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REVIEW ARTICLE

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The Non-Motor Symptoms Scale in Parkinson's disease: Validation and use

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The Non-Motor Symptoms Scale (NMSS) was developed and validated in 2007 as the first instrument for the comprehensive assessment of a range of non-motor symptoms in Parkinson's disease (PD). Thirteen years have elapsed since its introduction and extensive international validation with good psychometric attributes has been carried out. Here, we review the validation data of the NMSS and its cross-validity with other scales, and describe the key evidence derived from use of the NMSS in clinical studies. To date, over 100 clinical studies and trials have made use of it as an outcome measure, showing consistent and strong correlations between NMSS burden and health-related quality of life measures. Moreover, the scale has shown to be capable of detecting longitudinal changes in non-motor symptoms, where studies have shown differential changes over time of several of the NMSS domains. The scale has become a key outcome in several randomized clinical trials. Highlighting the prevalence and importance of non-motor symptoms to quality of life in patients with PD, the development of NMSS has also been useful in signposting clinical and biomarker based research addressing non-motor symptoms in PD.

KEYWORDS
non-motor symptoms, non-motor symptoms scale, Parkinson's disease

1 | INTRODUCTION

The Non-Motor Symptoms Scale (NMSS)[1] was first published in 2007, following several international validation studies, at a time when clinical research and practice were largely focussed on motor features,[2] with non-motor symptoms (NMS) frequently unrecognized.[3] As a broad range of NMS occurs in Parkinson's disease (PD),[4] the NMSS was developed to capture many of these symptoms and was modelled on the successful introduction of the Non-Motor Symptoms Questionnaire (NMSQ) as a screening tool. The NMSS has a total of 30 NMS grouped into nine domains: cardiovascular and falls, sleep/fatigue, mood/apathy, perceptual problems, attention/memory, gastrointestinal, urinary, sexual and miscellaneous (the latter consisting of pain, smell, weight change and hyperhidrosis), the time frame covered being the past month, and quantified by multiplying severity (score 0-3) and frequency (score 1-4) for each question (NMS symptomatic burden).[1] The range for the NMSS total scores is 0-360, and the original publication confirmed the high prevalence of NMS across all stages of PD.

Now, 13 years after its development and initial publication, the NMSS has been translated from English into many languages, including German,[5] Spanish,[6] Korean,[7] Brazilian,[8] Chinese,[9] Japanese[10] and Italian.[11] Over 100 papers have used the NMSS, reporting on its clinimetric properties, prevalence of NMS, correlation with demographic and clinical features and, importantly, on the effect of treatment in clinical trials. In this viewpoint, we aim to summarize the global validation/clinical use data for the NMSS and discuss the most relevant studies making use of the NMSS as an outcome measures, highlighting the contribution of this scale to the detection of NMS in PD.

2 | VALIDATION

The original validation study of the NMSS enrolled 242 PD patients from Europe, Japan and the USA (mean age 67.2 ± 11 years, disease duration 6.4 ± 6.0 years) and showed a mean NMSS score of 56.5 ± 40.7 (range: 0-243) with no floor and ceiling effects for the NMSS total score,[1] and satisfactory scaling assumptions and internal consistency for most domains. Test-retest study showed satisfactory reproducibility (ICC > 0.80) for all domains except cardiovascular (0.45). The second international validation (411 PD patients from 10 countries across three continents) confirmed that the scale as a whole was free of floor or ceiling effects and had robust clinimetric properties despite its multi-dimensional nature. Similar results were observed in a Chinese cohort and two additional validation studies (Table 1),[9]although certain NMSS domains have less favourable properties in terms of floor and ceiling effects. For example, the sexual dysfunction and perceptual domains in some studies had a higher percentage of patients where a ceiling effect was observed,[8,12] but still well within the acceptable range (around 2%).

2.1 | Convergent validity with other instruments addressing NMS

Various studies have either correlated NMSS total score with specific tools or addressed convergent validity against other instruments that include assessment of NMS in PD. The rater-administered NMSS showed a strong positive correlation with the NMSQ self-administered items, confirming the link between patient-reported and physician-gathered outcomes related to NMS in PD,[1] and quality-of-life measures (PDQ-8).

