Journal of the Neurological Sciences 373 (2017) 244–248

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Clinical short communication

Time for a strategy in night-time dopaminergic therapy? An objective sensor-based analysis of nocturnal hypokinesia and sleeping positions in Parkinson's disease☆

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ARTICLE INFO

Article history:
Received 2 October 2016
Received in revised form 19 December 2016
Accepted 22 December 2016
Available online 28 December 2016

Keywords:
Nocturnal hypokinesia
Nocturnal akinesia
Parkinson's disease
Sleep position
Supine
Sensors

ABSTRACT

Background: Nocturnal hypokinesia is a common night-time symptom in patients with Parkinson's disease (PD). However, there is still little understanding of the nature, and variations of severity of this symptom.
Objectives: To evaluate the severity of nocturnal hypokinesia and sleep positions in PD patients using multisite wearable sensors.
Methods: Nocturnal parameters and sleep positions in 18 PD couples were assessed and compared using wearable sensors (limbs and trunk) for one night in their homes. Nocturnal parameters included number, velocity, acceleration, degree, limb movements and the number of times they got out of bed.
Results: PD patients had significantly fewer episodes of turns in bed than their spouses ($p = 0.043$), which was associated with significantly slower speed ($p = 0.005$), acceleration ($p = 0.005$) and fewer degrees ($p = 0.017$). When we split the night into the first and second half, significant findings were mainly demonstrated in the second half of the night, including significantly fewer turns ($p = 0.02$) with smaller degrees ($p = 0.017$), slower speed ($p = 0.005$) and acceleration ($p = 0.007$). No significant differences in these parameters were shown in the first half of the night except for smaller degrees of turn in bed in PD patients ($p = 0.028$) and slower acceleration ($p = 0.037$). In addition, PD patients spent significantly more time in a supine position compared to their spouses ($p = 0.031$) with significantly less time in a prone position ($p = 0.041$).
Conclusion: Nocturnal hypokinesia gets worse as the night progresses. Treatment of nocturnal hypokinesia should aim at providing a continuous dopaminergic delivery that can achieve a sustained therapeutic level of dopamine throughout the night.

1. Introduction

Nocturnal hypokinesia/akinesia is defined as a condition where patients have difficulty in moving their body (mainly turning in bed) during sleep, causing them to stay in the same position for prolonged periods [1]. Although it is rated as one of the most common and troublesome night-time symptoms in patients with Parkinson's disease (PD), the recognition of this problem is still limited due to a lack of awareness and ability to observe and report the symptoms accurately to treating physicians by both patients and caregivers [2]. Disabilities related to nocturnal hypokinesia not only compromise a patient's night-time motor symptoms, but also negatively affect quality of life of both patients and caregivers [3]. In addition, the presence of nocturnal hypokinesia may also be associated with certain sleep positions (e.g. supine sleep) putting patients at significant risk of bed sores, and respiratory complications [4]. To date, there have been very few therapeutic trials that focus on nocturnal hypokinesia as their clinical outcome, probably due to inadequate understanding on the nature of this symptom, which is likely to occur but may vary in severity throughout the night [5].

While a number of studies involving semi-structured interviews and questionnaires have confirmed the existence of nocturnal hypokinesia as the common night-time symptom in PD patients, it is as yet unclear if the severity of nocturnal hypokinesia is different throughout the night [2,6]. As nocturnal hypokinesia is viewed as the longest 'off' period associated with the presence of early morning akinesia and a lack of night-time dopamine secretory peak, we postulate that the symptom of hypokinesia should get worse as the night progresses (e.g. the second half of the night) [2]. Understanding how nocturnal hypokinesia varies

☆ The authors have no conflict of interest.

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http://dx.doi.org/10.1016/j.jns.2016.12.045
0022-510X/

Table 1
Comparison of demographic data, nocturnal parameters and sleep position between Parkinson's disease (PD) patients and their spouses.

