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Short communication

Evaluation of nocturnal hypokinesia in Parkinson's disease using a novel patient/proxy questionnaire and correlations with objective monitoring

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ABSTRACT

Background: Nocturnal hypokinesia is a decreased ability to perform sufficient axial rotation and/or trunk flexion to turn in or get out of bed. Currently, there are no validated questionnaires specifically to assess nocturnal hypokinesia in PD patients.
Objective: To develop and validate a questionnaire to assess PD patients' problems associated with turning or getting out of bed.
Methods: The nocturnal hypokinesia questionnaire (NHQ) consists of 10 items, completed independently by patients and their caregivers. For validation, 76 patient-caregiver pairs completed the questionnaire and validity, agreement levels, and internal consistency assessed. In addition, 76 healthy couples served as controls. The NHQ and Modified Parkinson's Disease Sleep Scale (PDSS-2) were compared and 25 random patients-caregiver pairs were also assessed with objective night-time monitoring.
Results: Patient and caregiver scores showed a high level of agreement (Intra-class correlation: 0.84) with high internal consistency (KR-20 coefficient of 0.73 for patients and 0.69 for caregivers). No significant difference between the mean total NHQ scores as rated by patients and caregivers was observed. Mean NHQ scores from patients and caregivers were significantly higher than healthy controls ($p < 0.001$). Moderate correlations were found between the NHQ and PDSS-2 ($r = 0.32$, $p = 0.004$), and with objective monitoring (Number of turns: $r = -0.41$, $p = 0.04$, Degree of turn: $r = -0.44$, $p = 0.02$).
Conclusion: The NHQ is a reliable instrument to identify symptoms of nocturnal hypokinesia amongst PD patients. Strong patient-caregiver agreement supports the use of proxy evaluation by caregivers when patient's information is unobtainable.

1. Introduction

Nocturnal hypokinesia was recently defined as a decreased ability to perform sufficient axial rotation and/or trunk flexion to turn in or get out of bed [1]. However, in most cases, the problems related to night-time hypokinesia are not limited to axial rotation and trunk flexion, but also include abnormal limb movements and postures while in bed, and a decreased ability to coordinate axial and limb muscles to perform such movements. In clinical practice, the evaluation of nocturnal hypokinesia in PD patients is usually based on clinical interviews and specific items of validated questionnaires, with a reported prevalence of at least 50% amongst moderate stage patients [2,3]. Recently, continuous objective monitoring with body-worn sensors has provided another option to evaluate nocturnal mobility in patient's bedroom environment, with the ability to measure certain characteristics in PD patients, such as fewer, smaller and slower turns, and increased episodes of getting out of bed due to nocturia when compared to age-matched controls [4]. However, the use of night-time monitoring is still limited to research and clinical trials, and has yet to be employed in clinical practice.

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Despite the availability of the abovementioned instruments, there is currently no single method that is capable of capturing the different dimensions of nocturnal hypokinesia, which, by definition, is not just limited to turning in bed, but also encompasses getting out of bed, limb movements and posture while in bed, and the ability and coordination of axial and limb muscles to perform such movements. Moreover, certain symptoms may occur as part of the manifestations of nocturnal hypokinesia or as a result of treatment and related side effects, such as pain, stiffness, or dyskinesia. These modalities are not included in any existing questionnaires that are commonly used to elicit night-time problems amongst PD patients. For example, only one out of 15 items of the Modified Parkinson's Disease Sleep Scale (PDSS-2) inquire only one aspect of nocturnal hypokinesia (item #9: Did you feel uncomfortable at night because you were unable to turn around in bed or move due to immobility?) [5]. Obtaining the information on nocturnal hypokinesia from patients retrospectively during interviews can also be a real challenge as, in most circumstances, they are unable to recall their night-time symptoms accurately. On the other hand, physicians often obtain patient's night-time information from caregivers. Therefore, the objective of our study is to develop and validate nocturnal hypokinesia questionnaire (NHQ) that is completed independently by either PD patients or their caregivers to determine various aspects related to nocturnal hypokinesia as experienced by PD patients.

