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ORIGINAL COMMUNICATION

Expanded and independent validation of the NoMoFA scale for Parkinson's disease: the Italian version

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Abstract

Introduction Non-motor symptoms (NMS) in Parkinson's disease (PD) can fluctuate daily, impacting patient quality of life. The Non-Motor Fluctuation Assessment (NoMoFA) Questionnaire, a recently validated tool, quantifies NMS fluctuations during ON- and OFF-medication states. Our study aimed to validate the Italian version of NoMoFA, comparing its results to the original validation and further exploring its clinimetric properties.

Methods The scale underwent translation, back-translation, and cognitive pretesting before being administered to a calculated sample of > 200 PD patients. Each patient was assessed using a set of validated measures for assessing PD and cognitive state. We explored NoMoFA's feasibility, acceptability, factorial structure, internal consistency, convergent validity, test–retest reliability (the latter performed on 50 patients after 14 days), and the precision of the scale.

Results 227 PD patients (mean age 65.34, disease duration 9.31 years) were included, with 100% data computability. The scale was free from floor and ceiling effects, and included 7 factors (59.2% of the variance). Cronbach's alpha coefficient was 0.89, indicating strong internal consistency. The intraclass correlation coefficient (ICC) of 0.90 demonstrated satisfactory reproducibility. The NoMoFA Total score showed the strongest correlations with MDS-UPDRS Parts I ($r_S = 0.71$) and II ($r_S = 0.60$). Significant differences in NoMoFA scores were observed based on disease duration, H&Y score, and LEDD ($p < 0.0001$), but not age or sex. The Standard error of measurement (SEM) was 3.40 (for ½ $SD_{pooled} = 5.48$).

Conclusion The Italian version of the NoMoFA scale demonstrated strong reliability, validity and precision, making it a robust tool for assessing non-motor fluctuations in PD.

Keywords Parkinson's disease (PD) · Non-motor symptoms (NMS) · Non-motor fluctuations (NMF) · Non-Motor Fluctuation Assessment (NoMoFA) Questionnaire · Italian version

Introduction

Parkinson's disease (PD) is a neurodegenerative disease which has been traditionally considered as a "pure" movement disorder [1]. However, in the last decades, a significant amount of clinical and scientific evidence has defined PD as a complex and multifaceted disease, involving a constellation of both motor and non-motor symptoms (NMS) [1]. NMS are often present years before the clinical diagnosis of PD and tend to worsen during disease progression. Moreover, NMS proved to severely impact patients' quality of life, in some cases more than motor symptoms [1]. While fluctuations of motor symptoms in response to dopaminergic therapy have been historically recognized as a significant complication of the later stages of PD, it has been only recently demonstrated that many NMS can also have daily fluctuations [2]. Indeed, the relatively recent acknowledgment of the relevance of this phenomenon led to the definition of "non-motor fluctuations" (NMF), indicating the clinical status of daily changes in terms of presence and severity of a dynamic subset of NMS [3]. The relevance of differentiating static from fluctuating NMS relies in the fact that they may have different pathophysiology and responses

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to treatment. The recent recognition of the impact of NMS on quality of life has driven efforts to create valid and reliable questionnaires to capture and quantify NMS [4]. Some of these questionnaires have included items probing selected non-motor OFF symptoms, but none captures or quantifies the entire spectrum of NMF in both the ON- and OFF-medication conditions. In this context, the Non-Motor Fluctuation Assessment (NoMoFA) Questionnaire, a patient-derived and self-administered questionnaire that identifies and quantifies the severity of static and fluctuating NMS in people with PD, has been recently validated [5]. Given the high clinical and research significance of a validated tool able to reliably assess the NMS and NMF in patients with PD, we aimed to undertake a translation and cross-cultural adaptation of the questionnaire into Italian language, adhering to the scale translation protocol established by the International Parkinson and Movement Disorders Society (MDS) [6]. Moreover, we compared our results with those of the original validation study, adding new information on the NoMoFA clinimetric properties.

Methods

Study design

We conducted a translation and cross-cultural adaptation of the NoMoFA following published guidelines for this kind of studies in the field [6]. Authorization to use and adapt the original NoMoFA for research purposes was obtained from the MDS.

