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Sensor-based evaluation and treatment of nocturnal hypokinesia in Parkinson's disease: An evidence-based review

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ABSTRACT

The manifestations of nocturnal movements in Parkinson's disease (PD) are protean, with major disabilities related to nocturnal hypokinesia. While it can be assessed by clinical interviews and screening instruments, these are often inaccurate and prone to recall bias. In light of advances in sensor technology, we explored the use of sensors in the study of nocturnal hypokinesia, by performing a systematic review of the professional literature on this topic. Evidence suggests that nocturnal hypokinesia exists even in patients in the early stages, and PD patients turned significantly less and with much slower speed and acceleration than controls, partly related to low nocturnal dopamine level. We conducted another systematic review to evaluate the evidence of the efficacy of dopaminergic agents in the treatment of nocturnal hypokinesia. Several lines of evidence support the use of long-acting drugs or by continuous administration of short-acting agents to control symptoms. Sensor parameters could be considered as one of the important objective outcomes in future clinical trials investigating potential drugs to treat nocturnal hypokinesia. Physicians should be aware of this technology as it can aid the clinical assessment of nocturnal hypokinesia and enhance the quality of patient care. In addition, the use of sensors currently is being considered for various aspects of research on early diagnosis, treatment, and rehabilitation of PD patients.

1. Introduction

Nocturnal akinesia or hypokinesia refers to a condition where Parkinson's disease (PD) patients have difficulty in moving their body during sleep, causing them to stay in the same position for prolonged periods [1]. In most literature related to nocturnal hypokinesia in PD patients, impaired bed mobility is recognized, and is characterized by only a few episodes of turning in bed throughout the night, and these are accomplished very slowly with apparent difficulty [1–4]. These long periods of immobilization and experience of difficulty in changing positions are likely to affect other movements during the night, such as getting out of bed. These dynamics can lead to the development of pressure ulcers, a predisposition to aspiration, pneumonia, and asphyxia, which are common causes of death in PD patients. The situation described above represents a very common nighttime problem affecting 65–70% of PD patients, and was rated as the most troublesome nighttime symptom in 39% of patients [1,5]. These problems negatively affect sleep quality, and the quality of life (QOL) of the patients as well as posing a significant burden for caregivers [1,6].

Several mechanisms have been proposed to explain the presence of nocturnal hypokinesia in PD, supporting the possibility of multifactorial etiologies. These include degeneration of the reticulospinal and vestibulospinal tracts that control axial movements, low nocturnal dopamine levels, abnormal posture alignment, and even the process of aging [7,8]. Since the presence of nocturnal hypokinesia may reflect the status of undermedication in PD patients during the night, this manifestation could be viewed as one of the manifestations of wearing-off (WO) symptoms. This statement is supported by our recent study, which documented a significant correlation between the severity of the modified version of

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Parkinson's Disease Sleep Scale (PDSS), and the 9-item of WO questionnaire [5]. Furthermore, nonmotor WO has also been identified as an independent predictor of nocturnal disabilities in PD patients as determined by the modified version of Parkinson's Disease Sleep Scale (PDSS) [5].

For the purpose of this review, which focuses on the problem of nocturnal hypokinesia in PD, we explored the potential applications of emerging technology, particularly wearable sensors, on the measurement of nocturnal akinesia or hypokinesia, in addition to therapeutic options for this problem. We accomplished both tasks by performing systematic reviews on these two topics.

2. Assessing instruments of nocturnal hypokinesia

The acquisition of information on nocturnal hypokinesia can be accomplished in clinical practice through interviews, which are often very difficult and inaccurate. Sleep diaries are frequently used, but they mainly provide information on the number of times the patient left the bed, the time to sleep onset, total sleep time, number of daytime naps, and daytime awakenings without any details of nocturnal movements. Moreover, the lack of awareness of nocturnal symptoms by PD patients and caregivers, as well as their physicians, often results in these problems being overlooked [3]. With regards to scales, the Movement Disorder Society Task Force recommends the following scales for rating overall sleep problems, and daytime sleepiness in PD: 1) the PDSS; 2) the Pittsburgh Sleep Quality Index (PSQI); 3) the Scales for Outcomes in PD-Sleep (SCOPA); 4) the Epworth Sleepiness Scale (ESS); 5) the Inappropriate Sleep Composite Score (ISCS); and 6) the Stanford Sleepiness Scale (SSS) [9]. While these scales are able to provide information about the severity of sleep problems in PD, they do not process specific items in relation to nocturnal hypokinesia. The Modified Parkinson's Disease Sleep Scale (PDSS-2) has included a new item (#9: Did you feel uncomfortable at night because you were unable to turn around in bed or move due to immobility?) to rate the severity of nocturnal immobility [10]. Nocturnal Akinesia, Dystonia, and Cramp Score (NADCS) was specifically developed to determine the severity of nocturnal movements in PD patients, but its validity has not yet been established [11]. The Parkinson's Disease Quality of Life Questionnaire has a single item (among 37 questions) that rates nocturnal hypokinesia during the last three months as turning difficulties in bed [12]. Therefore, clinical interviews and the utilization of these scales are unlikely to comprehensively capture the presence and severity of nocturnal hypokinesia in PD. Moreover, these scales are retrospectively assessed, and interpreted, which makes them vulnerable to recall errors and other types of bias.