2. Methods

2.1. Questionnaire development

Discussions were held between a group of five PD experts who specialise in the care of PD and sleep disorders (three movement disorder and sleep neurologists, two PD specialist nurses), and a PD patient representing Chulalongkorn PD support group together with his caregiver, to determine the process of constructing a new questionnaire, as well as potential domains of burden worth exploring. All members were bilingual and all healthcare professionals had extensive experience, of at least 5 years, in the care of PD patients. In addition, one-on-one and group interviews were also conducted with patients and caregivers attending a local PD support group. The contents from all discussions were then transcribed and analysed to determinefour PD-specific themes that are related to nocturnal hypokinesia, including turning over in bed, getting out of bed, parkinsonian motor symptoms, and others (Supplementary data 1). Finally, ten items were generated for the NHQ, covering these four domains (Supplementary data 1). Each item was assigned a “yes/no” response for independent completion by patients and their caregivers based on their experience during the past week. The NHQ was then translated, according to translation standards, into Thai and back-translated into English, with modifications of the Thai wordings where necessary. Comprehension of all items was tested for content validity by another expert panel who were not involved with item generation. The index of item-objective congruence (IOC) was conducted on all questionnaire items, demonstrating a positive content validation of IOC index at least 0.6 on all items (Supplementary data 2).

2.2. Participants

PD patients were included if their diagnosis was in accordance to the UK Brain Bank criteria. Caregivers were defined as spouses, relatives, or friends who identified themselves as beingprimarily responsible for the care of the patient. The eligibility criteria included: age of at least 18 years, being able to understand and complete the self-rating questionnaire, and being clinically stable without a history of profound dementia or psychiatric disorders. In our setting,only caregivers who share the same bedroom environment with the patients were included in the study. Consent for participating in the study was obtained from all participants. Sample size was calculated by using medium effect size (Cohen's d = 0.5), desired statistical level of 0.8, and probability level of 0.05, giving the minimum sample size of 64 in each group. For the validation, 76 PD patient-caregiver pairs were recruited from the movement disorder outpatient clinic at Chulalongkorn Centre of Excellence for Parkinson's Disease and Related Disorders (ChulaPD, www.chulapd.org) between July and December 2017. Another set of 76 healthy couples served as controls. Ethical approval was given by the Human Ethics Committee of the Faculty of Medicine, Chulalongkorn University and the study was executed in accordance with the declaration of Helsinki. All patients provided written informed consent.

2.3. Instruments

In order to assess the NHQ against established measures of nocturnal symptoms in PD, all PD subjects were asked to complete the PDSS-2 and the Nocturnal Akinesia, Dystonia, and Cramp Score (NADCS). The PDSS-2 is the modified version of the PDSS, recommended by the Movement Disorder Society (MDS) for rating overall sleep problems both to screen and to measure severity [5,6]. All 15 items in the PDSS-2 are divided into three factor categories, representing motor symptoms at night, PD symptoms at night, and disturbed sleep respectively. Item# 9, referring to the difficulty of turning in bed as a result of nocturnal immobility, belongs to the category of PD symptoms at night. The NADCS has three components, exploring the severity of akinesia, dystonia, and cramp during the night via an ordinal scale [7]. In addition, a random sample of 25 patients-caregivers pairs were also assessed with night-time sensor monitoring (the NIGHT-Recorder, ChulaPD, Thailand) toprovide objective correlations [4,8]. Objective nocturnal parameters in this study consisted of the number of times, degree, velocity and acceleration of turning in bed as described in our prior study [4].