Non-motor fluctuation assessment (NoMoFA) questionnaire

The NoMoFA Questionnaire has a total of 27 items evaluating NMS over the past 2 weeks: loss of train of thought, distraction, difficulty planning, confusion, word-finding difficulty, excessive worry, fear, restlessness, hopelessness, loneliness/isolation, hallucinations, poor decision-making, impulsiveness, compulsiveness, poor short-term memory, difficulty handling stressful situations, apathy, low energy/fatigue, excessive daytime sleepiness, pain, numbness or tingling, shortness of breath, problems in vision, excess sweating, palpitations, and urinary symptoms. For each item, patients are asked about three aspects: presence, severity (mild, moderate, or severe, scored from 1 to 3 points), and state in which the symptom is worse (On, Off or Not difference). Total subscores (NoMoFA ON, NoMoFA OFF, and NoMoFA NoDif) are obtained as the sum of the item scores in each of these states. In addition, a total non-motor fluctuations subscore "NoMoFA ON + OFF" is obtained by the sum of the subscores "NoMoFA ON" and "NoMoFA OFF". The overall NoMoFA score, "NoMoFA Total", is calculated using the formula: "NoMoFA ON + OFF" + "NoMoFA NoDif "[5]. The scale includes instructions for use and a useful Scoring Table.

Procedure to obtain the NoMoFA Italian version

- Translation and back-translation were carried out by two different Italian neurologists for each step (RB and RE, and CAA and AR), fluent in English. Consensus on each translation and for the final Italian version after comparison with the original English version was achieved.
- A cognitive pretesting was conducted to evaluate the intelligibility of all questions and instructions and to gather feedback regarding the task's difficulty, as well as participants' interest, attention span, and any discomfort experienced during the scale administration. The provisional translated scale was administered to 10 PD patients by 2 evaluators external to the translator team, who collected questions and doubts from participants. These were incorporated into the revisions and retested until major issues were resolved. Following the cognitive pretesting phase, additional adjustments were made to the forward and back-translations, if necessary. After improving the quality of translations and considering the cognitive pretesting results, the final version for validation study (see supplementary materials) was obtained.

Validation

- Participating centers. Five Italian centers, Turin (coordinator center), Milan, Rome, Salerno, and Catania were involved in the validation phase. Patients' recruitment was carried out in the movement disorder clinics of these centers from August 2023 to July 2024.
- Inclusion criteria. Diagnosis of PD according to the 2015 MDS criteria [7], native Italian speaker, Mini-Mental State Examination (MMSE) score > 25 [8], stable antiparkinsonian medications for at least 3 months, and ability to provide informed consent.
- Exclusion criteria. Atypical parkinsonian syndrome, Hoehn and Yahr score (H&Y) > 4 [9], patients under legal protection, or any kind of disability impacting the possibility to complete the questionnaire.
- Patients' assessment and procedures. Demographic data such as age, sex and education, and clinical features encompassing age at onset, disease duration, antiparkinsonian treatment, and levodopa-equivalent daily dose (LEDD) [10] were collected. During the clinical examination, the H&Y, MDS Unified Parkinson's Disease Rating Scale (MDS-UPDRS, Parts I–IV) [11], and Montreal Cognitive Assessment (MoCA) [12] were collected. Patients completed the NoMoFA questionnaire

and the Wearing-Off Questionnaire (WOQ-19), a self-report measure used to screen for end-of-dose "wearing off" symptoms in patients with PD [13]. All the assessments were performed in ON state.

– Sample size. Around 7 (between 5 and 10) cases per scale item were ensured. Therefore, inclusion of at least 200 patients was planned. To evaluate the stability of the Italian version of the NoMoFA (test–retest reliability), a group of 50 patients repeated the scale 14 (± 2) days after the first evaluation.

Data analysis

Main data did not fit normal distribution (Shapiro–Francia test); therefore, non-parametric statistics were used for analyses. To characterize the sample, we used usual descriptive statistics (mean, standard deviation, percentage). For group comparison, the Mann–Whitney and Kruskal–Wallis tests were used. The following NoMoFA psychometric properties were explored:

