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RESEARCH ARTICLE

Expanded and Independent Spanish Validation of the MDS-Non Motor Rating Scale

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Abstract: Background: The Movement Disorder Society-sponsored Non-motor Rating Scale (MDS-NMS) assess the severity and disability caused by non-motor symptoms (NMS) in Parkinson's disease (PD).
Objective: This article encapsulates the formal process for completing this program and the data on the first officially approved non-English version of the MDS-NMS (Spanish).
Methods: The MDS-NMS translation program involves four steps: translation and back-translation; cognitive pre-testing to ensure that raters and patients understand the scale and are comfortable with its content; field testing of the finalized version; analysis of the factor structure of the tested version against the original English language version for the nine domains that could be analyzed in a confirmatory factor analysis. To be designated an "Official MDS translation," the confirmatory factor analysis Comparative Fit Index had to be ≥0.90.
Results: The Spanish MDS-NMS was tested in 364 native-Spanish-speaking patients with PD from seven countries. For all subjects with fully computable data with all domains of the MDS-NMS ($n = 349$), the Comparative Fit Index was ≥0.90 for the nine eligible domains. Missing data were negligible and moderate floor effect (42.90%) was found for the Non-Motor Fluctuations subscale. Item homogeneity coefficient was adequate, and the correlation of the MDS-NMS domains with other measures for related constructs was acceptable ($r_s \geq 0.50$).
Conclusions: The Spanish version of the MDS-NMS followed the IPMDS Translation Program protocol, reached the criterion to be designated as an Official Translation, and is now available on the MDS website.

Non-motor symptoms (NMS) are an important factor of the deterioration of the health-related quality of life (QoL) of patients with Parkinson's disease (PD).[1,2] NMS burden increases in their severity over time, impacting on patients' disability, caregivers' burden, and societal costs.[3] Assessment of NMS in PD are now crucial to value-based health care and recommended by patient-led organizations and the International Parkinson and Movement Disorder Society (IPMDS).[4] The IPMDS non-Motor PD Study Group recently developed and validated the International Parkinson and Movement Disorder Society-Non Motor Rating Scale (MDS-NMS) in English, an updated version of the Non-Motor Symptom Scale (NMSS).[5,6] The MDS-NMS was validated for use in PD using a sample of 402 English-speaking PD patients from America and England.

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Given the importance of NMS burden in PD, having a scale that is validated in multiple non-English languages is pivotal to international efforts to treat NMS. To obtain equivalent and locally validated non-English versions of the MDS-NMS, a Translation Program Protocol has been established by the IPMDS (www.movementdisorders.org).[7] The objective of this study was to organize and perform an independent validation of the MDS-NMS Spanish version following the IPMDS methodology for the translation and validation process.[8]

Methods

Study Design and Patients

This was an international, multicenter, observational, cross-sectional study. We invited for participation, Spanish-speaking patients from 14 Movement Disorders Units from Spain, and eight centers from North, Central, and South America (Mexico, Argentina, Colombia, Ecuador) and United States (Miami Florida and Boca Raton, Florida) at any age and disease stage, diagnosed with idiopathic PD as per the MDS-PD criteria,[9] and without significant cognitive impairment according to the judgment of the evaluating neurologist and a Montreal Cognitive Assessment (MOCA) score > 21.[10]

Ethical Aspects

Each site contributing to the study received approval of its respective ethics committee/IRB for participation, and the study was conducted according to Good Clinical Practice.[11] Patients provided signed informed consent before participating in this study.

Raters

Neurologists, members of the IPMDS, were invited by email to participate in this project.

Sample Size

The sample size for the translation study was based on the need for five subjects per item of the questionnaire to perform the statistical analysis.[12] Because there are 60 items (52 MDS-NMS items and 8 nonmotor fluctuations items) on the MDS-NMS, a sample of at least 300 was required.

Assessments

Socio-demographic, predominant hemi-body affected by PD, current use of antiparkinsonian drugs including the levodopa-equivalent daily dose (LEDD),[13] and other treatments, and PD historical data were obtained through an ad hoc questionnaire. In addition, the following rating scales were administered:

1. *MDS-NMS* (see Appendix): After the pilot study,[5] the final version of the MDS-NMS has 52 items, grouped according to clinical content into 13 domains: (A) Depression (5 items), (B) Anxiety (4 items), (C) Apathy (3 items), (D) Psychosis (4 items), (E) Impulse Control and Related Disorders (4 items), (F) Cognition (6 items), (G) Orthostatic Hypotension (2 items), (H) Urinary (3 items), (I) Sexual (2 items), (J) Gastrointestinal (4 items), (K) Sleep and Wakefulness (6 items), (L) Pain (4 items), and (M) Other (5 items; unintentional weight loss, decreased smell, physical fatigue, mental fatigue, and excessive sweating). Items are scored for frequency (from 0 [never] to 4 [majority of time]) and severity (from 0 [not present] to 4 [severe]), which are multiplied to generate the item total score. Scores for each domain and the total rating scale (maximum, 832 points) are calculated by summing the corresponding items.