2.4. Statistical analysis

Comparison of demographic data and clinical rating scales between groups were determined by Mann-Whitney *U* test. Chi-Square test was used to analyse relationships between categorical variables. Inter-rater agreement levels were assessed by Intra-class correlation for continuous variables, and Cohen's Kappa coefficient for ordinal variables. Kuder-Richardson 20 (KR-20) coefficient was used to determine the internal consistency of the NHQ according to the dichotomous options of response of the items. To evaluate the external validity of the NHQ, Spearman's rank correlation coefficient was calculated for correlations between the NHQ and the PDSS-2, NADCS, and objective data from sensor monitoring. A *p*-value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 22.0 software (SPSS Inc., Chicago IL).

3. Results

3.1. Sample characteristics

Table 1 outlines the characteristics of the 76 PD patient-caregiver pairs. The majority of caregivers were female spouses sharing the same bedroom environment. All 76 healthy couples were non-smokers and were without significant existing medical conditions.

3.2. NHQ questionnaire feasibility

The feasibility and face validity of the NHQ were established during interviews with neurologists, caregivers, patients, and healthy couples at the time of questionnaire development and during the recruitment stages of the study. All subjects took approximately 10 min to complete the NHQ, and all respondents were able to finish the NHQ once they had started it.

The NHQ characteristics can be seen in Table 2. The item rating of

Table 1
Clinical demographics of Parkinson's disease patient-caregiver pairs and healthy couples.

	Patient-caregiver pairs		Healthy couples (C)		*p*-value
	PD patients (N = 76)	Caregivers (N = 76)	Control (N = 76)	Caregivers (N = 76)	
Age (years)	65.59 ± 10.90	55.03 ± 16.06	64.30 ± 12.11	52.08 ± 15.83	$p^A = 0.681^{\beta}$, $p^B = 0.299^{\beta}$
Male gender	46 (60.5)	18 (23.7)	48 (63.2)	13 (17.1)	$p^A = 0.738^{£}$, $p^B = 0.314^{£}$
Relationship between caregivers and patients	Spouses: 52 (68.4%) Senior caregivers: 9 (11.8%) Children: 12 (15.8%) Relatives: 3 (3.9%)		Spouse 58 (76.3%) Senior caregivers 1 (1.3%) Children 14 (18.4%) Relatives 3 (3.9%)		$p = 0.076^{£}$
Hoehn and Yahr score	2.62 ± 0.93		–		-
Categories of Hoehn and Yahr score	Stage 1: 3 (3.9%) Stage 1.5: 10 (13.2) Stage 2: 16 (21.1%) Stage 2.5: 15 (19.7%) Stage 3: 19 (25%) Stage 4: 10 (13.2%) Stage 5: 3 (3.9%)		–		-
Disease duration (years)	6.43 ± 2.96		–		-
LED (mg)	965.60 ± 464.82		–		-
Total PDSS-2 score	18.59 ± 9.31		–		-
• Domain 1: Motor symptoms at night	4.85 ± 4.31		–		-
• Domain 2: PD symptoms at night	5.41 ± 4.42		–		-
• Domain 3: Disturb sleep	8.31 ± 3.53		–		-
Total NADCS score	3.93 ± 3.02		–		-
NADCS–akinesia sub-score	2.02 ± 1.31		–		-
NADCS–dystonia sub-score	0.95 ± 1.27		–		-
NADCS–cramp sub-score	0.96 ± 1.17		–		-

*: Statistically significant; $^{\beta}$: Mann-Whitney *U* test; $^{£}$: Chi-square test; Values in parentheses indicate percentage; A: Comparison between PD patients and control subjects; B: Comparison between PD caregivers and control spouses; LED: Levodopa equivalent dose; PDSS-2: Modified Parkinson's Disease Sleep Scale; NADCS: Nocturnal Akinesia Dystonia and Cramp Score.

Table 2
Nocturnal hypokinesia questionnaire scores of patient-caregiver pairs and healthy couples.