– *Feasibility and acceptability*. Data were considered of satisfactory quality if more than 95% was fully computable (without missing data or mistakes such as scores out of range, double scoring, etc.). The range of scores, difference between mean and median (arbitrary limit, 10% of the maximum possible score), floor and ceiling effect (maximum acceptable for both, 15%), and skewness (limits, − 1 to + 1) were calculated.
– *Dimensionality*. NoMoFA dimensionality was investigated through exploratory factor analyses (EFA) using the principal component analysis (PCA) and a parallel factor analysis (PFA). Appropriateness of the analyses was tested by Bartlett Test of Sphericity (standard, < 0.05) and Kaiser–Meyer–Olkin Measure of sampling adequacy (meritorious or better, ≥ 0.80). As in the pivotal validation study [5], a minimum loading of 0.40 was used as criterion for factor relevance, whereas item redundancy was considered if an item loaded on several factors by ≥ 0.40. The PFA characteristics and applied standards are detailed in Supplementary Material Section I. To confirm the adoption of "the most adequate" model, a clinical guidance was considered. Six neurologists participating in the present study were requested for grouping the NoMoFA items into domains according to their clinical experience, in a blind and independent manner. A multidimensional normal-ogive graded response model, Reckase's parameterization, was used to examine item discrimination (criterion, > 1.00).
– *Internal consistency and test–retest reliability*. Internal consistency was tested by the Cronbach alpha coefficient (criterion value, ≥ 0.70), corrected item-total correlation (criterion value, Spearman r ≥ 0.30), and item homogeneity (criterion value for a broad construct, ≥ 0.15). Weighted kappa with linear weights was used to determine the NoMoFA items test–retest reliability (stability), whereas intraclass correlation coefficient (ICC, 2-way random-effects model) was used for the NoMoFA subtotal and total scores. Kappa and ICC values ≥ 0.70 were considered satisfactory.
– *Convergent validity*. The convergent validity of the NoMoFA Total with other rating scales (H&Y, MDS-UPDRS, WOQ-19, MMSE, and MoCA) was assessed by means of Spearman's rank correlation coefficient (r_S). This statistic was also applied to evaluate the association of the NoMoFA scores with other variables (age, age at onset, disease duration, LEDD, and H&Y). Values of $r_S \geq 0.60$ were considered strong association. The hypothesis tested was that NoMoFA scores would show closer association (moderate to high) with measures for NMS and fluctuations and weaker correlation (weak to moderate) with the other measures and variables.
– *Known-group validity*. NoMoFA Total known-group validity was explored through Mann–Whitney and Kruskal–Wallis tests after grouping of patients by age (< 60, 60–64, 65–70, and ≥ 71 years), sex, disease duration (< 4, 4–7, 8–10, and ≥ 11 years), disease stage (HY < 3 was categorized as "mild"; HY = 3 as "moderate"; and HY > 3 as "severe"), and LEDD (< 400, 400–639, 640–1069, and ≥ 1070 mg/day). Age, disease duration and LEDD distribution for groups was obtained from their respective interquartile range.
– *Precision*. Precision of the NoMoFA Total was estimated by means of the Standard error of measurement (SEM). The smallest real difference (SRD; 95% confidence level) was also calculated. The corresponding equations are shown in the Supplementary Material Section I.

The standard values applied for the abovementioned clinimetric attributes appear in the Supplementary Material Table 1S. The analyses were carried out with STATA 15.1. (College Station, Texas 77,845 USA) and FACTOR Analysis 12.04.05 (Universitat Rovira I Virgili, Tarragona. Spain).

Results

Population

Two hundred and twenty-seven PD patients were included in the analysis. Their mean age (± SD) was 65.34 ± 8.53 years (range 41–90 years), with a predominance of men (67%). The age at onset of PD was 57.44 ± 9.40 years, and the disease duration was 9.31 ± 5.31 years. The distribution according to the H&Y stages was: 3.52% for stage 1, 77.1% for stage 2, 18.50% for stage 3, and 0.90% for stage 4. According to the

Table 1 Descriptive statistics of the assessments applied in the study

Variable	Mean	SD	Median	IQR	Minimum	Maximum
WOQ-19	4.40	3.68	4	0–7	0	16
MMSE	27.85	2.23	28	27–30	17	30
MoCA	24.63	3.54	25	23–27	11	30
LEDD	748.08	459.44	640	400–1070	0	2561.26
MDS-UPDRS I	10.27	6.56	9	5–14	0	29
MDS-UPDRS II	11.50	7.11	11	6–16	0	34
MDS-UPDRS III	28.57	12.83	27	19 – 36	6	65
MDS-UPDRS IV	4.59	4.23	4	0–8	0	16
NoMoFA ON	3.15	4.71	2	1–3	0	30
NoMoFA OFF	7.46	7.72	5	2–10	0	58
NoMoFA No Difference	9.51	7.87	7	4–12	0	45
NoMoFA ON + OFF	8.30	7.91	6	2–11	0	58
NoMoFA Total	14.23	11.11	11	6–20	0	64