3. Applications of sensors in the study of nocturnal hypokinesia in Parkinson's disease

With the advances of circuit technology, wearable sensors have been developed to monitor movement patterns in the daily lives of individuals and this capability has now been extended to PD patients. The advantages of wearable sensors include their ability to capture real-time data, thereby documenting real-life situations. They also allow physicians to obtain precise, accurate, and quantitative data. The accelerometer is a type of positional sensor, which functions by measuring acceleration along a sensitive axis based on Newton's second law (Force = Mass × Acceleration). Gyroscope is another type of angular velocity sensor measuring Coriolis force that arises in a rotating reference frame, which is proportional to the angular rate of rotation. The applications of sensors are expanding because they have the capacity to quantify dynamic accelerations with low-power consumption, and they come in small sizes making them suitable for the objective and ambulatory assessment of nocturnal movements. Motion sensors in the study of PD currently are based on an inertial measurement unit (IMU) that includes different types of sensors utilizing the technology of integrated micro-electro-mechanical systems (iMEMS), primarily accelerometers and gyroscopes. However, they differ in relevant technical aspects, including axial sensitivity (uni-, bi-, or tri-axial), frequency range, resonance frequency, damping and temperature drift.

The actigraph is a type of accelerometer that is built into a small, wrist watch-sized activity monitor that can record objective, long-term data on a patient's daily activities. The device consists of piezoelectric sensors that are sensitive in two or three directions, making it appealing for sleep investigators to apply this device for the identification of sleep vs. wakefulness. Specifically in PD, actigraphy has been used to compare sleep parameters in different subgroups of PD patients, and to assess the effects of medications, and interventions. The results of actigraphy compared with polysomnography (PSG) suggest that actigraphy may be useful for measurements of mean total sleep time, sleep efficiency, and wake-after-sleep onset in patients with mild to moderate PD. Because actigraphy registers nocturnal activities based on automatic scoring algorithms of the occurrence of suprathreshold motor activities and sleep is inferred from lack of movements, it can determine overall nocturnal activities, but lacks the ability to distinguish the nature of each activity. A significant degree of variability still occurs among individual patients with actigraphy [9]. Moreover, the position of actigraphy on the limbs also implies that it cannot directly monitor the activities of turning in bed, which are predominantly axial rotation, commonly referred to as nocturnal hypokinesia in the literature. This claim is supported by a study showing no significant differences in the actigraphic activities between PD patients with and without impaired bed mobility [3]. Therefore, in the following systematic review, we include only the application of axial sensors that are capable of capturing the activities of nocturnal hypokinesia in PD patients.

An electronic database search of titles and abstracts was performed using PubMed, EMBASE, Cochrane Library, life science journals, and online books to identify articles on the applications of sensors in the study of nocturnal hypokinesia in PD. The following terms were used for the literature search: Parkinson's disease AND nocturnal hypokinesia OR nocturnal akinesia OR early morning akinesia OR impaired bed mobility OR turning in bed OR roll over OR axial rotation OR sensor OR accelerometer OR gyroscope. A target search of bibliographies of relevant articles was also performed to identify additional studies for inclusion. Only original full-text articles published in English between January 1973 and August 2015 relating to sensors in the study of nocturnal hypokinesia in PD were included in this review. Review and editorial articles were excluded. Actigraphic studies were also excluded for the above reason. Two assessors (RB, JS) independently screened each paper and were required to agree on each study in order to be included in this review. We screened 252 titles and abstracts, from which 58 full-length articles were selected for further review. Of these, six articles fulfilled the selection criteria (Table 1) [3,4,13–16]. Except for one single case study without a matched control, all five studies had a case controlled design. A summary of all six studies, including subject details, sensor types, primary outcomes, and main results with conclusions, is provided in Table 1.

All studies involved a small number of PD subjects (<45 patients) with three studies utilizing patient's spouses as the controls [13,14,16]. All studies were performed in the patients' home environment with a period of one night of continuous recording with the exception of Louter's most recent study, which was performed on two occasions [4]. The sensors utilized in early studies were in the form of a rotational sensor consisting of a metal sphere

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