The Non-Motor Fluctuations (NMF) subscale has eight items: depression, anxiety, thinking or cognitive abilities, bladder symptoms, restlessness, pain, fatigue, and excessive sweating. Each item is scored for typical degree of change from "on" to "off" periods, from 0 (no change) to 4 (large). The sum of degree of change for the eight items is multiplied by the amount of time spent in the "off" state with NMS, which ranges from 1 (rarely) to 4 (majority of time). Maximum possible score is 128.

2. *MDS-Unified Parkinson's Disease Rating Scale* (*MDS-UPDRS*): The MDS-UPDRS includes four parts: part I, Non-motor Aspects of Experiences of Daily Living (nM-EDL); part II, Motor Aspects of Experiences of Daily Living (M-EDL); part III, Motor Examination (ME); and part IV, Motor Complications (MCompl). In addition, it contains the Hoehn and Yahr scale (HY), a tool for staging the severity of PD.[14]

3. *Wearing Off Questionnaire-19* (*WOQ-19*): This questionnaire includes nine items assessing motor fluctuations including tremor, difficulty in speech, weakness, problems with balance, slowness, reduced dexterity, general stiffness, muscle cramps, difficulty getting out of the chair (WOQ-19 Motor score); and 10 items evaluating non-motor fluctuations including anxiety, sweating, mood changes, numbness, panic attacks, cloudiness of mind, abdominal discomfort, feeling hot and cold, aches and pain (WOQ-19 Non-motor score).[15] For each item, patients were asked to check whether symptoms were present and whether they improved after the following dose of dopaminergic treatment: a cut off of 2 for the WOQ-19 Total score indicated a diagnosis of generic wearing off,[15] while a cut off of 1 for either the WOQ-19 Motor or Non-motor score specifically disclosed a diagnosis of motor or non-motor fluctuations, respectively.

Procedure

Assessments were performed during the "on" state when possible, and patient assessments between all centers were harmonized.

Phases in the development of the Spanish version of the MDS-NMS followed the prescribed protocol established by the IPMDS for official translations of the MDS-NMS:

1. *Translation, back-translation, comparison with the original, and amendments of the scale text.* A forward translation was developed by a third-party translation company experienced in the translation of rating scales and reviewed by the Spanish

Translation Committee created for this project. All wording was selected to meet the criterion of being at the 7th grade reading level. Documents were reviewed by the administrative team and reviewers independent of the Spanish organizers, and a draft translated scale was developed based on feedback. The back-translation obtained from a third-party translation company was reviewed by the MDS Translation Steering Committee, and the translation was then provisionally approved for Cognitive Pre-testing.

2. *Cognitive pre-testing*: This is a qualitative approach for assessing instrument completion regarding task difficulty for examiner and respondent, and respondent interest, attention span, discomfort, and comprehension.[16] The provisionally approved translation was administered to 20 PD patients and four raters for cognitive pre-testing. This phase identifies potentially culturally sensitive or complex items.[17] Based on the results of the initial cognitive pretesting, other round(s) of translation, back translation and cognitive pretesting could be required. Once cognitive pretesting was completed and no further problems were noted, the final translation could be approved as "Official Working Document".
3. *Field testing*: It was conducted on a large sample of an international sample of native Spanish speakers.
4. *Statistical analyses*, including validity testing, factor and clinimetric analyses.

Data Analysis

We conducted the following analyses.

Primary Analyses

Data quality which was established after checking for missing data (acceptable, <5%).[18]

Cognitive Pretesting: Data from the respondents (raters and patients) were analyzed using a framework approach.[19] Area of expressed difficult were examined and changes to the scale were made if necessary.