SD standard deviation. *IQR* interquartile range. *WOQ-19* wearing-off questionnaire-19 items, *MMSE* mini-mental status examination, *LEDD* levodopa-equivalent daily dose, *MDS-UPDRS* Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Parts I–IV, *MoCA* Montreal cognitive assessment. *NoMoFA* non-motor fluctuation assessment

WOQ-19, 72.70% of patients ($n = 165/227$) reported motor fluctuations and the number of NMS declared by patients was 9.37 ± 5.41. Descriptive statistics for the applied measures are shown in Table 1.

NoMoFA clinimetric properties

Feasibility and acceptability

The NoMoFA scores were fully computable for 100% of the sample. An overview of the distribution of the NoMoFA Total is illustrated in Fig. 1. The percentage of patients reporting the presence of specific symptoms varied widely across items, from as low as 9.3% (Item 12. Poor decision-making and Item 14. Compulsions) to as high as 73.1% (Item 18. Low energy/fatigue). The highest proportion of static (no-difference) symptoms was observed in Item 27 (constipation, 94.9%). Other items with high static symptom prevalence include Item 11 (hallucinations, 79.3%), Item 12 (poor decision-making, 81.0%), and Item 25 (palpitations, 79.4%). The highest proportion of fluctuating symptoms was observed in Item

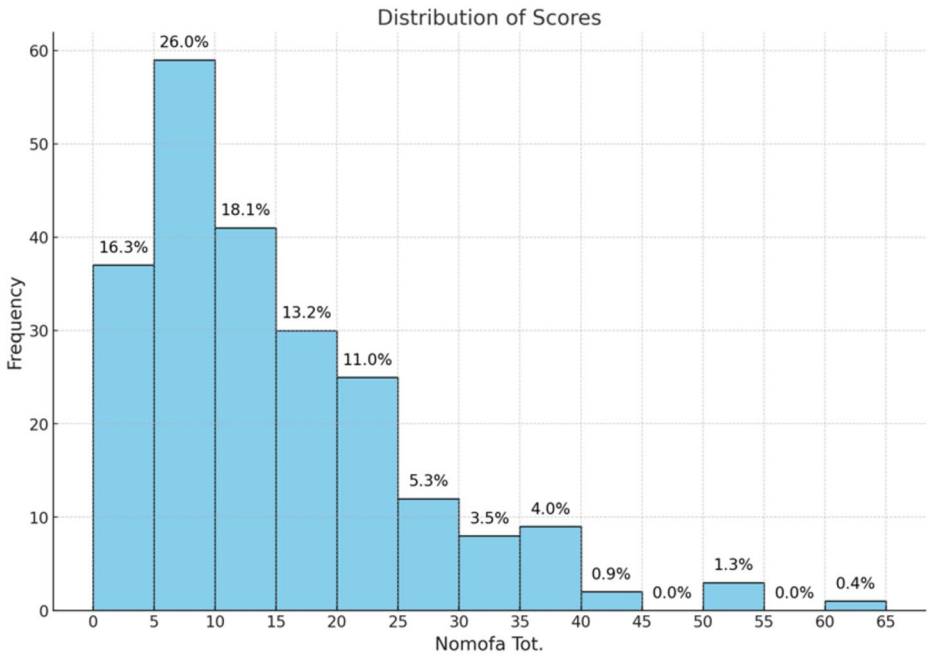

Fig. 1 Distribution of the NoMoFA Total scores in the sample. NoMoFA: Non-Motor Fluctuation Assessment

18 (low energy/fatigue, 55.4%), followed by Item 10 (loneliness, 44.0%) (Table 2).

The complete range of severity (0–3) was covered for 26 items with only Item 11 (Hallucinations) running from 0 to 2. The difference mean-median of the NoMoFA Total was 3.23 (< 10% of the maximum possible score = 8.1). All the NoMoFA items showed high floor effect but none showed ceiling effect over the limit. Eight items reached skewness greater than 2 (items 4, 7, 10, 11, 12, 13, 14, and 23) (Supplementary material, Table 2S). Concerning the NoMoFA subtotal and total scores, their skewness, floor and ceiling effects are shown in Table 3. NoMoFA Total showed no skewness and presented floor and ceiling effects clearly under the threshold value 15%.

