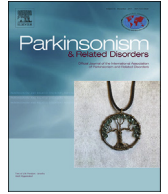




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## Review article

## Getting a good night sleep? The importance of recognizing and treating nocturnal hypokinesia in Parkinson's disease

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## ABSTRACT

When Parkinson's disease (PD) patients are asked about the quality of their sleep, their answers are dominated by difficulties associated with impaired mobility in bed, medically referred to as nocturnal hypokinesia. Nocturnal hypokinesia is symptomatic from the mid-stage of the disease, affecting up to 70% of PD patients, and contributes to poor sleep quality, and increased carer burden. Here we explore four areas of nocturnal hypokinesia that are relevant to clinical practice, namely: manifestations and definition; clinical assessment and objective monitoring; etiologies and contributing factors; and evidence-based therapeutic approaches. In addition, we provide an operational definition of what constitutes nocturnal hypokinesia and outline different methods of assessment, ranging from clinical interviews and rating scales to objective night-time monitoring with inertial sensors. Optimal management of nocturnal hypokinesia in PD begins with recognizing its manifestation by inquiring about cardinal symptoms and contributing factors from, not only patients, but also carers, followed by formal assessment, and the application of individualized evidence-based treatment. Night-time dopaminergic treatment is the primary therapy; however, careful clinical judgment is required to balance the benefits with the potential adverse events related to nocturnal dopaminergic stimulation. Future studies are needed to explore the practicality of home-based objective assessment of nocturnal hypokinesia, new therapeutic options not limited to dopaminergic medications, and non-pharmacologic approaches, including training on compensatory strategies and bedroom adaptations.

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## 1. Introduction

"This need of change of position is principally exhibited at night in bed by the more infirm, who are incapable of attending on themselves. ....Half an hour, a quarter of an hour, has scarcely elapsed until they require to be turned again, and if their wish be not immediately gratified they give vent to moans, which sufficiently testify to the intense uneasiness they experience."

JM Charcot, Lecture on the Diseases of the Nervous System, 1877

Charcot's statement probably represents the earliest description

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of what we nowadays refer to as 'nocturnal hypokinesia', medically defined as difficulty changing body position in bed [1]. However, it was not until 1988, in Lee and colleagues' landmark study, that an inability to turn over in bed was identified as PD patients' most troublesome night-time symptom, experienced by two-thirds of the studied population [2]. Since then nocturnal hypokinesia has been variously described in the medical literature as impaired bed mobility, inability to turn in bed, disordered axial movements, nocturnal immobility, and nocturnal wearing-off [1,3–6]. In addition, the much early term 'axial apraxia' illustrated the difficulties PD patients face in performing axial rotation in the horizontal plane despite sufficient levodopa treatment [7,8], but may also represent nocturnal hypokinesia as well. Based on these descriptors, nocturnal hypokinesia has been identified in 54–70% of PD patients, and negatively affects sleep quality, sleep efficiency, and quality of life of patients as well as imposing significant burden on carers [1–3], [5,6].

Despite its high prevalence, nocturnal hypokinesia is often overlooked, with physicians dismissing night-time symptoms in PD as of secondary importance [9] and compounded by patient ignorance [10]. Interestingly, low levels of self-reported night-time symptoms are contradicted by how troublesome PD patients rate sleep problems or how frequently night-time problems are identified when they are specifically assessed through the completion of validated questionnaires [1,5,11,12]. A recent patient survey indicated that difficulty turning in bed was the most challenging motor symptom to improve with dopaminergic medication [13]. Therefore, the objective of this article is to inform practicing neurologists about this common, but neglected, night-time symptom in PD, focusing on its clinical manifestations, assessment methods, etiologies and contributing factors, and give evidence-based therapeutic options, along with a practical treatment algorithm.

## 2. What movements constitute nocturnal hypokinesia?

It is difficult to define nocturnal hypokinesia as abnormal night-time movements in PD are myriad, including periodic limb movements in sleep (PLMS), painful dystonia, dyskinesia, tremor, and motor features of rapid eye movement sleep behavior disorder (RBD) [14–16]. Some occur as a result of depleted dopaminergic neurons or low efficacy of dopaminergic medication, with other causes including degeneration of sleep-wake regulatory centers and the waking effect of dopamine. While certain night-time movements have distinctive features (e.g. PLMS is associated with rhythmical extension of the big toe and dorsiflexion of the ankle) [16], characteristic movements for nocturnal hypokinesia have never been described. Traits that are related to nocturnal hypokinesia usually involve difficulties with turning in bed and getting out of bed, both features reflect the impairment of axial movements in PD patients [1,3,4,17].