Factor Analysis: R (Version 4.2.0) packages *lavaan* and *psych* were used to do the primary confirmatory and secondary exploratory factor analyses, respectively. We used an adjusted weighted least square (WLSMV) approach to factor estimation that minimizes the weighted sum of squared differences between observed and estimated correlation matrices not counting diagonal elements. To assist in interpretation of the factors we used an orthogonal VARIMAX rotation that constrains the factors to be uncorrelated. Any participants with missing values were deleted from analysis of that domain only. Thus, the sample size from domain to domain could vary. The investigators obtained participants' approval to collect the data. Data without patient names or medical record numbers were transferred to the analytic team via a secure website.

Confirmatory factor analysis (*CFA*): CFA was used to determine if the factor structure for the English language MDS-NMS[20] could be confirmed in data collected using the Spanish translation. We evaluated the CFA results based on the Comparative Fit Index (CFI) for only nine of the subscales with more than three items.[21] Because two items (as in Orthostatic Hypotension and Sexual subscales) and three items (as in Apathy and Urinary subscales) lead to under-identified and saturated models, respectively, we could not obtain valid model fit results. Therefore, CFAs were conducted for each of the 10 subscales (nine domains of the MDS-NMS plus the NMF subscale) that met this requirement. According to the protocol, to establish a successful translation and to designate that translation as an Official MDS translation of the MDS-NMS, we required that the CFI for each eligible subscale of the translated MDS- NMS be 0.90 or greater relative to the English language version. Mean and variance adjusted weighted least square (WLSMV) estimator was used to confirm model fit.

Secondary Analysis

Exploratory Factor Analysis (*EFA*): We conducted EFA for each of the subscales (13 domains of the MDS-NMS plus the NMF subscale) to explore the underlying factor structure without the constraint of a pre-specified factor structure, and once the factors were chosen, an item was retained in a factor if the factor loading for that item was 0.40 or greater. We used the orthogonal VARIMAX rotation to assist the interpretation of the factors, which sets the factors to be uncorrelated.

Tertiary Analysis

We used the IBM-SPSS v.28 for these statistical analyses. The primary variables in the study had non-normal distribution (Shapiro–Wilk Test, all $p < 0.001$). To establish the homogeneity of the included PD sample, we compared the main sociodemographic and clinical characteristics using the Fisher's exact and chi-squared test for categorical variables and T-Student, ANOVA, Mann–Whitney U, and Kruskall-Wallis tests, based on the normal and non-normal distribution of the numerical variables, respectively.

Prevalence of NMS was based on scores ≥1 in each MDS-NMS item, domain, and total scale, denoting the presence of a symptom (0 = no symptom present). For comparison, the prevalence of NMS assessed with the MDS-UPDRS and WOQ-19 NMS was obtained using the same method.

Following the original English validation procedure,[6] we assessed the following clinimetric properties: *Acceptability*: Floor and ceiling effect (satisfactory threshold, ≤ 15%)[22]; skewness (criterion values, from −1 to +1)[23]; and range of observed versus theoretical values; *Internal consistency*: For each domain (1) interitem correlation (standard values, 0.20–0.75)[24]; (2) item homogeneity coefficient calculated as the average corrected item-total interitem correlation by domain (standard, 0.15 for broad domains)[25]; (3) corrected item-total correlation (standard, ≥0.40)[18]; and (4) Cronbach's α (standard, ≥0.70)[22]; *Hypotheses testing*: For convergent validity, we hypothesized that MDS-NMS domains would be highly associated (Spearman rank correlation coefficient value, $r_s > 0.50$),[26] with corresponding components of the MDS-UPDRS part 1, and NMF subscale with the WOQ-19NMS, and moderate or weak correlation ($r_s = 0.20–0.50$) with other PD severity measures. The known-