	Patient-caregiver pairs		Healthy couples		*p*-value
	PD patients (N = 76)	Caregivers (N = 76)	Control (N = 76)	Spouses (N = 76)	
Total NHQ score (points)	4.57 ± 2.54	4.28 ± 2.40	0.80 ± 1.24	0.80 ± 1.28	$p^A = 0.45^{\beta}$, $p^B = 0.84^{\beta}$ $p^C < 0.001^{\beta*}$, $p^D < 0.001^{\beta*}$
NHQ domain 1 score (Turning in bed, points)	1.17 ± 0.86	1.06 ± 0.81	0.10 ± 0.35	0.11 ± 0.36	$p^A = 0.39^{\beta}$, $p^B = 0.78^{\beta}$ $p^C < 0.001^{\beta*}$, $p^D < 0.001^{\beta*}$
NHQ domain 2 score (Getting out of bed, points)	1.01 ± 0.86	0.98 ± 0.82	0.19 ± 0.54	0.26 ± 0.62	$p^A = 0.84^{\beta}$, $p^B = 0.49^{\beta}$ $p^C < 0.001^{\beta*}$, $p^D < 0.001^{\beta*}$
NHQ domain 3 score (Parkinsonian motor symptoms, points)	2.32 ± 1.52	2.24 ± 1.53	0.48 ± 0.77	0.42 ± 0.69	$p^A = 0.69^{\beta}$, $p^B = 0.67^{\beta}$ $p^C < 0.001^{\beta*}$, $p^D < 0.001^{\beta*}$
NHQ domain 4 score (Others, points)	0.05 ± 0.22	0.04 ± 0.19	0.01 ± 0.11	0.00 ± 0.00	$p^A = 0.71^{\beta}$, $p^B = 0.31^{\beta}$ $p^C = 0.17^{\beta*}$, $p^D = 0.07^{\beta*}$

*: Statistically significant; $^{\beta}$: Mann-Whitney *U* test; A: Comparison between PD patients and caregivers; B: Comparison within control group; C: Comparison between PD patients and control subjects; D: Comparison between PD caregivers and control spouses; NHQ: Nocturnal hypokinesia questionnaire.

each item was either 'Yes' (1) or 'No' (0) and the mean total score of NHQ as rated by PD patients was not significantly different from the score rated by the caregivers (Patients: 4.57 ± 2.54 vs. Caregivers: 4.28 ± 2.40, $p = 0.10$). However, both patients' and caregivers' scores were significantly higher than the healthy couples' scores ($p < 0.001$), confirming the specificity of NHQ items for nocturnal hypokinesia as experienced by PD patients. The distribution of this score indicates mild to moderate symptoms of nocturnal hypokinesia for most patients. Importantly, the internal consistency of the NHQ items was good, as confirmed by KR-20 coefficient of 0.73 and 0.69 for patients and caregivers respectively (Supplementary data 3). Therefore, all ten items were included in a final version of the NHQ.

3.3. Inter-rater agreement between PD patients and caregivers

The Intra-class correlation coefficient for the total NHQ score, when rated by patients and caregivers as a measure of interrater agreement, was 0.84, demonstrating a good agreement for the NHQ when rated by either PD patients or their caregivers (Supplementary data 4). When considering the agreement of individual NHQ items, the strongest coefficient was observed for item #4 enquiring about the need for assistance to get out of bed (0.97), followed by item #5, which enquires about presence of axial stiffness during the night or in the early morning (0.76). However, the coefficient values of all NHQ items were above 0.4, indicating at least moderate strength of agreement for all items.

3.4. Convergent validity

The convergent validity was supported by moderate correlations of the NHQ with the PDSS-2 (r = 0.32, $p = 0.004$) as well as its PD symptoms at night sub-score (r = 0.42, $p < 0.001$), and PDSS item #9

on nocturnal immobility (r = 0.37, $p = 0.001$) (Supplementary data 5). Similar correlations were also observed between the NHQ and the NADCS total score and its sub-scores on akinesia and dystonia. In this study, we attempted to determine the correlation between the NHQ and the objective measurement of turning in bed in 25 PD subjects and their caregivers. Moderate correlations were also observed between the NHQ and the number of turns (r = −0.41, $p = 0.04$) and the degree of turning in bed (r = −0.44, $p = 0.02$) respectively (Supplementary data 5).