Parameters	PD patients ($n = 18$) mean (SD)	Spouses ($n = 18$) mean (SD)	p-Value
Demographic data			
• Sex	14 M; 4 F	4 M; 14 F	
• Age (years)	64.9 ± 7.6	63.8 ± 8.5	0.632
• TMSE	27.0 ± 1.9	27.9 ± 1.4	0.248
• Age of onset (years)	55.0 (10.0)		
• Duration of the disease (years)	10.0 (5.4)		
• Hoehn & Yahr staging	2.53 (0.44)		
• Total UPDRS	46.89 (20.78)		
• UPDRS III	22.94 (8.31)		
• Presence of nocturnal hypokinesia	60%		
• Total LED (mg)	953.06 (451.89)		
• Nighttime LED (mg) (controlled-release levodopa, $n = 13$)	68.89 (48.46)		
	PD patients ($n = 18$)	Spouses ($n = 18$)	p-Value
Nocturnal parameters (full night analysis)			
• Total sleep time (min)	447.0 (59.9)	477.8 (116.2)	0.271
• Number of turns in bed (times)	7.6 (6.7)	11.7 (6.6)	0.043[a]
• Velocity of turns in bed (degree/s)	610.8 (238.8)	1154.8 (362.0)	0.005[a]
• Acceleration of turns in bed (degree/s^2)	53.6 (20.2)	159.4 (71.6)	0.005[a]
• Degree of turns in bed (degree)	44.0 (23.1)	77.4 (23.8)	0.017[a]
• Number of getting out of bed (times)	1.9 (1.2)	1.2 (1.1)	0.075
• Number of upper limb movements (times)	31.0 (16.4)	25.5 (10.6)	0.347
• Number of lower limb movements (times)	18.4 (8.7)	21.1 (12.7)	0.953
Nocturnal parameters (first half of the night analysis)			
• Number of turns in bed (times)	5.7 (5.5)	5.2 (3.4)	0.226
• Velocity of turns in bed (degree/s)	647.87 (508.4)	941.81 (730.58)	0.093
• Acceleration of turns in bed (degree/s^2)	55.57 (40.37)	125.17 (108.42)	0.037[a]
• Degree of turns in bed (degree)	46.87 (28.29)	74.35 (41.91)	0.028[a]
• Number of getting out of bed (times)	1.5 (0.7)	0.6 (0.8)	0.257
Nocturnal parameters (second half of the night analysis)			
• Number of turns in bed (times)	3.3 (3.1)	6.5 (3.6)	0.020*
• Velocity of turns in bed (degree/s)	573.71 (417.26)	1367.78 (537.63)	0.005*
• Acceleration of turns in bed (degree/s^2)	51.56 (35.31)	193.65 (118.38)	0.007*
• Degree of turns in bed (degree)	41.21 (27.14)	80.37 (16.41)	0.017*
• Number of getting out of bed (times)	0.8 (0.9)	0.5 (0.5)	0.008*
Nocturnal parameters (1st vs. 2nd half of the night analysis in PD patients)	PD patients (1st half of the night)	PD patients (2nd half of the night)	p-Value
• Number of turns in bed (times)	5.7 (5.5)	3.3 (3.1)	0.048*
• Velocity of turns in bed (degree/s)	647.87 (508.40)	573.71 (417.26)	0.959
• Acceleration of turns in bed (degree/s^2)	55.57 (40.37)	51.56 (35.31)	0.721
• Degree of turns in bed (degree)	46.87 (28.29)	41.21 (27.14)	0.646
• Number of getting out of bed (times)	1.5 (0.7)	0.8 (0.9)	0.054
Sleep position (full night analysis)	PD patients ($n = 18$)	Spouses ($n = 18$)	p-Value
• Prone position	0.69 (2.45) [0.15%]	18.58 (31.67) [3.89%]	0.041*
• Right lateral position	72.37 (69.12) [16.19%]	137.56 (105.39) [28.80%]	0.094
• Left lateral position	57.38 (110.00) [12.84%]	112.28 (99.53) [23.50%]	0.039*
• Supine position	316.58 (133.17) [70.82%]	209.37 (108.64) [43.82%]	0.031*

Wilcoxon Signed Ranks test was used for the comparison of nocturnal parameters.
TMSE: Thai Mini-Mental Status Examination.
* Refers to p-value ≤ 0.05 indicating statistical significance.

throughout the night has significant therapeutic implications on the use of continuous dopaminergic delivery during the night to achieve a sustained therapeutic benefit, particularly in advanced PD patients [5]. Recently, we have demonstrated that the severity of nocturnal hypokinesia can be quantified with the use of inertial sensors [7,8]. Therefore, in this study, we aim to evaluate the differences in the severity of nocturnal hypokinesia by comparing the ability to turn in bed, getting out of bed, and sleep positions between PD patients and their spouses during the first and second half of the night.

2. Patients and methods

2.1. Parkinson's disease couples

We included 18 PD patients who had spouses whose age did not differ from the patients by >10 years. We excluded patients if they were bedridden, had history of other neurologic or musculoskeletal disorders that may compromise the ability to turn in bed, and took any hypnotic or sedative drugs. All PD patients were allowed to continue on their usual medications. Clinical demographics and rating scales including Hoehn & Yahr (HY) stage and Unified Parkinson's Disease Rating Scale (UPDRS) were evaluated in all patients. The UPDRS axial score was calculated as the summation of the items 18, 22, 27, 28, 29, and 30 of the UPDRS section 3 [9]. Levodopa equivalent dose (LED) was determined using a standardized protocol with the bedtime LED calculated from the amount of dopaminergic medications that patients took at bedtime. All spouses were carefully examined by two independent neurologists (JS and RB) to ensure they had no signs of Parkinsonism. We also excluded subjects with restless leg syndrome, periodic limb movement disorders, chronic insomnia, and history of cerebrovascular disorders, which may increase or decrease limb movements in affected individuals. Spouses were selected as controls because they shared the same