TABLE 1 *Demographic data of Spanish speaking population (N = 364)*

Male, *N* (%)	211 (58.0)
Ethnicity, *N* (%)	
American Hispanic/Spaniard	338 (92.9)
Race, *N* (%)	
White	243 (66.8)
Other	118 (32.4)
Married (%)	263 (72.70)
Living with family (%)	315 (86.5)
Age, years, Mean (SD)	64.12 (10.28)
PD duration, years, Mean (SD)	8.80 (7.20)
Education, years, Mean (SD)	12.35 (4.89)
Total levodopa daily equivalent dose, Mean (SD)	847.67 (457.44)
Antidepressants, yes (%)	98 (26.90)
Anxiolytics, yes (%)	78 (21.40)
Antipsychotics, yes (%)	10 (2.7)
Urinary disturbances treatment (%)	11 (3.00)
Sleep disturbances treatment (%)	32 (8.80)
HY stage, *N* (%)	
1	18 (4.9)
2	238 (65.3)
3	90 (24.7)
4	18 (4.9)
MDS-NMS, Mean (SD) [range]	
Depression	8.44 (13.79) [0–80]
Anxiety	8.62 (10.73) [0–64]
Apathy	4.34 (7.56) [0–48]
Psychosis	1.65 (5.34) [0–60]
Impulse control disorder	1.73 (4.31) [0–60]
Cognition	8.75 (12.42) [0–88]
Orthostatic Hypotension	1.90 (3.74) [0–32]
Urinary	8.94 (10.69) [0–48]
Sexual	4.41 (7.46) [0–32]
Gastrointestinal	7.82 (8.50) [0–38]
Sleep	11.66 (11.64) [0–80]
Pain	7.72 (8.59) [0–49]
Others	12.10 (10.86) [0–57]
NMS Total	88.07 (73.47) [1–489]
NMF Total	10.41 (14.55) [0–88]
MDS-UPDRS Mean (SD) [range]	
Part 1	11.26 (7.55) [0–38]
Part 2	12.71 (9.59) [0–44]
Part 3	31.27 (18.63) [1–105]
Part 4	4.39 (4.48) [0–20]
WOQ-19 Total Mean (SD) [range]	14.00 (2.49) [8–16]
WOQ-19 MS Mean (SD) [range]	18.50 (3.72) [13–22]
WOQ-19 NMS Mean (SD) [range]	33.00 (5.93) [25–38]

Abbreviations: SD, standard deviation; PD, Parkinson's Disease; HY, Hoehn and Yahr; MDS-NMS, Movement Disorder Society–sponsored Nonmotor Rating Scale; MDS-UPDRS, Movement Disorder Society–sponsored Unified Parkinson's Disease Rating Scale; WOQ-19 = Wearing Off Questionnaire-19 items.

groups validity of the MDS-NMS and NMF was tested by determining the difference in total scores for subgroups based on sex, age, PD duration, HY, predominant hemibody affected, and LEDD. To provide similar descriptive results compared with the original validation,[6] we stratified the population in similar tertiles.

Results

Sample Characteristics

We included 364 PD patients, 160 (44%) from Spain and 204 from North, Central, and South America (56%). Centers provided between 5 and 45 cases to the study cohort. When the PD sample from Spain was compared to the American PD sample, no significant differences were found in terms of age ($P = 0.39$), PD duration ($P = 0.11$), education ($P = 0.84$), and gender ($P = 0.52$), except for higher HY stage in the American PD sample ($P < 0.001$). Sociodemographic and clinical characteristics are detailed in Table 1.

Cognitive Pretesting

The responses from the 20 patients and 4 raters (samples of 5 patients and 1 rater each from Argentina, Mexico, Spain, and the United States) were collated and subjected to framework analyses identifying common themes and concerns. No major concerns or problems were identified, and the final translation was designated an Official Working Document and approved for use in the validation phase.

Primary Analyses

Data quality: Fully computable data were available in 349 subjects (96%) for all domains of the MDS-NMS, one subject (0.3%) had missing data in the depression domain, one subject (0.3%) had missing data in the impulsive control and related disorders,

cognition, and orthostatic hypotension domains, three subjects (0.8%) in the urinary and sexual dysfunction domains, and three subjects (0.8%) in the sleep and wakefulness, pain and other domains, respectively.

Factor analysis: Table S1 displays the CFA results for each of the 10 eligible subscales (9 domains of the MDS-NMS plus the NMF subscale). All 10 subscales of the Spanish MDS-NMS satisfied our pre-specified criterion of Comparative Fit Index ≥0.90 in comparison with the English-language factor structure.

Secondary Analyses

Exploratory Factor Analysis: The results of the EFA displaying the factor structures for results for all domains of the MDS-NMS and the NMF subscale are included in the Table S2 and Figure 1.

