to-understand way: a continuous quantitative score reflecting the severity of tremor was displayed in a graph, demonstrating the changes in the condition of each patient during the day (25). Long-time continuous monitoring information will help physicians with adjustment of a patient's medication dose and frequency.

FOG and fall risk are two major causes of secondary injures in PD patients, which occur occasionally in daily life, and are therefore hard to observe and evaluate during short visits to doctors. With the help of wearable sensors, continuous monitoring is achievable now, making it possible to detect the FOG in real-time and predict the fall risk. Weiss A et.al equipped subjects with body-fixed sensors and collected objective data for 3 days (26). After analyzing the acceleration measurements recorded, they found significant differences between fallers and non-fallers. Additionally, the acceleration measurements showed significant correlation with previously validated measures of fall risk (26). In another sensor-based three day study investigating gait abnormalities among PD patients who suffered from FOG, demonstrated that freezers have altered gait variability and consistency under daily-life conditions (27). Researchers also found that these measures were associated with the impact of FOG on daily functions, which were derived from the new FOG-questionnaire (evaluating the subject's perceptions of FOG severity and its impact) (27). Wearable devices could not only detect the occurrence of FOG, but also reduce the subsequent falling risk. When FOG was detected, an assistant system provided a rhythmic auditory signal that helped the patient to resume walking. At least half of the participants showed a positive effect (28).

Using a home-based motion measurement system, researchers could also evaluate the medication effect. Levodopa is one of the major medications in PD, widely used among the PD patients because of its high effectiveness and economical price. However, long-term use may cause some patients to suffer the serious complication of significantly disabling fluctuations and dyskinesia, referred to as levodopa-induced dyskinesia (LID). Wrist-worn sensors could not only detect the presence of LID with a sensitivity of 0.73 and a specificity of 1.00 (29), but they also demonstrate a correlation coefficient of 0.81 between clinician and model scores (30). Tsipouras *et al*. carried out a study, testing subjects under real-life conditions (31). They reported that the proposed method performed with high accuracy for LID assessment, including detection of LID symptoms and the classification of their severity (31).

To maximize the feasibility and benefit of objective measurement tools in the early diagnosis of PD, researchers are paying more attention to the analysis of real world activity patterns, rather than examinations in lab-based environments. A computer based at-home testing device (AHTD) was tested on early-stage, unmedicated PD patients with disease duration over 6 months (32). After analyzing a massive amount of data, researchers found that a change in tremor was a significant predictor of change in UPDRS (P=0.047) (32). The AHTD consisted of a series of motor tasks that the participants could perform at home, while another activity monitor—activPAL, was able to collect data of daily living activity (33). Eighty-nine newly diagnosed PD patients and 97 controls wore an activPAL for 7 days. Key results showed significant differences in the volume and pattern of daily ambulatory activity in newly diagnosed PD patients compared with controls (33).

### *Home-based monitoring depending on fixed motor tasks*

Monitoring patients in a continuous way without supervised and standardized motor tasks is not the only way to design a home-based monitoring system. Patients could also provide disease-related information by doing video-guided motor tasks at home (25,31). An algorithm was developed to estimate the clinical scores provided by a neurologist when observing patients performing the same motor tasks. The classification errors of this remote UPDRS assessment system were 3.4% for tremor, 2.2% for bradykinesia and 3.2% for dyskinesia, demonstrating that clinical UPDRS score can be reliably estimated under the help of the remote UPDRS assessment system based on wearable sensors (23).

Tapping performance could be tested in patients' home environment using a battery of tests implemented in a touch-pad handheld computer (34). This approach showed discriminative ability between early PD and controls, as well as strong correlations between computed global tapping severity (GTS) score and visually assessed GTS scores (34).

