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How well do Parkinson's disease patients turn in bed? Quantitative analysis of nocturnal hypokinesia using multisite wearable inertial sensors

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ABSTRACT

Background: Nocturnal hypokinesia/akinesia is a distressing symptom in patients with Parkinson's disease (PD). However, it is difficult to accurately monitor these symptoms based on clinical interviews alone.
Objectives: To quantitatively compare nocturnal movements of PD patients with their spouses by using multisite inertial sensors and to correlate these parameters with disease severity scores.
Methods: Nocturnal movements in 19 PD couples (mild-moderate stage) were assessed and compared using wearable sensors (limbs and trunk) for one night at their homes. Nocturnal parameters included number, velocity, acceleration, degree, and duration of rolling over, number of getting out of bed, and limb movements. Each activity was compared to sleep diary, and video recording for accuracy.
Results: PD patients significantly had fewer rolling over ($p = 0.048$), turned with smaller degree ($p = 0.007$), less velocity ($p = 0.011$), and acceleration ($p < 0.001$), but had more episodes of getting out of bed ($p = 0.03$, nocturia) when compared to their spouses. Moderate and significant correlations were observed between the mean duration of rolling over and the Unified Parkinson's Disease Rating Scale-Axial score, and Nocturnal Akinesia Dystonia and Cramp Score. The number of leg movements (predominant side) significantly correlated with REM behavior disorder single-question screen. Episodes of nocturia correlated with total and bedtime levodopa equivalent dose. Several other correlations were also observed.
Conclusion: Our study was able to demonstrate quantitatively the presence of nocturnal hypokinesia in PD patients. This problem correlated with daytime axial motor and nonmotor symptoms. Treatment strategy for PD should be based on a comprehensive review of both day- and nighttime symptoms.

1. Introduction

Nocturnal symptoms of Parkinson's disease (PD) contribute significantly to a reduced quality of life for both patients and their caregivers [1,2]. It is considered to be a good practice for treating physicians to utilize a 24-h treatment strategy to adequately monitor and control symptoms that occur both during the day and at night [3,4]. This concept is particularly important since as high as 96–98% of PD patients suffer from disease-related nocturnal problems [1,5]. Depending on the study methods used, common and troublesome symptoms identified in most studies were nocturia (57–80%), sleep disorders (40–80%), nocturnal hypokinesia (50–82%), neuropsychiatric and cognitive disorders (30%) [1,5–9].

Nocturnal hypokinesia/akinesia is a condition where PD patients have difficulty in moving their body during sleep so that rolling over or turning in bed and getting out of bed is restricted. The

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consequence of these long periods of immobilization and difficulty changing position includes the development of pressure ulcers, predisposition to aspiration pneumonia, and asphyxia, which is a potential cause of death in PD patients [10]. Furthermore, it can also be a burden to caregivers, which contributes to a poor quality of life [2,11]. Due to the nocturnal nature of these symptoms, patients and caregivers often are unable to observe and report them accurately resulting in a low recognition of nighttime problems in clinical practice [3,12].

The issues of nocturnal hypokinesia and inability to get out of bed have been raised as the most common nighttime problems in PD in two original studies between 1987 and 1988 [5,12]. In the study by Lees et al., the inability to turn over in bed was experienced by 65% of PD patients and was rated as the most troublesome problem in 39% of patients from a national survey of 220 PD patients [5]. Subsequent studies observed a similar finding in which patients attributed their impaired mobility at night to general movement difficulties, pain or stiffness, or weakness and they utilized different strategies to overcome these problem [8]. Not only PD patients turned less frequently than their spouses, their turns were also slower with smaller amplitudes [13]. A recent study also identified the problem of nocturnal hypokinesia negatively affects sleep quality in PD [6].

In clinical practice, the acquisition of information about nocturnal hypokinesia by history taking, a physical examination, or a questionnaire is often very difficult and inaccurate. Moreover, the lack of awareness of nocturnal symptoms by PD patients, caregivers, and their physicians often will result in these problems being overlooked. With the advances in sensor technology, wearable sensors have been developed to monitor movement patterns in the daily life of individuals and this capability has now been extended to PD patients [14,15]. The advantages of wearable sensors are their ability to capture real-time data, thereby documenting real-life situations, allowing physicians to obtain precise, accurate, and quantitative data. Therefore, the aim of our study was to evaluate the patterns of nocturnal hypokinesia and the ability of getting out of bed in PD patients by utilizing multisite wearable sensors and to correlate these findings with standardized clinical rating scales.