Tertiary Analyses

Data Acceptability: The MDS-NMS total scores showed no significant floor and ceiling effects (0.50%, 0.30%, respectively), but

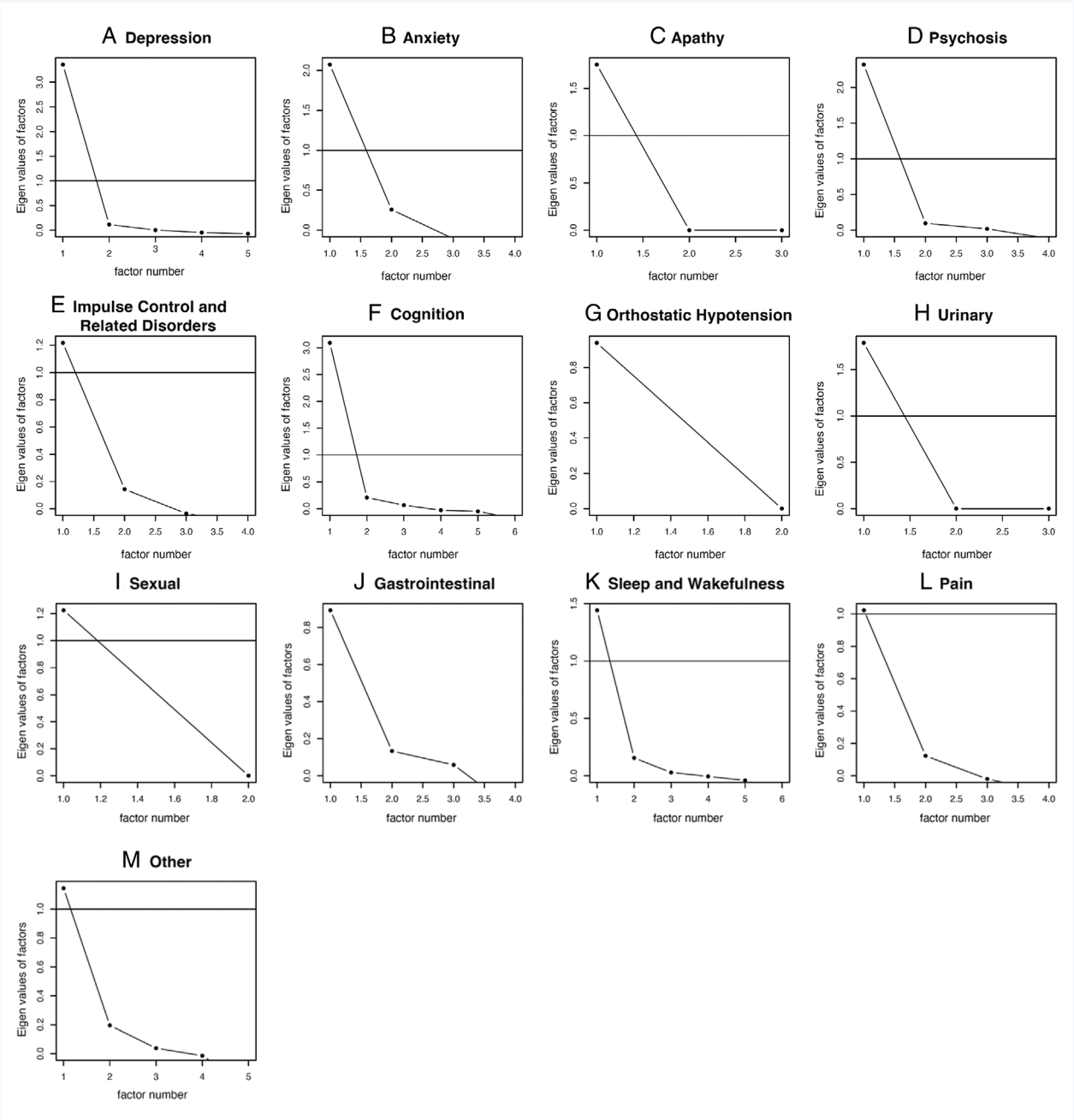

FIG 1. Scree plots of items A to M of the MDS-NMS.