Several studies have shown the link between the NMSS total scores and a range of other tools assessing PD symptoms. The NMSS showed moderate to strong correlation coefficients (r(S) ≥0.3) with: (a) sleep scales,[9,11,12] such as the Pittsburgh Sleep Quality Index, PD Sleep Scale (PDSS) and Epworth Sleepiness Scale (ESS); (b) neuropsychiatric scales,[9,11,12-14] including the Geriatric Depression Scale (GDS), Hamilton Anxiety rating scale (HAM-A), Beck Depression Index (BDI), Neuropsychiatric Inventory (NPI) and Scales for Outcomes in Parkinson's disease (SCOPA) cognitive and psychiatric problems scales; (c) autonomic scales, limited so far to SCOPA-Autonomic [11,12]; and (d) the UPDRS part III motor scale.[15] An overview of these scales and the associated correlation strength is presented in Table 2 and Figure 1. Additionally, the NMSS has been validated against instruments assessing specific NMS such as cognition, sleep, neuropsychiatric symptoms, autonomic symptoms and olfaction, detailed below.

These data show that the NMSS can pick up a broad range of NMS and has the potential to be used to identify specific NMS in PD, which can then be further explored with scales more dedicated to the specific problem.

2.2 | Neuropsychiatric features and Cognition

The NMSS mood/apathy domain was strongly associated with SCOPA cognition (SCOPA-COG) total scores,[14] while the self-completed Hospital Anxiety and Depression Scale (HADS) correlated strongly with NMSS sleep/fatigue, mood/cognition and gastrointestinal domains in two studies.[15] Other scales with significant associations include those between the Beck Depression Inventory and NMSS mood/apathy and perceptual domains; Neuropsychiatric Inventory with the NMSS sleep/fatigue, mood/apathy and perceptual domains; and the Epworth Sleepiness Scale with the NMSS sleep/fatigue domain. An overview of these associations is provided in Table 2.

In terms of links with specific cognitive measures, Koh and colleagues showed a moderate inverse correlation (r(S) = −0.291) between MMSE and NMSS total scores.[7] This was also observed in a Chinese study, where the inverse correlation between MMSE and NMSS was also moderate (r = −0.19), although in the same study the association between NMSS domain 3 and the MMSE was better (r = −0.47).[9] The latter highlights that the cognition domain of the NMSS may prove useful to identify (the risk for) cognitive problems

