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The Nondeclaration of Nonmotor Symptoms of Parkinson's Disease to Health Care Professionals: An International Study Using the Nonmotor Symptoms Questionnaire

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Abstract: The nonmotor symptoms (NMS) of Parkinson's disease (PD) are less well recognised and can be more troublesome to patients and carers than classical motor features. NMS are frequently missed during routine consultations and such under-recognition may have implications on quality of care given that many NMS are treatable. To determine the proportion of patients not declaring NMS to healthcare professional (HCP) as assessed by self completion of the NMS questionnaire (NMSQuest), a validated, self-completing questionnaire with 30 items. Multicentre international study. The data was collected from PD patients across all age groups and stages attending outpatient clinics in specialist and care of the elderly settings. 242 patients recruited and undeclared NMS ranged from 31.8% (diplopia) to 65.2% (delusions). The most frequently nondeclared symptoms were delusions, daytime sleepiness, intense and vivid dreams, and dizziness. In many, appropriate treatments for undeclared NMS were started only after these were recognised following completion of NMSQuest. NMS of PD are frequently undeclared at routine hospital consultation and may be related to the fact that patients often do not link these symptoms with PD or may be too embarrassed to discuss these. Use of NMSQuest allows patients to flag symptoms which may be otherwise undeclared and remain untreated when potential treatments exist. © 2010 Movement Disorder Society

Key words: nonmotor symptoms; Parkinson's disease; nondeclared; NMSQuest; quality of life

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The nonmotor symptoms (NMS) of Parkinson's disease (PD) are a key cause of disability and contribute to the deterioration of quality of life (QoL) in PD. Therefore, recognition of NMS is important for delivery of modern and comprehensive healthcare for PD patients.[1,2] NMS of PD occur throughout the course illness from early to late disease. Although some NMS of PD, such as, depression, dementia, dysautonomia,

and sleep problems, are well recognised, whereas others, such as, dribbling of saliva, weight changes, sexual problems, and visual problems are less known.[1,3] Some NMS can be related to dopaminergic treatment, for example, dopamine dysregulation syndrome, drug-induced hallucinations or psychosis, and postural hypotension, whereas fluctuations in motor responses also may have major nonmotor components.[1]

In spite of the importance of NMS, these symptoms are not well recognized in clinical practice. A study conducted in the US reported that existing depression, anxiety, and fatigue are not identified by neurologists in over 50% of consultations, and existing sleep disturbance in over 40%.[4] Additionally, a UK Brain Bank based study reported that 21% of the sample as presenting or premotor features, such as, pain, anxiety, and urinary dysfunction. These patients were more likely to be misdiagnosed initially and received inappropriate medical interventions.[5] The importance of recognising NMS is underpinned by the fact that many of NMS of PD, contrary to common perception are treatable and may respond to dopaminergic therapy.[6]

The NMSQuest is the first self completed 30 item screening tool containing nine NMS domains designed for rapid screening of NMS, empowering the patient and caregiver to flag up relevant NMS that may not be otherwise discussed in consultations.[7] Pilot validation study assessing feasibility, validity, and acceptability of the NMSQuest has been published and the questionnaire has been independently validated and recommended for use in routine clinical practice by the Department of Health in the UK as part of the 18-week treatment pathway for PD.[8,9] In this multicentre international study, we report observations from the use of NMSQuest across PD clinics and the percentage of NMS declared on NMSQuest that may not have been previously discussed with the healthcare professionals (HCP).

PATIENTS AND METHODS

PD patients (with the aid of caregivers when necessary) completed the NMSQuest (details of completion of NMSQuest has been described previously),[7,8] whereas waiting to be seen by the HCP. Nondemented, consecutive PD patients of all ages and in all stages of the disease were included as long as they satisfied the UK PD brain bank criteria.[10] Only patients with no previous experience of using NMSQuest were included to avoid potential bias in eliciting NMS patients were recruited from both teaching hospital (KCH, London, Bremerhaven, Germany), general hospital neurology clinic (University Hospital Lewisham) and care of the elderly movement disorders clinics (KCH and Sothern General Hospital, Glasgow) or research units (Alzheimer Disease Research Unit, Madrid, Spain). Routine demographic details and drug history were noted. Where appropriate locally cross cultural validated versions were used as used in the original NMSQuest validation and subsequent prevalence studies.

After completion of NMSQuest (which relates to problems active in the past month), patients were specifically asked if they had discussed the positive symptoms previously with any HCP and, if not, why. Declaration of NMS prompted appropriate review and management of individual symptoms in all patients.