TABLE 2 *Data Acceptability*

Domains $N = 364$	Mean (SD)	Median (range)	Skewness	Floor (%)	Ceiling (%)
Depression	8.44 (13.79)	3.00 [0–80)	2.60	32.10	0.50
Anxiety	8.62 (10.73)	4.00 [0–64)	2.11	19.80	0.50
Apathy	4.34 (7.56)	1.00 [0–48]	2.79	47.80	0.50
Psychosis	1.65 (5.34)	0.00 [0–60]	6.47	76.10	0.30
IC and related disorders	1.73 (4.31)	0.00 [0–60]	3.73	72.80	0.30
Cognition	8.75 (12.42)	4.00 [0–88]	2.85	21.40	0.30
Orthostatic hypotension	1.90 (3.74)	0.00 [0–32]	3.75	57.10	0.30
Urinary	8.94 (10.69)	4.00 [0–48]	1.45	26.40	1.10
Sexual	4.41 (7.46)	0.00 [0–32]	2.09	57.70	3.00
Gastrointestinal	7.82 (8.50)	5.00 [0–38]	1.26	19.50	0.30
Sleep and wakefulness	11.66 (11.64)	8.00 [0–80]	1.85	8.00	0.30
Pain	7.72 (8.59)	6.00 [0–49]	1.71	21.70	0.30
Others	12.10 (10.86)	9.00 [0–57]	1.14	11.80	0.30
MDS-NMS total score	88.07 (73.47)	70.00 [1–489]	1.58	0.50	0.30
NMF change	4.77 (5.63)	3.00 [0–24]	1.21	42.90	0.80
NMF time in "off"	1.22 (1.16)	1.00 (0–4)	0.41	39.30	2.20
NMF total score	10.41 (14.55)	4.00 [0–88]	1.99	42.90	0.30

Abbreviations: SD, standard deviation; IC, Impulse Control; MDS-NMS, Movement Disorder Society–sponsored Nonmotor Rating Scale; NMF, NonMotor Fluctuation.

TABLE 3 *Reliability*

Domain $N = 364$	Interitem correlation	Item homogeneity coefficient	Item-total correlation	Cronbach's α
Depression	0.01–0.77	0.64	0.59–0.72	0.897
Anxiety	0.03–0.77	0.49	0.44–0.70	0.785
Apathy	0.20–0.61	0.57	0.54–0.64	0.796
Psychosis	0.04–0.44	0.59	0.55–0.70	0.826
IC and related disorders	0.04–0.37	0.24	0.07–0.36	0.548
Cognition	0.17–0.49	0.51	0.41–0.66	0.861
Orthostatic hypotension	0.43	0.43	0.43[a]	0.556
Urinary	0.12–0.46	0.58	0.50–0.70	0.801
Sexual	0.66	0.66	0.66[a]	0.545
Gastrointestinal	0.15–0.44	0.21	0.02–0.30	0.499
Sleep and wakefulness	0.12–0.47	0.23	0.08–0.37	0.625
Pain	0.20–0.46	0.22	0.10–0.31	0.497
Others	0.12–0.44	0.15	0.009–0.18	0.429
NMF change★ ($n = 208$)	0.03–0.43	0.53	0.21–0.57	0.817

Abbreviations: IC, Impulse Control; MDS-NMS, Movement Disorder Society–sponsored Nonmotor Rating Scale; NMF, NonMotor Fluctuation.
[a]These domains have only two items; therefore, values are like inter-item correlation.

TABLE 4 *Items Convergent Validity*

MDS-NMS	MDS-UPDRS	Spearman R
A.Depresion	1.3Depression	0.68
B.Anxiety	1.4 Anxiety	0.62
C.Apathy	1.5 Apathy	0.69
D.Psychosis	1.2 Hallucinations/ psychosis	0.44
E.IC and related disorders	1.6 Dopamine dysregulation syndrome	0.55
F.Cognition	1.1 Cognitive	0.64
G.Orthostatic hypotension	1.12 Lightheadedness	0.59
H.Urinary	1.10 Urinary problems	0.77
I.Gastrointestinal	1.11 Gastrointestinal	0.59
I.Gastrointestinal	2.2 Saliva and drooling	0.50
I.Gastrointestinal	2.3 Swallowing	0.48
K.Sleep and wakefulness	1.7 Sleep problems	0.44
K.Sleep and wakefulness	1.8 Daytime sleepiness	0.45
K.Sleep and wakefulness	2.9 Turning in bed	0.34
L.Pain	1.9 Pain	0.72
M.Others	1.13 Fatigue	0.55
NMF	**WOQ-19 NMS**	**Spearman R**
2. Anxiety	3. Anxiety	0.50
3. Thinking or cognitive abilities	13. Cloudy mind	0.45
6. Pain	15. Muscle cramps	0.32
6. Pain	18. Pain	0.50
8. Excessive sweating	4. Sweating	0.54
8. Excessive sweating	17. Feeling Hot and Cold	0.55

Note: Spearman rank correlation coefficients. All *P* values <0.0001.
Abbreviations: MDS-NMS, Movement Disorder Society–sponsored Nonmotor Rating Scale; MDS-UPDRS, Movement Disorder Society–sponsored Unified Parkinson's Disease Rating Scale; WOQ-19, Wearing Off Questionnaire-19 items; NMF, Nonmotor Fluctuation.