TABLE 1 Validation data for the Non Motor Symptoms Scale

	Item-Total correlation (Cronbach's alpha)			Domain-Total correlation			Test-Retest		
Study	Chaudhuri et al 2007[1]	Martinez-Martin et al 2009[12]	Wang et al 2009[9]	Cervantes-Arriaga et al 2010[6]	Cova et al 2017[11]	Chaudhuri et al 2007[1]	Martinez-Martin et al 2009[12]	Wang et al 2009[9]	Koh et al 2012[7]
Country	Europe USA Japan	Brazil India Japan USA Venezuela Europe	China	Mexico	Italy	Europe USA Japan	Brazil India Japan USA Venezuela Europe	China	Korea
Number of patients	242	411	126	150	71	242	411	126	102
Cardiovascular		(0.53)		NA	0.35	0.45	0.72		0.58
Light headedness	0.46	0.43	0.30			0.53	0.68	0.28	
Fainting			0.09			0.49	0.84	1.00	
Sleep/fatigue		(0.58)		0.86	0.80	0.92	0.77		0.70
Daytime sleepiness	0.32	0.26	0.51			0.85	0.75	0.94	
Fatigue	0.47	0.45	0.61			0.95	0.70	0.69	
Sleep initiation	0.36	0.40	0.61			0.87	0.65	0.86	
Restless legs	0.47	0.34	0.44			0.74	0.62	0.84	
Mood/apathy		(0.85)		0.35	0.71	0.93	0.91		0.76
Loss of interest	0.65	0.67	0.62			1.00	0.81	0.78	
Lack of motivation	0.68	0.68	0.55			0.50	0.77	0.83	
Feeling nervous	0.61	0.55	0.50			0.88	0.70	1.00	
Feeling sad	0.62	0.65	0.61			0.90	0.89	0.87	
Flat mood	0.62	0.56	0.65			0.62	0.70	0.82	
Anhedonia	0.65	0.70	0.58			0.82	0.63	0.70	
Perceptual		(0.45)		0.25	0.32	0.83	0.71		0.77
Hallucinations	0.37	0.31	0.22			0.77	0.85	1.00	
Delusions	0.44	0.27	0.25			0.86	0.68	1.00	
Diplopia	0.42	0.25	0.31			0.31	0.56	0.28	
Attention/memory		(0.77)		0.44	0.57	0.94	0.83		0.76
Concentration	0.54	0.53	0.47			0.94	0.65	0.72	
Forgetfulness	0.73	0.73	0.52			0.93	0.78	0.86	
Forget to do things	0.66	0.59	0.23			0.87	0.67	1.00	
Gastrointestinal		(0.49)		0.30	0.62	0.84	0.78		0.79
Sialorrhoea	0.23	0.32	0.37			0.96	0.71	0.53	
Dysphagia	0.24	0.43	0.34			0.60	0.80	0.40	
Constipation	0.21	0.22	0.45			0.99	0.79	0.96	

(Continues)

TABLE 1 (Continued)

	Item-Total correlation (Cronbach's alpha)				Domain-Total correlation				Test-Retest			
Urinary	(0.72)				0.26	0.70	0.83		0.83			0.78
Urgency	0.51	0.53	0.37				0.68		0.81	0.86		
Frequency	0.58	0.59	0.42				0.64		0.76	0.74		
Nocturia	0.51	0.51	0.50				0.94		0.79	0.52		
Sexual dysfunction		(0.52)	0.19		NA	0.26	0.94		0.67		0.93	
Interest	0.65	0.36	0.19				1.00		0.69	0.73		
Problems having sex							0.65		0.67	1.00		
Miscellaneous		(0.44)			0.43	0.54	0.65		0.81		0.59	
Pain	0.17	0.35	0.42				0.63		0.70	0.60		
Taste/smell	0.30	0.23	0.37				0.95		0.73	0.51		
Weight change	0.10	0.20	0.32				0.78		0.71	0.40		
Hyperhidrosis	0.15	0.22	0.40				0.83		0.81	0.68		

and high domain scores should prompt clinicians to explore cognitive problems in their patients.

2.3 | Sleep

NMSS total scores strongly correlate with the PD Sleep Scale (PDSS) total scores.[12] Strong associations of the NMSS total scores, and the NMSS sleep domain, have been shown with the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Geriatric Depression Scale (GDS) and Hamilton Anxiety Scale (HAM-A).[9] Wang et al also reported significant associations between the Sleep/fatigue domain of the NMSS and the PSQI and the ESS.[9] Other scales that were significantly associated with the NMSS sleep/fatigue domain were the NPI and BDI scales (Table 2). As such, the sleep/fatigue domain of the NMSS may be used as a brief screening tool for identifying sleep disorders in PD.

2.4 | Autonomic

NMSS total score correlate positively with SCOPA-Autonomic scores (SCOPA-Aut).[11,12] For the NMSS domain scores, significant associations were observed between the NMSS sleep/fatigue, gastrointestinal, urinary and sexual domain scores with SCOPA-Aut, demonstrating the ability of the NMSS to identify and signpost autonomic symptoms in PD[11,12] (Table 2). In addition, some authors have explored the link between specific autonomic symptoms and the NMSS. Hommel et al, for example, showed that 48.5% of PD patients with orthostatic hypotension declared symptoms (score of one or over on NMSS domain 1), whereas 43.4% of patients with symptoms had no orthostatic hypotension.[16] How the detection rate of the NMSS for these symptoms relates to other scales, however, remains unclear as no other autonomic scales where included in this study. Further efforts should be put into the identification of how the NMSS is able to identify and grade autonomic symptoms.