The Wii was a video game console released by Nintendo in 2006 which was very popular in the United States. Two of the Wii peripherals: the Nintendo Wii remote and the Wii balance board were able to be repurposed as home-based motion monitoring equipment for PD (35-38). The Wii Balance Board is a wireless balance board accessory for the Wii, with multiple pressure sensors capable of measuring the user's center of balance, which could be used in the assessment of postural instability. Clark *et al*. examined its validity comparing with the 'gold standard'—a laboratory-grade force platform (35,39). Both of the two devices exhibited excellent center of pressure (COP) path length test-retest reliability (35). In another study with an improved signal processing scheme, intra-class correlation coefficient (ICC) point estimates for concurrent validity were noticeably higher compared with Holmes *et al*.'s result (ICCs, 0.92–0.98 *vs*. 0.77–0.89) (36). The Wii Remote is an infrared based handheld pointing device that can detect movement in three dimensions, making it possible to measure upper limb movement in patients. A mini-game that included target shooting, target holding and button tapping (38), made the Wii remote testing enjoyable to do, which helped increase the patients' compliance. The Wii remote testing system showed impressive discriminative ability between PD patients and the control group, making it a promising home-based detecting tool for PD (38). Certain motor symptoms like tremor could be detected from some specific metrics using Wii remote. It could also perform as an indicator of PD severity, with a clear correlation between patient self-rating scores of tremor severity and metric obtained (37).

## Severity evaluation/progression tracking

In clinical practice, evaluation of PD severity mainly depends on clinicians' personal judgement, with the help of common rating scales such as UPDRS. However, the strong dependence on clinicians' experience makes such an evaluation subjective and therefore less reliable. If objective measures were proven to be correlated with the generally accepted 'gold standard'-UPDRS overall or sub-score, it is reasonable to believe that the objective measuring system may become an alternative to the current rating scales in the progression tracking of PD.

Volkow *et al*. found a strong correlation between the dopamine receptors in PD and the motor task characterized by RFT (rapid finger-tapping test) (40), which made it a potential objective metric to determine the PD stages. There were two systems that could be used to evaluate the RFT objectively—a computer vision method using a webcam (41) and a system consisting of an accelerometer and touch sensors (42). These two systems are not quite comparable although the basic principles are different: one is designed based on image analysis technique; the other is based on wearable sensor technology. The accelerometer-based system showed discrimination ability between PD patients and the control group (42). The computer vision system made a novel contribution by testing the correlation between quantitative parameters and clinical ratings: one of the measures referred to as "cross-correlation between the normalized peaks" showed a strong correlation with clinical ratings; and by using a support vector machine classifier and 10-fold validation, the computer vision system could categorize the patients between UPDRS-FT levels with an accuracy of 88% (41).

Lewek *et al*. reported a significant reduction in the amplitude of arm swing asymmetry (ASA) in early PD, leaving unresolved questions as to whether the ASA difference was caused by the asymmetry in rigidity and bradykinesia, the breakdown of the central synchronization between the arms during walking, or a possible combination of those factors (19). One study investigating the arm swing coordination during walking, posted the hypothesis that differences between PD group and healthy controls could be observed in both the amplitude of the arm swing accelerations and their coordination (43). The objective measure maximum cross correlation (MXC) was calculated, reflecting the degree of statistical dependence between the arms, as well as the degree of inter-limb coordination during gait (43). Higher ASA was found in PD subjects and significant correlation was found between ASA and UPDRS scores of limbs. However MXC exhibited significant correlation with the tremor sub-score of the limbs (43).

The measure of postural sway jerk as proven to be a promising measure for early diagnosis, not only exhibiting correlation with the gold-standard-laboratory measures of postural sway derived from a force-plate, but also the PIGD sub-score related to clinical postural instability (44).

Rapid alternating movement (RAM) is the very useful task often used for the evaluation of bradykinesia in clinical practice, and it can be objectively measured by using a foam handball in subjects' hands that is attached to angular displacement sensors (45). Two of the features (mean and maximal velocity) derived from the RAM task were found to have a statistically significant correlation with the clinical score (45).

## Limitations

There are two prime limitations in tracking progression of PD using objective tools. The first problem was the lack of a reliable and objective "gold standard" which could accurately reveal the condition changes during the course of the disease. Clinical scales are most frequently used as the "gold standard" in most publications, such as the UPDRS score, however they are non-linear, provide only a snapshot of the condition, and have high inter-rater variability. Some lab-based equipment such as the 'force plate system', and 'pressure sensitive walking mats' are expensive and limited to only a subset of PD symptoms.