TABLE 5 *Hypothesis Testing and Convergent/Divergent Validity*

	MDS-NMS Total Score Spearman R	NMF Total score Spearman R
Age	0.16 ⋆	0.03⋆⋆
Age at onset	−0.2	−0.29
Education (years)	−0.06⋆⋆	−0.01⋆⋆
PD duration	0.18	0.27
LEDD	0.19	0.34
Hoehn & Yahr	0.29	0.35
WOQ-19 NMS total score	0.42	0.54
WOQ-19 MS total score	0.33[&]	0.18[&]
MDS-UPDRS part I	0.80	0.59
MDS-UPDRS Part II	0.58	0.48
MDS-UPDRS Part III	0.26[&]	0.21[&]
MDS-UPDRS Part IV	0.45	0.61

Note: Spearman rank correlation coefficients. *P* values are <0.0001, except for ⋆=0.002, and ⋆⋆>0.05. [&]The Spearman R coefficients between the MDS-NMS/NMF with the WOQ-19 MS and MDS-UPDRS Part III indicate divergent validity.
Abbreviations: LEDD, Levodopa equivalent daily dose; MDS-NMS, Movement Disorder Society–sponsored Nonmotor Rating Scale; MDS-UPDRS, Movement Disorder Society–sponsored Unified Parkinson's Disease Rating Scale; WOQ-19, Wearing Off Questionnaire-19 items; NMF, Nonmotor Fluctuation.

the NMF showed a floor effect (42.90%) and adequate ceiling effect (0.30%) (Table 2). There were no ceiling effects for individual domains, but floor effects ranged from a low of 8.00% (sleep and wakefulness) to a high of 78.10% (impulse control disorders and related disorders), in line with results from the validation sample. As a whole, there was a positive skewness that was higher than the standard, mirroring the floor effect.

Internal consistency: These results are shown in Table 3. Some items of the MDS-NMS and in the NMF subscale had an inter-item (within domain) and corrected item-total correlation coefficient less than the 0.20 standard value, but the item homogeneity coefficient was more than the 0.15 threshold value for all domains.

Hypothesis testing: *Convergent Validity*: MDS-NMS domains correlated 0.34–0.77 with the corresponding MDS-UPDRS items, and NMF subscales 0.32–0.50 with the corresponding WOQ-19 NMS items (Table 4). The correlation between the MDS-NMS and NMF total scores with the MDS-part 1–4 ranged from 0.26 to 0.80, and 0.21 to 0.59, respectively. With the WOQ-19 NMS and MS, correlations with MDS-NMS were 0.42, and 0.33, and with the NMF: 0.54 and 0.18, respectively (Table 5); *Know-Groups Validity*: Using the MDS-NMS, 99.5% of the sample showed at least one NMS, compared to the 90.9% with the MDS-UPDRS part I. The MDS-NMF identified 57.1% of the sample with NMF, and 59.1% with the WOQ-19.

The total MDS-NMS and NMF subscale scores showed no significant differences between subgroups defined by age, and predominant affected PD hemibody. However, MDS-NMS and NMF scores increased significantly in females, with higher HY stage, PD duration, and LEDD (Table S3). Likewise, in terms of

severity, after adjusting for multiple comparisons, depression and anxiety domains, and total NMS, MDS-UPDRS part 1 and WOQ-19 NMS total scores were higher in females than males (Table S4). Comparisons of prevalence for NMS domains and MDS-UPDRS items are shown in Table S5.

Discussion

The IPMDS has organized a worldwide program to provide official and clinimetrically validated versions of several MDS-owned rating scales. Several official non-English versions are currently in progress for the MDS-NMS, but the Spanish MDS-NMS is the first completed program for this scale. Of note, we have addressed the various cultural differences that may be present in an international language such as Spanish. To achieve this international validation, we have achieved harmonization across the major Spanish-speaking cultures in Spain and the Americas. Based on the results of this study, the Spanish version of the MDS-NMS fulfills the clinimetric criteria to be designated as an MDS-approved Official Translation (http://www.movementdisorders.org/publications/rating_scales). The overall factor structure of the Spanish version was consistent with that of the English version based on the high CFIs for the 10 eligible subscales of the MDS-NMS in the confirmatory factor analysis (CFI ≥ 0.90).