2.5 | NMSS total and non-motor burden grading

A study of 935 PD patients introduced the concept of NMS burden (NMSB) grading based on cut-off scores for the NMSS: 0) no NMS; 1) Mild (NMSS scores 1-20); 2) Moderate (NMSS scores 21-40); 3) Severe (NMSS scores 41-70); and 4) Very severe (NMSS scores 71 and higher).[17] Using this grading, the authors reported that severity levels of NMSB and motor grading are not well correlated, and that even PD patients with mild HY stages could have severe burden of NMS.[17] This observation was further developed to underpin the concept of non-motor endophenotypes within PD.[18] NMSB grading provides a simple tool, alongside motor measures, for the stratification of patient cohorts.

2.6 | NMSS in epidemiological studies and progression patterns

The reproducible and validated nature of the NMSS has enabled it to be used as a structured outcome measure in multiple large cohort studies.[19] Several currently active cohort studies are using the NMSS as an outcome measure, for example the Spanish COPPADIS-2015 study.[20] In previous studies, it was shown that NMS and NMS burden are not strongly related either to age or disease duration.[21] Guo et al reported in 616 PD patients that, although the mean affected number of NMS and NMMS score increased with disease duration, NMS progression rate appeared to be largely symptom-specific.[22] On the other hand, specific determinants reported for NMS or NMS burden include sex, Impulse Control Disorder (ICD) (eg ICARUS study)[23] and most recently seasonal variation.[24] In the latter study, it was shown that not only NMSS total scores, but also domain scores for cardiovascular symptoms, perceptual problems and sleep demonstrate seasonal fluctuation.[24] The knowledge gained from some of the here mentioned studies has been instrumental in selecting the relevant outcomes for clinical studies and, moreover, have started to highlight that many factors influence NMS in PD and should be taken into account for proper study interpretation.

2.7 | Quality of life: Correlations with QoL scores

The NMSS is not only a useful tool for the identification of specific NMS in PD, but also for the identification of overall NMS burden, underlined by the consistently reported strong link between NMS (burden) and quality of life (QoL) in PD,[19,25] for example between the NMSS total score and the Parkinson's Disease Questionnaire-39 (PDQ-39) and EQ-5D (r(S) 0.57-0.70).[12] Several large studies (n > 500 patients) have confirmed these findings,[26,27] with female sex as an independent predictor for worse QoL related to NMS.[28] NMS burden is not only related to QoL in patients, but also in caregivers where especially disability and mood of PD patients affect caregiver stress and burden assessed through the Zarit Caregiver Burden Inventory and Caregiver Strain Index.[29] The strong link between the NMSS and QoL highlights the need of having a non-motor instrument as an outcome in clinical trials and other clinical studies.

2.8 | Relationship with motor features

The relationship between the NMSS, its domains and several motor symptoms, including tremor and postural instability, in PD has been examined and it was reported that these symptoms were moderately, yet significantly, associated[15,30] (Table 2). Of interest, however, interventions aimed at improving motor symptoms do not necessarily improve NMS. Dafsari et al showed that DBS, Apomorphine and Intrajejunal Levodopa infusion are capable of inducing strong improvements in UPDRS part III scores, alongside with a strong improvement of NMSS total scores and domains such as the sleep/fatigue, mood/cognition, urinary and miscellaneous, but not of all the individual domains.[31]