Data Analysis

Prevalence of each NMS was calculated by computing the number of positive responses (symptoms) and calculation of percentage related to the number of patients in the sample. For each item, the proportion of nondeclared NMS was calculated based on the percentage of patients declaring to suffer the symptom. For each NMSQuest domain, the number of declared symptoms (positive) and nondeclared symptoms was determined. Mann-Whitney and Kruskal-Wallis tests were used for comparisons. The Spearman rank correlation coefficient was applied to determine associations. Statistical analysis was carried out with Stata/IC 10.1 (Stata Corp. LP, College station, TX).

RESULTS

A total of 242 patients, mean (±standard deviation) age 68.0 ± 10.0 (range 34–91 years), male 63.2%, were examined. There were no significant differences among participant countries in relation to this characteristic. Disease duration was 8.0 ± 5.8 (range 1–28 years), with shorter disease duration in German patients (6.4 ± 5.9) and longer in Spanish patients (8.9 ± 5.5) (Kruskal-Wallis test, $P = 0.01$). Twenty two percent had tremor dominant PD, whereas 39.5% had akinesia dominant PD and 38.3% had mixed pattern of PD. The distribution of patients by HY stage is shown in Table 1 and showed significant differences by country (chi-squared, $P = 0.002$).

The number and percentage of "positive" and "nondeclared" symptoms are shown in Table 2. The mean of total NMSQuest positive symptoms was 10.9 ± 5.6 and the mean of undeclared symptoms was 4.6 ± 4.1 (42.8% of the positive). Range of proportions for undeclared NMS was from 31.8% (diplopia) to 65.2%

TABLE 1. *HY stage and recruitment in the three countries in current study*

Hoehn and Yahr stage	n	Germany	Spain	United Kingdom
1	22	7	8	7
2	121	5	62	54
3	66	14	18	34
4	26	4	10	12
5	6	1	2	3

N = 241 (one missing).

(delusions). Delusions, daytime sleepiness, intense and vivid dreams, and dizziness were the most frequently nondeclared symptoms. In regard to the NMSQuest dimensions/domains, the percentage of undeclared symptoms ranged from 36.8% (miscellaneous) to 50.0% (hallucinations/delusions), Table 3.

Although mean positive NMSQuest scores did not differ significantly among the countries, mean undeclared NMS was significantly lower in Spanish patients (3.2 ± 3.0) compared with the German (5.5 ± 3.7) and the UK patients (5.6 ± 4.6) (Kruskall Wallis test, $P = 0.0001$).

There were not significant differences in the number of nondeclared NMS by sex. Only the domain depression/anxiety showed a marginal difference (Mann-Whitney test, $P = 0.04$), with more undeclared symptoms for women (0.45 ± 0.67) than for men (0.29 ± 0.57).

The number of undeclared NMS showed a low correlation with age ($r_S = \pm 0.14$; $P = 0.03$), and further analysis suggest that patients aged ±75 declared significantly less NMS to the HCP than patients ±75 years (5.0 ± 4.1 vs. 3.8 ± 4.0; Mann-Whitney test, $P = 0.01$). NMS were present significantly more in akinesia dominant PD compared with the other subtypes (Kruskal-Wallis test, $P = 0.008$); however, there was no difference in the percentage of undeclared NMS between the three subtypes of PD.

When asked about why these were not declared the patients and caregivers responded by outlining the following reasons:

a) They were not aware some of these symptoms may have been related to PD (delusions, RBD, intense and vivid dreams, pains, dribbling of saliva, insomnia),

TABLE 2. *Number and percentage of positive and undeclared nonmotor symptoms*

		Positive		Non-declared	
Items		N	%	n	%*
1	Dribbling	101	41.7	46	45.5
2	Taste/smelling	103	42.9	41	39.8
3	Swallowing	65	27.0	24	36.9
4	Vomiting	38	15.8	16	42.1
5	Constipation	115	47.5	53	46.1
6	Bowel incontinence	15	6.3	5	33.3
7	Bowel emptying incomplete	65	27.0	31	47.7
8	Urgency	145	59.9	61	42.1
9	Nocturia	157	64.9	69	43.9
10	Pains	111	45.9	45	40.5
11	Weight	55	22.7	21	38.2
12	Remembering	124	51.2	55	44.4
13	Loss of interest	82	33.9	35	42.7
14	Hallucinations	41	17.0	17	41.5
15	Concentrating	121	50.0	46	38.0
16	Sad, blues	118	48.8	45	38.1
17	Anxiety	101	41.7	40	39.6
18	Sex_drive	90	37.3	41	45.6
19	Sex_difficulty	82	34.3	37	45.1
20	Dizzy	94	38.8	47	50.0
21	Falling	70	29.3	28	40.0
22	Daytime sleepiness	84	34.7	44	52.4
23	Insomnia	114	47.3	50	43.9
24	Intense, vivid dreams	84	34.7	44	52.4
25	Acting_out during dreams	93	38.7	41	44.1
26	Restless Legs	99	41.1	36	36.4
27	Swelling	91	37.6	33	36.3
28	Sweating	74	30.6	25	33.8
29	Diplopia	44	18.2	14	31.8
30	Delusions	23	9.5	15	65.2

*Frequency and percentage calculated on the number of positive responses.