2. Patients and methods

2.1. Patients

Participants in this study were patients at Chulalongkorn Centre of Excellence on Parkinson's Disease & Related Disorders (CUPD) with the diagnosis of PD according to the Unified Kingdom Parkinson's Disease Society Brain Bank criteria who had spouses whose age did not differ from the patients by more than 10 years. Exclusion criteria were: 1) patients and/or spouses who were bedridden; 2) a history of other neurological disorders or other muscle and joint diseases; and 3) a history of hypnotic or sedative drugs use. In addition, all spouses were carefully examined by two independent neurologists (JS and OJ) to detect any signs of parkinsonism or any of the above exclusion criteria so that they could represent healthy controls. Spouses were selected as controls because they shared similar sleeping environments as well as nighttime activities to PD patients. The study was approved by the Human Ethics Committee of the Faculty of Medicine, Chulalongkorn University. All subjects gave informed consent before entering the study in accordance with the declaration of Helsinki. This study was registered at www.clinicaltrials.gov (NCT02352727).

2.2. Methods

Multisite inertial sensors (the NIGHT-Recorder) used in this study were developed under the collaboration of CUPD and the National Electronics and Computer Technology Center, Thailand. The details of technical development and experimental verification of the NIGHT-Recorder have been described elsewhere [16]. The sensor module consists of 16-bit digital-output triaxial integrated microelectromechanical system (iMEMS) accelerometer and gyroscope that are capable of measuring linear and angular accelerations in three translational planes (*x,y,z*). The recordings were obtained using a 10-Hz sampling rate with a low pass filtering at 12 Hz.

All participant clinical characteristics were evaluated by a movement disorder neurologist (RB). The severity of PD was evaluated by two independent neurologists (JS and OJ) to include the Hoehn & Yahr (HY) staging, and the Unified Parkinson's Disease Rating Scale (UPDRS). Both physicians had to agree on their rating assessments. In the case of a discrepancy, both physicians assessed the evidence again, and arrived at a consensus. The UPDRS axial score was calculated as the summation of the items 18, 22, 27, 28, 29, and 30 of the UPDRS Section Section 3 [17]. To quantify the severity of nocturnal symptoms, the Nocturnal Akinesia Dystonia, and Cramp Score (NADCS), and the Modified Parkinson's Disease Sleep Scale (MPDSS) were recorded in the patient group [18,19]. The MPDSS has been validated and tested in Thai PD patients and demonstrated good reliability (Cronbach's alpha = 0.842) [1,19]. The presence of Rapid Eye Movement (REM) sleep Behavior Disorder (RBD) was identified from a single-question screen (RBD1Q) as proposed by Postuma et al. (a sensitivity of 93.8% and a specificity of 87.2%) [20]. The RBD1Q consists of a single question, answered “yes” or “no”, as follows: “Have you ever been told, or suspected yourself, that you seem to ‘act out your dream’ while asleep?”. This question was translated into Thai by RBD expert investigators (RB and OJ) fluent in English and Thai languages. The RBD1Q has also been validated and tested in Thai PD patients demonstrating good reliability (Cronbach's alpha = 0.866). The diagnosis of restless legs syndrome (RLS) was made if subjects fulfilled all the four essential diagnostic criteria for RLS of the National Institute of Health-International Restless Legs Syndrome Study Group (NIH-IRLSSG) [21]. Levodopa equivalent dose was determined by using a standardized protocol. Bedtime LED was calculated from the amount of dopaminergic medications that patients took at bedtime using the same protocol.

Both patients and spouses wore the triaxial accelerometers on both wrists, both ankles, and trunk for one night in their normal bedroom environment. The orientation of axis *x,y,z* on the patient is shown in Supplementary Fig. 1. Signal processing was performed using a forward derivative method on the angular data to obtain its derivatives on the Sleep Motion Analyzer software (version 1.0) running on MATLAB (Version 7.8.0.347, R2009a). The detailed technical analysis of the data was described in the prior literature [16]. Subjects were instructed to complete a sleep diary for sleep times and the episodes of getting out of bed if awakened. All subjects were also videotaped during sleep. Sleep times were defined as the period that the subjects were in bed excluding the first and the last 5 min. If any discrepancies occurred between sleep times as provided by subjects' records and sleep times registered by the accelerometer, the registration by the accelerometer was synchronized with the data reported by the subjects. All PD subjects were allowed to continue on their usual medications.

Nocturnal parameters that were included in this study consisted of the numbers of times the subjects rolled over, the number of times they got out of the bed, and limb movements. Supplementary data 1 describes different outcome parameters in categories, descriptions, and units. The characteristics of rolling over include degrees, duration, velocity, and acceleration. Rolling over in bed is defined as a series of unconscious motions during sleep involving