We included a representative sample of patients with mild–moderate PD severity according to the HY stage. Interestingly, considering the high prevalence (99.5%) and burden of NMS (mean: 88.07 ± 73.47, range: 1–489), in addition to levodopa and other dopaminergic drugs, very few patients were receiving specific treatment for NMS, mostly antidepressants (26.90%) and anxiolytics (21.40%).

Concerning the validation aspects, the data quality was very satisfactory for all sections of the MDS-NMS and NMF, considering the existence of 52 and 8-item questionnaires, respectively, indicating the scale's excellent feasibility. In the present study, only 208 (57%) patients experienced NMF, which might explain the high floor effect on the NMF total score. Compared to the original English version of the MDS-NMS,[6] similar item homogeneity coefficients and Cronbach's alpha values were found, indicating a good internal consistency.

As hypothesized, convergent validity between the MDS-NMS domains and other scales measuring similar constructs was satisfactory. The MDS-NMS identified a high prevalence of NMS and NMF in the included sample, similar to the MDS-UPDRS and WOQ-19 NMS. Due to differences between the rating scales, their components are not equivalent, showing slight differences in prevalence rates. MDS-NMS and NMF scores correlated moderately with individual MDS-UPDRS parts I, II, IV, and WOQ-19 NMS. The correlation between motor fluctuations severity observed in the MDS-UPDRS part IV with MDS-NMS and NMF, supported recent studies reporting the association of motor fluctuations with a greater increase in the NMS burden.[27]

The MDS-NMS domains also showed a satisfactory discriminative ability to differentiate between patients grouped according to the PD and HY staging at a point in time. In agreement with other authors, we found a higher burden of NMS in females,[28,29] also with the MDS-UPDRS part I, II, and WOQ-19 NMS, indicating similar capabilities to detect gender NMS burden differences. The most affected NMS domains in females were depression and anxiety using the MDS-NMS. Of note, although not statistically significant in terms of PD motor asymmetry, we found that patients with predominant left extremities affected by PD (right brain hemisphere) had a higher NMS burden than the right one. This finding was consistent with brain asymmetry, and its association with NMS severity found in another PD cohort, suggesting increased susceptibility or awareness in the right hemisphere for NMS.[30]

Limitations of the study are related to potential sample selection bias as data come from specialized clinical units. However, the multicenter, international collaboration and wide sample are circumstances buffering that bias. As per exclusion criteria excluding patients with significant cognitive impairment, the sample distribution showed a predominance of patients with mild/moderate PD according to the HY stage. Finally, data about longitudinal validity and interpretability were not available.

On the other hand, the benefits of translating and validating the MDS-UPDRS into Spanish will include the possibility of reaching millions of individuals worldwide, including healthcare professionals and PD patients. Approximately 21 countries worldwide speak Spanish as their official language, and Spanish is spoken by more than 492 million individuals worldwide.[31] This validation will also unify PD clinical assessments, eventually improving patient outcomes. Its availability now allows for large clinical trials that use the MDS-NMS as a pivotal outcome to include study sites, investigators, and patients from these countries when new treatment protocols emerge.

In conclusion, the cross-cultural adaptation of the scale and the confirmation that the MDS-NMS Spanish version is structurally equivalent to the original English measure is relevant for future transnational studies enrolling patients from Spanish-speaking countries.

Author Roles

(1) Research project: A. Conception; B. Organization; C. Execution. (2) Analysis: A. Design; B. Execution; C. Review and Critique. (3) Manuscript Preparation: A. Writing of the first draft; B. Review and Critique.

EC: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B.
SL: 1A, 1B, 2A, 2B, 2C, 3B.
PMM: 1A, 1B, 2A, 2B, 2C, 3B.
GS: 1A, 1B, 2A, 2B, 2C, 3B.
JL: 2B, 2C, 2C, 3B.

DC: 2B, 2C, 2C, 3B.
AGB: 1C, 3B.
PM:1C, 3B.
DSG: 1C, 3B.
MSD: 1C, 3B.
MRV:1C, 3B.
CS: 1B, 3C.

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J.L.: Salary: Duke University.

D.C.: Salary: Duke University.

A.G.B.: Salary: Research Unit, Hospital Universitario Spain.

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Appendix

A.1. Spanish & American team participants

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Supporting Information

Supporting information may be found in the online version of this article.

Table S1. Spanish Confirmatory Factor Analysis (CFA)

Table S2. Spanish Exploratory Factor structures for subscales of MDS-NMS

Table S3. Known-Groups Validity

Table S4. NMS Severity Comparison between males and females

Table S5. NMS Prevalence Comparisons