3 | NMSS IN CLINICAL TRIALS

3.1 | Randomized trials

A total of eight randomized, placebo-controlled, trials have made use of the NMSS as an outcome. Of these, two studies examined the effect of Rotigotine on NMS. In a post hoc analysis of the RECOVER trial,[32] Chaudhuri et al showed that in 178 PD patients on rotigotine, fatigue, symptoms of depression, anhedonia and apathy improved, compared to 89 patients on placebo, using the NMSS.[33] In a subsequent study, using the NMSS as a primary outcome measure, however, the superiority of Rotigotine over placebo could not be confirmed.[34] Other large-scale randomized controlled trials (RCTs) using the NMSS as a (secondary) outcome measure are the Exenatide[35] and the PANDA[36] trials. In neither trial did the study medication, Exenatide and oxycodone-naloxone, respectively, have an effect on NMS, as measured by the NMSS. Also, the DUOGLOBE study (DUOdopa/Duopa in Patients with Advanced Parkinson's Disease—a GLobal OBservational Study Evaluating Long-Term Effectiveness (DUOGLOBE), a non-interventional post-marketing observational study of PD patients treated with Levodopa continuous intestinal gel (LCIG) (NCT02611713)), is making use of the NMSS as an outcome and the results are awaited with interest.[37] These studies show that many therapies, alongside the often pronounced motor effects, have non-motor effects as well and can be captured through instruments such as the NMSS.

3.2 | Open-label and comparative trials

The NMSS was explored as a primary outcome measure in PD for the first time in a trial of Intrajejunal Levodopa infusion in 2009, where, in an European multicentre study, it was shown that LCIG improved NMSS scores.[38] Martinez-Martin et al subsequently showed an improvement of NMSS total and domain scores with apomorphine continuous treatment in an open-label comparative study of 17 patients.[39] In a separate report, all advanced treatment in PD were shown improve NMSS scores, although distinct NMSS defined effect profiles were associated with each treatment option.[31] As such, the NMSS has facilitated the description of the broad improvements in NMS after the introduction of device-aided therapies.

4 | ADVANTAGES AND DISADVANTAGES OF THE NMSS

The identification and quantification of NMS burden and specific symptoms is of crucial importance as these symptoms are strongly

TABLE 2 Association of the Non Motor Symptoms Scale and its domains with other assessments tools

	Study and PD population	Tool	r(S)	Reference
Total scores	Wang et al 2009 126 patients	PSQI ESS GDS HAM-A	0.63 0.38 0.45 0.52	9
	Cova et al 2017 71 patients	BDI NPI ESS SCOPA-Aut MDS-UPDRS part I	0.56 0.65 0.45 0.66 0.85	11
	Martinez-Martin et al 2009 411 patients	SCOPA-Aut SCOPA-Motor SCOPA-PC SCOPA-Cog CISI-PD PDSS	0.64 0.44 0.51 0.44 0.49 0.53	12
	Campos et al 2015 76 patients	SCOPA-Cog	-0.36	14
	Swick et al 2014 287 patients	MDS-UPDRS part III	0.35	15
Domain 1 Cardiovascular/falls	Cova et al 2017 71 patients	ESS MDS-UPDRS part I	0.41 0.46	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.12 Light headedness	0.62	13
	Martinez-Martin et al 2009 411 patients	SCOPA-Aut	0.62	13
Domain 2 Sleep/fatigue	Wang et al 2009 126 PD patients	PSQI ESS	0.66 0.42	9
	Cova et al 2017 71 patients	BDI NPI ESS SCOPA-Aut MDS-UPDRS Part I	0.57 0.55 0.37 0.35 0.75	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.7 Sleep problems 1.8 Daytime sleepiness 1.13 Fatigue	0.70	13
	Martinez-Martin et al 2009 411 patients	PDSS	0.56	13
Domain 3 Mood/cognition	Wang et al 2009 126 PD patients	GDS HAM-A	0.41 0.47	9
	Cova et al 2017 71 patients	BDI NPI MDS-UPDRS Part I	0.58 0.66 0.40	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.3 Depressed mood 1.4 Anxious mood 1.5 Apathy	0.80	13
Domain 4 Perceptual/ hallucinations	Cova et al 2017 71 patients	NPI	0.40	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.2 Hallucinations/psychosis	0.70	13
	Martinez-Martin et al 2009 411 patients	SCOPA-PC	0.53	13

(Continues)

TABLE 2 (Continued)