TABLE 3. *Declared (positive) and nondeclared symptoms analysed according to NMSQuest domains*

NMS Questionnaire—domains	Positive	Non-declared	%*
Gastrointestinal	2.1 ± 1.6	0.9 ± 1.1	43.5
Urinary	1.3 ± 0.8	0.5 ± 0.8	43.2
Sexual function	0.7 ± 0.9	0.3 ± 0.7	45.8
Cardiovascular	0.7 ± 0.7	0.3 ± 0.6	45.6
Apathy/attention/memory	1.4 ± 1.2	0.6 ± 0.9	41.5
Hallucinations/delusions	0.3 ± 0.6	0.1 ± 0.4	50.0
Depression/anxiety	0.9 ± 0.8	0.4 ± 0.6	38.9
Sleep disorder	2.0 ± 1.5	0.9 ± 1.2	45.2
Miscellaneous	1.6 ± 1.1	0.6 ± 0.8	36.8

Mean ± standard deviation.
*Percentage calculated on the number of positive responses.

b) They were embarrassed to discuss these issues with the HCP unless they were prompted (sexual problems, incontinence of bowel),
c) The consultation time was mostly preoccupied by discussion on motor symptomatology and as such no or little time was available for discussion of any NMS related issues.

These answers were obtained as complementary information, but were not tabulated for quantitative analysis.

DISCUSSION

This international study reports some key observations in the "routine" clinical care of patients with PD. These are:

a) A range of NMS of PD are often undeclared to HCP unless a specific tool, such as, the NMSQuest is used.
b) The "nondeclaration" of NMS occurs across several countries in Europe irrespective of the setting status (teaching hospital, general neurology clinic, research unit) and, therefore, is likely to be translated as a whole to PD patients attending hospital clinics.
c) The undeclared symptoms include several potentially treatable NMS, such as, EDS, low mood, dribbling of saliva, insomnia, RBD, RLS, and following this study, appropriate referrals and treatments were started in several cases.
d) Relatively younger patients declare NMS less frequently compared with older (±75 years) patients.

We included a reasonable "real life" patient population, across all age groups to address the issue of "nondeclaration" of NMS in outpatient clinics. The validated and internationally used NMSQuest allowed us to use an instrument that empowers PD patients and carers to flag NMS in clinics.[7] Only "NMSQuest naive" patients were used for the study so that patients were not previously exposed to NMSQuest. Answers to NMSQuest related to problems active in the last month and in all, therefore, undeclared symptoms related to current active problems, which were not flagged in their last consultation/meeting with a HCP. The spread of the clinics allowed assessment of patients in specialised to general neurology clinics to reduce potential bias. Patients with disease severity rated from mild PD to severe PD based on Hoehn and Yahr staging were included as long as they were able to complete NMSQuest in a satisfactory fashion. However, as is reflected in many observational studies, the proportion of stage 5 PD (HY stage) was low.

In line with previous observation reported in the international NMS prevalence study,[8] we observed that the mean NMS reported on use of NMSQuest was around 10. In contrast, the mean of "undeclared" NMS was 4.65 ± 4.07 (42.8% of the positive) indicating that on average there are four undeclared NMS per patient. The range of undeclared NMS was wide with delusions, daytime sleepiness, intense and vivid dreams, and dizziness being the most undeclared, whereas potentially treatable NMS, such as, dribbling of saliva, low mood, insomnia, REM behaviour disorder, restless legs syndrome type symptoms, and falls were also often undeclared (Table 2). When analysed by NMSQuest domains (Table 3), there was a more even spread of nondeclared symptoms grouped by domains ranging from 36.7% (miscellaneous including pain, weight change) to 50% (hallucinations, delusions).

A key issue that emerges from this study is that many of the undeclared NMS are treatable. These include targeted dopaminergic or nondopaminergic therapy for depression, low mood, insomnia, EDS, RBD, RLS dribbling of a saliva, pains, anxiety to mention a few.[6] It is well recognised that NMS, such as, depression, EDS, falls are key determinants of health related QoL in PD.[11–14] It is, therefore, reasonable to speculate that in our patient group, undeclared NMS has the potential to adversely affect QoL as it is likely that without the use of an empowering tool, such as, the NMSQuest such symptoms would not have been addressed.