On the other hand, as Parkinson's disease is an aggravating disease, the measures regarding the course of the disease are supposed to deteriorate over time. Researchers have investigated the possibility of postural sway becoming an objective marker of progression: this objective measure did deteriorate over one year only in untreated PD patients despite minimal changes in neither UPDRS motor scores nor PIGD sub-score (11). However, it's unlikely for patients not to take parkinsonian medication on clinical trials. Although there has not been solid evidence that medication could slow down the degeneration of dopamine neurons and change the disease course, it is necessary to characterize the effect of PD medication.

Another important limitation of an objective measuring system is the lack of representative measures, as most of the multi-dimensional motions are presented in the form of separate physical parameters. Taking gait performance for example, it could only be presented in separate parameters like cadence, stride length, and gait cycle time, instead of being integrated into one easily understandable index. Using classifiers, patients and controls could be distinguished. However, almost none of the individual gait parameters would be representative enough to evaluate the overall gait performance. An integrated and comprehensive metric is needed in the future. In Daneault *et al*.'s study investigating bradykinesia (45), only moderate correlation was observed between the objective measures and clinical scores. One inevitable reason is that clinical evaluation combines measures of bradykinesia, hypokinesia, and motor coordination while the quantitative features were only related to velocity (mean and maximal velocity).

It should be noted that objective measuring tools are not always superior compared with traditional rating scales. In the analysis of tremor, wearable sensors provide precise linear measures of tremor amplitude, whilst rating scales are crude and nonlinear. Nevertheless, this advantage is mitigated by the natural variability in tremor amplitude (46). Studies suggest that wearable transducers were no more sensitive to clinical changes than a 0-4 rating scale (47,48). The minimum detectable change in tremor is comparable between sensors and rating scales (47,48).

## Future work

A sensor-based objective analysis system of movement disorders is one of the most challenging tasks in medical engineering. Although great progress has been made in recent years, there is still much room for improvement. First, to increase the feasibility of such a tool being used in clinic conditions, the reliability and validity should be tested in large clinical trials. Meanwhile, a set of data from healthy controls should be collected to establish a baseline of quantitative motor function metrics.

To enhance the accuracy and stability of a biomechanical measure system, integration of data from different body segments seems to be the most logical approach. An example system is called PERFORM (49), which is an intelligent closed-loop system integrating a wide range of wearable sensors, allowing physicians to remotely monitor the condition changes of the patients, adjust medication schedules, and individualize therapy. In a study regarding gait measurement, researchers were working on combining the data from wrist and sternum sensors with the data from foot sensors (50).

With the prevalence of smart phones, the ease of developing medical apps will help increase the feasibility of objective measuring tools of PD. ResearchKit is an open source platform released by Apple Inc. in 2014, which could help researchers and developers to create medical apps. With ResearchKit, researchers could take advantages of data derived from millions of iPhone users. It is undoubtedly a valuable resource to the development of an objective measurement tool of Parkinson's disease. Several mobile-based apps have been designed and tested on PD patients. "PD Dr" is a mobile cloud-based mHealth app, which collects quantitative and objective information about PD and is capable of home-based monitoring of PD symptoms. Similarly, mPower is also a relatively mature smartphone app, which has a combination of surveys, structured tasks, and passive measures. A team from National University of Singapore described a foundation of smartphone-based app referred as "SmartMOVE", managing to combine the quantification of gait performance and rhythmic auditory cueing system together (51). This innovative application showed great potential to reduce the falling risks in advanced PD patients.

As the objective measurement of PD matures, researchers have been trying to apply it into clinical studies, such as evaluating the effect of rehabilitation programs (52), understanding the pathophysiological mechanisms of PD medication, and improving treatment evaluation. It is reasonable to believe that in the near future, the objective measuring systems of motor symptoms will be widely used in Parkinson's disease as well as other movement disorders.

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## Footnote

*Conflicts of Interests:* The authors have no conflicts of interest to declare.

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