Table 3 Acceptability parameters of the NoMoFA scores

	Skewness	Floor effect	Ceiling effect
NoMoFA ON	4.06	5.5	1.8
NoMoFA OFF	2.65	2.2	0.7
NoMoFA No Difference	1.73	1.4	0.5
NoMoFA ON + OFF	2.35	2.1	0.7
NoMoFA Total score	1.37	1.3	0.4

NoMoFA Non-motor fluctuation assessment

Dimensionality

Initially, we performed an exploratory factor analysis (EFA) using the principal component analysis (PCA) method and found 7 factors, explaining 59.2% of the variance. Considering the original validation study, in which 2 factors were identified, we tried the maximum-likelihood factor and the principal factor methods, obtaining 20 and 15 factors, respectively. These latter solutions were considered non-satisfactory and, therefore, abandoned. Next, a parallel factor analysis was carried out on a 7-factor solution, as proposed by the PCA. Several rotations potentially applicable to our

Table 2 Presence and characteristics of symptoms in the NoMoFA

NoMoFA item	Symptom present (%)	Static	Fluctuating	I–T Cor	Kappa$_W$
1. Loss of train of thought	38.8	62.5	37.5	0.58	0.68
2. Distraction	34.8	58.2	41.8	0.50	0.64
3. Difficulties in planning	27.3	56.5	43.5	0.61	0.68
4. Confusion in simple tasks	11.5	57.5	42.5	0.56	0.62
5. Difficulty in finding words	52.0	63.0	37.0	0.54	0.81
6. Excessively worried	49.3	70.5	29.5	0.60	0.76
7. Fear (feeling scared)	14.1	56.8	43.2	0.39	0.77
8. Restlessness	46.3	56.6	43.4	0.54	0.74
9. Sadness/hopelessness	37.0	57.1	42.9	0.60	0.67
10. Loneliness/isolation	22.0	56.0	44.0	0.48	0.83
11. Hallucinations	12.8	79.3	20.7	0.28	0.93
12. Poor decision-making	9.3	81.0	19.0	0.46	0.53
13. Impulsiveness	15.4	63.9	36.1	0.38	0.55
14. Compulsions	9.3	61.9	38.1	0.27	0.74
15. Poor short-term memory	50.7	77.4	22.6	0.47	0.81
16. Difficulty in stressing situations	37.0	61.9	38.1	0.62	0.77
17. Apathy/loss of interest	30.4	69.6	30.4	0.53	0.77
18. Low energy/fatigue	73.1	44.6	55.4	0.54	0.75
19. Excessive daytime sleepiness	50.2	60.0	40.0	0.54	0.82
20. Painful sensations	48.5	63.6	36.4	0.46	0.83
21. Strange sensations	36.6	62.6	37.4	0.47	0.69
22. Shortness of breath	26.6	63.3	36.7	0.43	0.83
23. Problems with vision	22.5	78.4	21.6	0.31	0.80
24. Excessive sweating	34.8	73.4	26.6	0.40	0.68
25. Palpitations	26.9	79.4	20.6	0.33	0.88
26. Urinary frequency or urgency	59.0	79.0	21.0	0.39	0.83
27. Constipation	60.8	94.9	5.1	0.28	0.80

MDISC item multidimensional discrimination, *I-T Cor.* corrected item-total correlation, *Kappa$_W$* weighted kappa with linear weights

data were tried with similar results: most components loading clearly on a factor and several others loading on none or on 2 or 3 factors. From the clinical survey, a 7-domain solution (range 5–7) was proposed by majority, including well-defined (coincidentally located by at least two-thirds of the participants) 26 items and 8 items that could be located into 2 to 4 different domains. According to the clinical survey, the items 12, 16, 21, and 23 (which could not be assigned to a specific domain due to excessive dispersion) were the most ambiguous to be grouped. Therefore, a final PFA solution with 7 factors and the best indices of goodness of fit was adopted (Table 4 and Supplementary Material Section II). Adequacy of sampling, item loadings on the respective factors, and goodness of fit indices appear in the Supplementary Material, Section II. The item multidimensional discrimination (MDISC) values appear in the Supplementary Material Section II (parallel factor analysis). Five items (18, 19, 21, 26 and 27) did not reach the criterion value > 1.00.