	Study and PD population	Tool	r(S)	Reference
Domain 5 Attention/memory	Wang et al 2009 126 PD patients	MMSE	-0.47	9
	Cova et al 2017 71 patients	BDI MDS-UPDRS Part I	0.50 0.40	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.1 Cognitive impairment	0.74	13
	Martinez-Martin et al 2009 411 patients	CISI-PD	0.51	13
Domain 6 Gastrointestinal	Cova et al 2017 71 patients	BDI ESS SCOPA-Aut MDS-UPDRS Part I	0.32 0.33 0.56 0.45	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.11 Constipation	0.58	13
	Martinez-Martin et al 2009 411 patients	SCOPA-Aut	0.65	13
	Swick et al 2014 287 patients	UPDRS part III	0.44	15
Domain 7 Urinary	Cova et al 2017 71 patients	UPDRS Part III MoCA SCOPA-Aut UPDRS Part I	0.33 -0.37 0.72 0.63	11
	Martinez-Martin et al 2015 434 patients	MDS-UPDRS Part I 1.10 Urinary problems	0.65	13
	Martinez-Martin et al 2009 411 patients	SCOPA-Aut	0.65	13
Domain 8 Sexual	Cova et al 2017 71 patients	SCOPA-Aut	0.50	11
	Martinez-Martin et al 2009 411 patients	SCOPA-Aut	0.51	13
Domain 9 Miscellaneous	Cova et al 2017 71 patients	BDI NPI ESS SCOPA-Aut MDS-UPDRS Part I	0.56 0.65 0.45 0.66 0.85	11
	Martinez-Martin et al 2009 411 patients	SCOPA-Aut thermoregulatory	0.51	13

Note: Data only shown in case of moderate (0.30-0.59) or strong (≥0.60) significant correlation magnitude levels (*r*(S)).

Abbreviations: Aut, Autonomic; BDI, Beck Depression Index; CISI-PD, Clinical Impression of Severity Index—Parkinson's disease; Cog, Cognitive; ESS, Epworth Sleep Scale; GDS, Geriatric Depression Scale; HAM-A, Hamilton Anxiety Rating Scale; MDS-UPDRS, Movement Disorder Society—Unified Parkinson's Disease Rating Scale; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; NPI, Neuropsychiatric Inventory; PC, Psychiatric disturbances; PD, Parkinson's disease; PDSS, Parkinson's Disease Sleep Scale; PSQI, Pittsburgh Sleep Quality Index; SCOPA, Scales for Outcomes in Parkinson's disease.

linked to QoL in PD. The NMSS is a very useful tool in this respect, and several studies have confirmed that the NMSS total score is largely free of floor or ceiling effects, in addition to other robust clinimetric properties in this multi-dimensional scale. Moreover, even though the scale is rater-administered, it is strongly associated with self-administered NMS questionnaire items, confirming that the NMSS reflects patient-reported outcomes. Its importance in flagging up and quantifying NMS is reflected by its increasing use in academic and commercial trials.

Despite the great success the NMSS has had in clinical and other research endeavours, the instrument has limitations, including the fact that it groups together symptoms not necessarily related to each other. The latter is mainly the case in the miscellaneous domain of the NMSS, where four non-related symptoms (weight change, hyperhidrosis, change in smell/taste and pain) have been grouped together. A high score on the domain does not provide direct information about the individual symptoms. In addition, less prevalent symptoms are likely to produce high