### 2.1. Turning in bed

Although turning in bed may be viewed as a simple event involving primary axial rotation, it is, in fact, a complex sequential motor skill that involves many steps. A typical turn begins with throwing back bed covers (arms or legs), shifting the pelvis (axial), turning the head (axial), bringing the arm across the body in the direction of rolling (arm), and swinging the legs over (legs) (Fig. 1a–c) [18]. Therefore, turning or rolling over in bed represents a continuum of movements, requiring a sequence of coordination patterns involving limb (both upper and lower limbs), and axial (head, neck, and trunk) muscle coordination.

Movement impairment means strategies employed by PD patients to turn in bed differ from age-matched healthy individuals. In a video analysis of 38 PD patients (Hoehn & Yahr (HY) 1–2: 46%; 3–4: 54%), 82% reported difficulties with turning in bed, with 18% unable to turn either way, with various strategies used to overcome the problem, including hip-hitching, sitting, or using supports [3]. Despite the small number of subjects, this study emphasized that it is an inability to perform axial rotation which impairs the PD patients' ability to turn in bed. Another study, using the Kings College Hospital (KCH) rating scale with a sub-score for axial rotation, found significant correlation between axial rotation impairment and difficulty with turning in bed, again highlighting axial rotation as an important component of successful turning [4]. In addition, objective analysis of turning in bed with axial inertial sensors revealed that, in PD patients, turns were smaller, slower, and fewer in number compared to age-matched controls [17].

### 2.2. Getting out of bed

In most cases, to get out of bed requires a continuum of movements beginning with turning to enable a rise from a supine to a seated position, followed by moving to the edge of the bed, putting both feet onto the bedroom floor, and ending with successful standing (Fig. 1c–f). From a biomechanical perspective, this involves a series of complex sequential motor skills, including trunk flexion, pivot movements of the pelvis with thigh abduction, and completed by standing. Existing findings indicate that healthy older women are more likely to use lateral trunk flexion and rotation with weight bearing through the elbow to facilitate getting out of bed, rather than the commonly adopted strategy in young women of trunk flexion in the sagittal plane at the beginning of the rise [19–21]. In addition, compared to older adults without PD, PD patients were less likely to use a 'rotation' strategy and tended to sit up from a supine position by using both arms to push their torso in a vertical plane, and the time PD patients took to get out of bed was significantly longer than age-matched controls, with long pauses between each movement [19]. A recent video-analysis study also yielded similar findings, showing that PD patients frequently used their upper limbs to get out of bed (55%) while a lateral roll strategy was employed by only 27% of patients [22].

It seems that axial rotation represents a core movement when turning in bed, while trunk flexion is an essential component of getting out of bed. Therefore, based on analysis of previous clinical descriptions, we propose that the operational definition of 'turning in bed' be 'the ability to perform an axial rotation from one static position to the another', while the definition of 'getting out of bed' be 'the ability to sit up from a supine position primarily using trunk flexion, followed by thigh abduction, weight bearing on both legs and successful standing'. So, if these two operational definitions are followed, then nocturnal hypokinesia can be defined as 'a decreased ability to perform sufficient axial rotation and/or trunk flexion to turn in, or get out of, bed as a result of axial and limb muscle incoordination'.

## 3. Assessment methods for nocturnal hypokinesia: what is applicable in clinical practice?

Currently, information about a patient's experience of nocturnal hypokinesia is acquired during clinical consultations, but often neither patient nor carer recognize or recall this symptom by themselves or they underestimate its severity [6]. Sleep diaries can be used, but they principally provide data related to time to sleep onset, total sleep time, number of daytime naps, and daytime awakenings without any detail of nocturnal movements. The International Parkinson and Movement Disorder Society (IPMDS) Task Force recommends the following scales for rating, screening, or measuring the severity of sleep problems, and daytime sleepiness in PD: 1) the PD Sleep Scale (PDSS); 2) the Pittsburgh Sleep Quality Index (PSQI); 3) the Scale for Outcomes in PD-Sleep (SCOPA-Sleep); 4) the Epworth Sleep Scale (ESS); 5) the Inappropriate Sleep Composite Score (ISCS); and 6) the Stanford Sleepiness Scale (SSS) [23]. However, they do not process specific items that are related to nocturnal hypokinesia. For example, the ESS and SSS only provide information that is related to daytime sleepiness, not nocturnal sleep. Only, the modified Parkinson's Disease Sleep Scale (PDSS-2), not the PDSS, has an item included (out of 15 items; #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 [24]. Other scales to consider are: the Nocturnal Akinesia, Dystonia, and Cramp Score (NADCS), which was specifically developed to determine the severity of nocturnal movements in PD patients, but its validity has not been established

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