Internal consistency and test–retest reliability

Cronbach's alpha coefficient of the NoMoFA was 0.89 and the corrected item-to-correlation values ranged from 0.27 (Item 14. Compulsions) to 0.62 (Item 16. Difficulty in stressing situations), with 3 items (11, 14, and 27) lower than the criterion value 0.30 (Table 2). The item homogeneity was 0.17, just over the minimum 0.15 standard for broad constructs.

Fifty patients completed the NoMoFA for a second time after 13.8 ± 6.16 days. The difference in the number of symptoms declared on both occasions (10.74 ± 0.78 vs 11.38 ± 0.88) was not significant. For items, the kappa values ranged from 0.53 (Item 12. Poor decision-making) to 0.93 (Item 11. Hallucinations). Eighteen items showed kappa values > 0.70 (Table 2), and the ICC for the NoMoFA Total was 0.90 (95% CI = 0.84–0.94).

Convergent validity

The NoMoFA Total reached the highest correlation coefficients with MDS-UPDR Parts I ($r_S = 0.71$) and II ($r_S = 0.60$). The association with other measures was weak or moderate, as was the correlation with other variables, except with the number of symptoms declared in the NoMoFA ($r_S = 0.96$) (Table 5).

Table 5 Correlation of NoMoFA with other variables and convergent validity

	NoMoFA total	*p*
Age	0.14	0.05
Age at onset	− 0.04	NS
PD duration	0.30	0.001
LEDD	0.39	0.001
Number of symptoms	0.96	0.001
WOQ-19	0.45	0.001
MMSE	− 0.29	0.001
MoCA	− 0.41	0.001
Hoehn and Yahr	0.32	0.001
MDS-UPDRS Part I	0.71	0.001
MDS-UPDRS Part II	0.60	0.001
MDS-UPDRS Part III	0.30	0.001
MDS-UPDRS Part IV	0.47	0.001

LEDD levodopa-equivalent daily dose, *WOQ-19* wearing-off questionnaire-19 items, *MMSE* Mini-mental state examination, *MoCA* Montreal cognitive assessment, *MDS-UPDRS* Movement Disorder Society—Unified Parkinson's Disease Rating Scale, *NoMoFA* non-motor fluctuation assessment, *NS* not significant

Table 4 Dimensionality of the NoMoFA according to factor analyses and clinical survey

Exploratory factor analysis—principal component		Parallel factor analysis		Clinical survey	
Factors	Items	Factors	Items	Factors	Items
Cognition and urinary	1, 2, 5, 15, 16, 26	Cognitive disorder	1, 2, 4, 5, 12, 15, 16	Cognition	1, 2, 3, 4, 5, 15, 16
Dysautonomic disorder	25, 27	Dysautonomic disorder	22, 25, 26, 27	Dysautonomia	22, 24, 25, 26, 27
Mood and apathy	6, 8, 9, 10, 16, 17	Mood and apathy	6, 8, 9, 10, 16, 17	Mood	6, 7, 8, 9, 10, 17
Abnormal sensations, pain, dyspnea	20, 21, 22	Abnormal sensations, pain, dyspnea	7, 20, 21, 22	Sensations, pain	20, 21
Feel scared, hallucinations	7, 11	Feel scared, hallucinations	7, 11	Hallucinations	11
Control disorder	4, 12, 13, 14	Control disorder, sleepiness, sweating	12, 13, 14, 19, 24	Control disorder	12, 13, 14
Sleepiness, vision, sweating	19, 23, 24	Problems vision and sweating	23, 24	Fatigue, sleepy	18, 19
Do not load in any factor	3, 18		3, 18		23
Load on two or more factors	16		7, 12, 16, 22, 24		12, 16, 21, 23

EFA-PCA exploratory factor analysis, *NoMoFA* non-motor fluctuation assessment, *PCA* principal component analysis

Known-groups validity

Difference of NoMoFA Total was significant for PD duration, H&Y-based severity levels, and LEDD groups (Kruskal–Wallis test, $p < 0.0001$) but not for the different groups of age and sex (Table 6).

Precision

The SEM value of the NoMoFA Total was 3.40 (1/2 $SD_{pooled} = 5.48$) and the SRD resulted in 9.42.