The range of undeclared NMS items was 33.2% (diplopia) to 65.2% (delusions). During the study, the following undeclared NMS were specifically addressed in terms of management and treatment with successful outcomes as follows:

Dribbling of saliva (45.5% undeclared) and swallowing difficulty (36.9% undeclared): referral to speech and language therapy and nutritional advice,
Urinary urgency (42.1% undeclared): referral to urologist for bladder care,
REM behaviour disorder (RBD, 44.1% undeclared): further confirmation was sought and referral for polysomnography was made in appropriate cases, whereas others received treatment with clonazepam or melatonin.

Daytime sleepiness (52.4% undeclared), constipation (46.1% undeclared), unexplained pains (40.5% undeclared), sadness and blues (38.1% undeclared), restless legs type symptoms (36.4% undeclared), and insomnia (43.9% undeclared) were treated as appropriate with medications with satisfactory outcomes. In addition, patients that were assessed in the research unit were advised to visit their doctors for discussing the results with the NMSQuest.

No relationship with undeclared NMS and sex of the patient was observed. Although, akinesia dominant PD reported a greater number of NMS, there was no difference in undeclared NMS between the three clinical subtypes of PD. Surprisingly, we found older patients declared NMS more frequently than younger patients. We are unable to explain this observation apart from the fact that questions on NMS are generally more likely to be asked in older patient consultations and younger patients may not be too forthcoming in declaring some NMS, which may be perceived as socially embarrassing. The rate of undeclared NMS was significantly lower in the Spanish centre. This may reflect a better understanding of NMS and longer consultation times allowed in these clinics.

Akinesia dominant PD patients reported more NMS than tremor dominant subtype (Table 3), however, all three subtypes has similar rates of undeclared NMS.

In conclusion, this study indicates that NMS in PD continues to be poorly detected in wider clinical practice. Part of this is related to nondeclaration of NMS by patients, on average four NMS per patient. Unless prompted by a simple self completing instrument, such as, the NMSQuest, many such symptoms may not be declared leading to a potentially suboptimal patient care, increased cost of care[14] and compromised QoL. This has been translated to routine clinical practice in the UK, where the government department of health has recommended NMSQuest to be routinely used in the "18 week pathway" for treatment and management of PD.

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REFERENCES

1. Chaudhuri KR, Healy D, Schapira AHV. The non motor symptoms of Parkinson's disease. Diagnosis and management. Lancet Neurol 2006;5:235–245.
2. Aarsland D, Larsen JP, Goek Lim N, et al. Range of neuropsychiatric disturbances in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 1999;67:492–496.
3. Naidu Y, Chaudhuri KR. Early Parkinson's disease and non motor issues. J Neurol 2008;255 (Suppl 5):33–38.
4. Shulman LM, Taback RL, Rabinstein AA, Weiner WJ. Non-recognition of depression and other non-motor symptoms in Parkinson's disease. Parkinsonism Relat Disord 2002;8:193–197.
5. O'sullivan SS, Williams DR, Gallagher DA, et al. Non motor symptoms as presenting complaints in Parkinson's disease: a clinicopathological study. Mov Disord 2008;23:101–106.
6. Chaudhuri KR, Schapira AHV. The non motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. Lancet Neurol 2009;8:464–474.
7. Chaudhuri KR, Martinez-Martin P, Schapira AHV, et al. An international multicentre pilot study of the first comprehensive self-completed non-motor symptoms questionnaire for Parkinson's disease: the NMSQuest study. Mov Disord 2006;21:916–923.
8. Martinez-Martin P, Schapira AHV, Stocchi F, et al. Prevalence of non motor symptoms in Parkinson's disease in an international setting; study using non-motor symptoms questionnaire in 545 patients. Mov Disord 2007;22:1623–1629.
9. National Health Service, Department of Health. UK. The 18 week commissioning pathway for treatment and management of

tremor disorders. Available at: www.18weeks.nhs.uk. Neurology, Tremor Pathway. Accessed on 29 August, 2009.
10. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181–184.
11. Global Parkinson,'s Disease Survey Steering Committee. Factors impacting on quality of life in Parkinson's disease: results from an international survey. Mov Disord 2002;17:60–67.
12. Schrag A, Jahanshahi M, Quinn N. What contributes to quality of life in patients with Parkinson's disease? J Neurol Neurosurg Psychiatry 2000;69:308–312.
13. Martinez-Martin P, Serrano-Duenas M, Forjas MJ, Serrano MS. Two questionnaires for Parkinson's disease: are the PDQ- 39 and PDQL equivalent? Qual Life Res 2007;16: 1221–1230.
14. Findley L, Aujla M, Bain PG, et al. Direct economic impact of Parkinson's disease: a research survey in the United Kingdom. Mov Disord 2003;18:1139–1145.