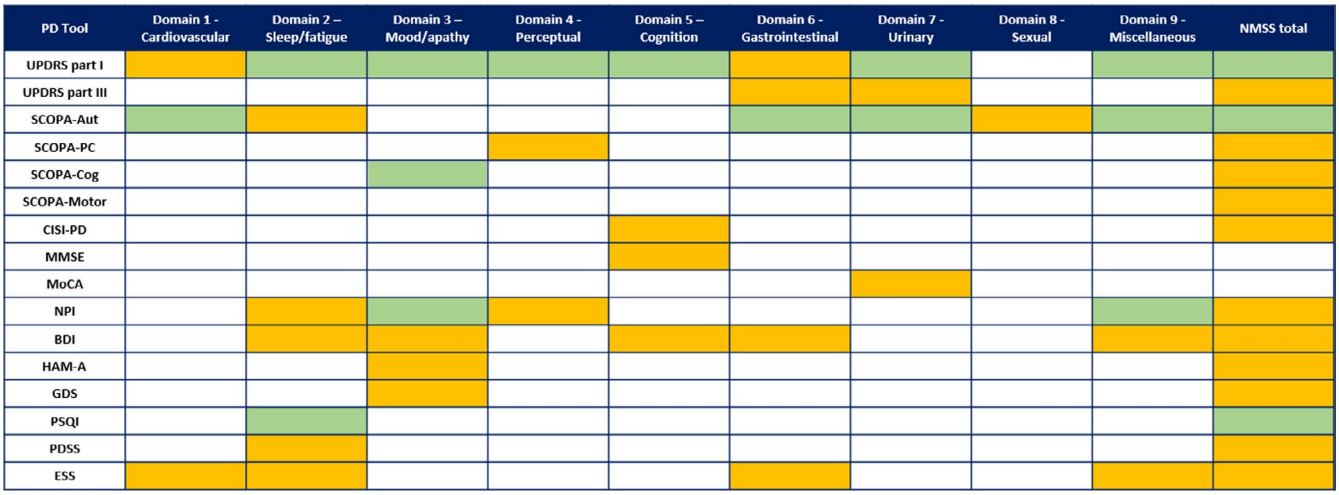

FIGURE 1 Association of the Non-Motor Symptoms Scale and its domains with other assessments tools. Only associations with a *r*(S) value of 0.3 or higher are shown. Amber indicates a *r*(S) value of 0.30-0.59, green a value of ≥ 0.60, and white indicates that the association was either not examined or the *r*(S) value was <0.30; exact values and references are provided in Table 2. Abbreviations: Aut, Autonomic; BDI, Beck Depression Index; CISI-PD, Clinical Impression of Severity Index - Parkinson's disease; Cog, Cognitive; ESS, Epworth Sleep Scale; GDS, Geriatric Depression Scale; HAM-A, Hamilton Anxiety Rating Scale; MDS-UPDRS, Movement Disorder Society—Unified Parkinson's Disease Rating Scale; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; NPI, Neuropsychiatric Inventory; PC, Psychiatric disturbances; PD, Parkinson's disease; PDSS, Parkinson's Disease Sleep Scale; PSQI, Pittsburgh Sleep Quality Index; SCOPA, Scales for Outcomes in Parkinson's disease

floor effects for their domains, such as perceptual problems and sexual dysfunction.[1] Other limitations of the scale, in terms of validity, include low internal consistency for some domains, mainly the perceptual/hallucinations and sexual dysfunction domains. The correlation between NMSS scores and both disease duration and motor scores is low, and the diversity of NMSS is likely to preclude a homogeneous linear score progression over time. The latter is an inherent problem to comprehensive non-motor scales, and also applies to the updated version of the NMSS and the Movement Disorder Society Non-Motor Scale (MDS-NMS) where some of the outlined issues with the NMSS have been addressed.

5 | CONCLUSIONS

The development and worldwide validation of NMSS provided, for the first time, a roadmap for clinical quantification of the broad burden of NMS in PD patients. The scale has been validated with acceptable psychometric properties as a reliable and reproducible outcome measures. To date, over 100 original research studies have made use of the NMSS as an outcome measure, clearly demonstrating the high prevalence and burden of NMS in PD. Given the relevance of the NMSS and the identified shortcomings, a revised expanded version (the MDS-NMS) was sponsored by the International Parkinson Disease and Movement Disorder Society and very recently was validated.[40] It is likely that the MDS-NMS would be used accompanying motor measures such as the MDS-UPDRS in clinical trials.

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CONFLICT OF INTEREST

KRC and PMM were involved in the development of the Non-Motor Symptoms Scale. The authors report no conflict of interest.

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