Discussion

The NoMoFA is an instrument specifically designed for the evaluation of NMF in patients with PD. This study was aimed to translate and validate the scale in Italian language, comparing the results with the original validation study and adding new information on its clinimetric properties.

As a whole, the acceptability of the Italian version of the NoMoFA was satisfactory. Data quality was excellent, with 100% of data fully computable. The total NoMoFA score was free of floor and ceiling effects, although the skewness value (1.37) was slightly higher than the standard limit (1.0). This asymmetry was consistent with the floor effect present in the NoMoFA items and their skewness (only 8 items with skewness < 1.0) (Table 2S), a finding already detected in the original validation study [5]. This scale assesses a variety of symptoms that are frequently unrelated to each other and experienced only by a proportion of the patients (Table 2), explaining the higher floor effect. In this sense, our findings align with studies on other scales focused on a variety of NMS that showed relatively lower prevalence of several of these symptoms [14, 15]. Interestingly, low energy/fatigue (item 18) was endorsed as both the most frequent overall and most fluctuating NMS, a finding coincident with the pivotal NoMoFA validation study [5].

Table 6 Known-groups validity of the NoMoFA

Groups	NoMoFA total score	*p*
Age		0.11
< 60	12.27 ± 9.12	
60–64	12.40 ± 10.97	
65–70	14.77 ± 10.62	
≥ 71	16.82 ± 12.74	
Sex		0.08§
Male	15.07 ± 11.65	
Female	12.52 ± 9.78	
Disease duration		0.0001
< 4	10.38 ± 11.37	
4–7	12.89 ± 10.34	
8–10	17.18 ± 12.25	
≥ 11	16.24 ± 9.29	
H&Y Severity level		0.0001
Mild	12.45 ± 10.01	
Moderate	21.07 ± 12.42	
Severe	33.00 ± 9.90	
LEDD		0.0001
< 400	8.53 ± 7.75	
400–639	12.49 ± 10.38	
640–1069	15.81 ± 11.10	
≥ 1070	19.30 ± 11.87	

NoMoFA non-motor fluctuation assessment

p Kruskal–Wallis test, except § (Mann–Whitney test)

In the present study, NoMoFA clearly was a multidimensional measure. Given the difference in findings with the pivotal validation study, we tested several applicable factor analysis solutions and, finally, a clinical-based guide and the best goodness of fit to make the final decision. In Table 4 and the Supplementary Material Section II, we display the results of the methods applied and the interpretation in terms of "factors" to allow the reader obtaining a full information on the issue. For this multidimensional tool, most of the items showed adequate discriminative ability. As in the first validation study, five items were under the criterion value, but they were not coincident except for "Item 21. Strange sensations".

Regarding internal consistency, the Cronbach's alpha and the other parameters (corrected item-total correlation and item homogeneity) showed overall acceptable results. The alpha value was coincident with the previous validation study and only a slight difference was found in the item–total correlation. In the present study, only three items (11, 14, and 27; 11% of all items in the scale) showed item–total correlation values lower than the < 0.30 threshold applied here. Eight items showed values < 0.40 (7 in the original study, which used this criterion 0.40). In summary, both intrinsically and comparatively, the internal consistency of the NoMoFA Italian version was considered satisfactory. Regarding the stability, 18 NoMoFA items (67%) showed kappa values higher than the 0.70 threshold. Although we applied the same method of analysis as the original study, the results are quite different. Apparently, a threshold of 0.30 was used in the first validation, but we followed the recommended 0.70 threshold (Supplementary Material Table 1S). Nonetheless, Item 11 (Hallucinations) showed the highest kappa value and the ICC indicated satisfactory NoMoFA Total reproducibility in both studies.

The convergent validity analysis found that NoMoFA score was strongly associated with the MDS-UPDRS Part I (non-motor symptoms experiences of daily living), and II (motor experiences of daily living). The association with other scales and variables was moderate or weak, as

predicted. The pattern of association with the four sections of the MDS-UPDRS and H&Y was quite similar between the present and the first validation studies. Other scales and variables differ between the studies, making direct comparison impossible. Overall, the known-group validity analyses indicated that the NoMoFA scale could distinguish between groups based on disease duration, H&Y severity levels, and LEDD, demonstrating the instrument's sensitivity to these known degrees of PD severity. As per the results in the present study, NoMoFA Total scores are higher for increasing PD duration and H&Y stage (Table 6), supporting the notion that also NMF tend to increase in frequency and severity during the disease course. Noteworthily, the analysis shows that NoMoFA Total increases with aging and is higher in males in our cohort, although differences did not reach statistical significance.