4. Discussion

In this study, we have developed the NHQ that is specific to PD and displays good content validity and reliability when implemented by either PD patients or their respective caregivers. Significant correlations have been demonstrated between the NHQ and a number of standard rating scales and in particular the objective monitoring, providing a strong evidence for its validity in capturing the full spectrum of nocturnal hypokinesia in PD patients.

One unique feature of the NHQ is that it can be completed by either PD patients or their caregivers, provided that he/she shares the same bedroom environment with the patient. Our data supports the use of proxy evaluation for nocturnal hypokinesia by caregivers, thus providing a practical application for physicians to acquire reliable night-time information from caregivers when the same information may not be obtained from patients for several reasons, for example patient's inability to recall or communicate effectively [9,10]. Indeed, the use of proxy evaluation in PD is not new and a successful example is shown by the proxy assessment of health-related quality of life using PD Questionnaire-8 and EuroQol-5 dimension [11]. To investigate about nocturnal hypokinesia in clinical practice, we recommend that the NHQ is provided to patients, particularly those who are at risk of developing night-time mobility problems, including those with a HY of at least stage 2 and the presence of day-time or early morning off [1]. The NHQ should be first attempted by patients but caregivers can be consulted for additional information or act as a proxy when patient's information deems inadequate or unreliable. According to our own experience, the majority of patients and caregivers reported more than one aspect of nocturnal hypokinesia with a mean of four symptoms amongst moderate-stage patients.

In addition to proxy evaluation, the NHQ offers several further advantages to its use in a clinical setting, including being a self-administered and simple instrument, which can be completed within 10 min in the majority of PD patients. The ‘yes’ or ‘no’ response makes it a simple screening instrument that does not require detailed knowledge of responders for interpretation. The subjects were asked to complete the NHQ based on their experience within the past week, limiting the possibility of recall bias or error. As the NHQ evaluates different symptom dimensions of nocturnal hypokinesia, the identified symptom can also be individually targeted for treatment. While the PDSS-2 is recommended as a screening tool and a measure of severity for overall sleep impairment, it is not an ideal scale for comprehensive assessment of nocturnal hypokinesia [6]. However, the PDSS-2 and NHQ can complement each other where the PDSS-2 is used to evaluate overall night-time disturbances in PD patients, followed by a specific assessment of nocturnal hypokinesia by the NHQ when the PDSS-2 item on nocturnal immobility is identified to be frequentor troublesome to the patients. Since there is currently no gold standard for diagnosing nocturnal hypokinesia, a cut-off point for the NHQ cannot be determined, but the score range reflects the number of symptoms that are considered relevant to nocturnal hypokinesia. Uneven gender distribution, reflected by male predominance in both patients (60.5%) and control subjects (63.2%) could be a potential limitation although no statistical differences were foundwhen compared between these two groups. Another limitation of our questionnaire is a lack of non-motor assessment ofnight-time symptoms (e.g. sleep dysfunctions, urinary symptoms), which may co-exist in PD patients with nocturnal hypokinesia. Future studies are needed to explore the relationship between nocturnal non-motor symptoms and nocturnal hypokinesia to provide a holistic approach of night-time symptoms in PD.

To conclude, nocturnal hypokinesia represents one of many common night-time PD symptoms that are deemed by many patients as disabling to their quality of life, but potentially neglected by physicians [1,12]. While no specific instrument is currently available for the evaluation of night-time motor symptoms, the NHQ could be offered as a self-rated instrument by patients who are suspected of suffering from nocturnal hypokinesia with proxy evaluation by caregivers when direct patient's information is not possible. The NHQ can also be considered as a screening tool for those with night-time motor problems [1]. The presence of nocturnal hypokinesia as identified by the NHQ should prompt physicians to investigate causes and coexisting nocturnal symptoms in their patients, and, importantly, to consider therapeutic options where indicated.

Conflicts of interest

The authors have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2018.09.023.

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