Finally, the NoMoFA scale seems to show satisfactory precision, as evidenced by the SEM value. The SEM represents "the standard error of an observed score with a particular test that obscures the true score" and is sample-independent [16]. According to this parameter, NoMoFA Total can reliably distinguish differences of 3.40 points on a maximum score of 81. The SRD (9.42 in the present study) is based on the SEM and represents the minimal change in the score "that can be interpreted as a real difference" [17], providing an estimate of the scale's responsiveness. These findings suggest that the scale has satisfactory sensitivity to change, although this attribute should be properly established through longitudinal studies.

Our study has some limitations. First, despite efforts to ensure a balanced representation of disease severity, most of our participants were classified as having mild to moderate PD. This distribution is consistent with challenges faced in similar studies, such as the first NoMoFA validation study [5], where recruiting patients with advanced disease proved difficult. Consequently, our findings may be less generalizable to individuals with severe PD, who often face greater challenges in attending outpatient subspecialty clinics and are more likely to be in long-term care settings. Second, while the SEM and SRD of the NoMoFA scale suggest an appropriate sensitivity, the study did not include a longitudinal follow-up to assess the responsiveness of the scales over time. Future studies should incorporate longitudinal designs to evaluate the scale's ability to detect changes in symptom severity and disease progression (18). In addition, the factor analysis identified a 7-factor solution that accounted for a significant portion of the variance (68%). However, several items did not load on any factor or loaded on different factors, indicating potential issues with these items. Further research is needed to explore these findings and refine the factor structure of the scale.

Conclusion

NMS in PD are highly frequent and invalidating, and most of them show fluctuations, as seen with motor symptoms. The recently developed NoMoFA scale is the first and only scale designed to assess NMS in PD considering their presence, severity and fluctuations in relation to the dopaminergic therapeutic status of patients. The Italian NoMoFA scale, here translated from the English version and validated, showed strong potential as reliable and valid tool for evaluating NMF in PD. Its high data quality, robust psychometric properties, and ability to distinguish between known groups make it valuable for clinical practice and research. Further studies, particularly those including more diverse and severely affected populations, as well as longitudinal designs, will be crucial in continuing to validate and refine this new scale, ensuring its efficacy in various clinical contexts.

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Data availability The dataset used and analyzed during the current study will be made available by the corresponding author upon request to qualified researchers (i.e., affiliated to a university or research institution/hospital).

Declarations

Conflict of interests Roberta Balestrino: no relevant financial or non-financial interests to disclose. Domiziana Rinaldi: no relevant financial or non-financial interests to disclose. Silvia Galli: no relevant financial or non-financial interests to disclose. Alberto Romagnolo: no relevant financial or non-financial interests to disclose. Roberto Erro: no relevant financial or non-financial interests to disclose. Claudia Ledda: no relevant financial or non-financial interests to disclose. Giulia Donzuso: no relevant financial or non-financial interests to disclose. Marina Picillo: supports from the Italian Ministry of Health, the Italian Ministry of University and Fondazione della Società Italiana di Neurologia. Speaker honoraria from Abbvie. Claudio Terravecchia: no relevant financial or non-financial interests to disclose. Federica Agosta is Associate Editor of NeuroImage: Clinical, has received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and receives or has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, AriSLA (Fondazione Italiana di Ricerca per la SLA), the European Research Council, the EU Joint Programme – Neurodegenerative Disease Research (JPND), and Foundation Research on Alzheimer Disease (France). Paolo Barone: research grant from M.J. Fox Foundation; Advisory Board of: Roche, UCB, Abbvie, Zambon, Bial, Chiesi. Leonardo Lopiano: speech honoraria from Zambon, Bial, Abbvie, UCB. Alessandra Nicoletti: no relevant financial or non-financial interests to disclose. Massimo Filippi is Editor-in-Chief of the Journal of Neurology, Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology; received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards

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Ethical approval Approval from the independent Research Ethics Committee of each hospital was also obtained. The study was registered in clinicaltrials.gov (n°NCT06406374). All the participants gave their written informed consent prior to enrollment.

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