Original scientific paper
Izvorni znanstveni rad

Med Jadert 2025; 55(2):105-112
DOI: https://doi.org/10.57140/mj.55.2.2

Psychometric properties of the Croatian version of the Non-motor Symptoms Scale in Parkinson's disease

Psihometrijska svojstva hrvatske verzije „Non-motor Symptoms Scale" skale kod bolesnika oboljelih od Parkinsonove bolesti

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Summary

Objectives: The objective was to evaluate the psychometric properties of the Croatian version of the Non-Motor Symptoms Scale (NMSS), a tool to assess non-motor symptoms (NMSs) in Parkinson's disease (PD).

Methods: A cross-cultural adaptation of the NMSS into Croatian and a psychometric analysis of the translated version of the NMSS was carried out in PD patients. NMSS includes nine domains: cardiovascular, sleep/fatigue, mood/cognition, perceptual problems/hallucinations, attention/memory, gastrointestinal tract, urinary, sexual function and miscellaneous. The quality of data was descriptively analysed, and Cronbach's alpha coefficient assessed internal consistency. Pearson correlations were performed on the nine domains. The level of significance was set to $p<0.05$.

Results: 76 PD patients were assessed (mean age 68.4±9.6 years; 45% women; mean length of disease 8.7±4.6 years). Mean NMSS score was 110.68±58.76, where the more common NMSs in PD patients were related to the following domains: mood/cognition (22.86 %), sleep/fatigue (19.74 %), sexual function (13.65 %) and urinary (11.58 %). Cronbach's alpha for the NMSS total score was 0.92 (range for domains: 0.48-0.96). Total NMSS score was highly correlated with each of the nine domains (Pearson correlation range: 0.45-0.82).

Conclusions: The Croatian version of NMSS can be considered a comprehensive and helpful measure for NMSs in Croatian-speaking PD patients.

Key words: Croatia, Parkinson's disease, non-motor symptoms, Non-Motor Symptoms Scale

Sažetak

Cilj: Cilj ovoga rada bio je evaluirati psihometrijska svojstva hrvatske verzije 'Non-motor Symptoms Scale' skale, pomagala koje se koristi u procjeni nemotoričkih simptoma kod bolesnika oboljelih od Parkinsonove bolesti.

Metode: Međukulturalna adaptacija 'Non-motor Symptoms Scale' skale na hrvatski jezik i

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Primljeno/*Received* 2024-12-12; Ispravljeno/*Revised* 2025-05-11; Prihvaćeno/*Accepted* 2025-05-15

psihometrijska analiza prevedene verzije navedene skale, vršila se na bolesnicima oboljelim od Parkinsonove bolesti. 'Non-motor Symptoms Scale' skala uključuje devet domena: kardiovaskularni sustav, spavanje/umor, raspoloženje/spoznaja, vidljivi problemi/halucinacije, pažnja/memorija, gastrointestinalni trakt, urinarne tegobe, seksualna funkcija i domena razno. Podaci su opisno analizirani, a unutarnja dosljednost procijenjena je pomoću Cronbach alpha koeficijenta. Pearsonove korelacije primijenjene su na svih devet domena, a razina značajnosti postavljena je na $p<0,05$.

Rezulati: U istraživanje je ukupno bilo uključeno 76 bolesnika koji boluju od Parkinsonove bolesti (prosječna starost 68,4±9,6 godina, 45 % žene, prosječno trajanje bolesti 8,7±4,6 godina). Srednja vrijednost ukupnog rezultata 'Non-motor Symptoms Scale' skale iznosila je 110,68±58,76, pri čemu su češći nemotorički simptomi bili povezani sa sljedećim domenama: raspoloženje/spoznaja (22,86 %), spavanje/umor (19,74 %), seksualna funkcija (13,65 %) i urinarne tegobe (11,58 %). Cronbach alpha koeficijent za ukupni rezultat 'Non-motor Symptoms Scale' skale iznosio je 0,92 (raspon za domene od 0,48 do 0,96). Ukupni rezultat 'Non-motor Symptoms Scale' bio je visoko povezan sa svih devet domena (Pearsonova korelacija bila je u rasponu od 0,45 do 0,82).

Zaključak: Hrvatska verzija 'Non-motor Symptoms Scale' skale može se smatrati sveobuhvatnim i korisnim instrumentom koji pomaže mjerenje nemotoričkih simptoma kod bolesnika koji boluju od Parkinsonove bolesti na hrvatskom govornom području.

Ključne riječi: Hrvatska, nemotorički simptomi, 'Non-Motor Symptoms Scale' skala, Parkinsonova bolest

Introduction

Parkinson's disease (PD) is a progressive neurological disorder which is characterized by a dopamine deficiency that is associated with tremor, rigidity, bradykinesia and gait problems. In the last decade, PD has been also recognized as implying non-dopaminergic dysfunction and non-motor symptoms (NMSs) which appear at all stages of disorder[1] and have a notable impact on PD patients' health and quality of life.[2-5] NMSs mainly consider neuropsychiatric symptoms, sleep disorders, autonomic dysfunction, gastrointestinal symptoms and sensory symptoms.[6] NMSs associated with PD are sadly often under-recognized and remain untreated in the early stages of the disease. The exact prevalence and severity of non-motor symptoms in early PD (before initiation of antiparkinsonian drugs) remains unclear.[7]

In order to respond to the need for quantification of PD symptoms, various instruments have been recently developed and validated to assess and advance their detection. Several instruments are available for the quantification of motor feature (Unified Parkinson's Disease Rating Scale, UPDRS) and health-related quality of life (Parkinson's Disease Questionnaires - PDQ 8 and 39), but until year 2006, no scale had yet been developed or validated specifically for the assessment of the full range of NMSs observed in PD. In the mentioned year, Chaudhuri et al. developed and validated a self-reported questionnaire for PD patients for NMS (NMSQuest). NMSQuest consisted of 30 common symptoms scored "yes" or "no," and it is designed to provide a quick screen for problematic NMSs for clinical management.[8]

Because NMSQuest is not a rating scale, nor is it intended to evaluate the effect of treatment, Chaudhuri et al. developed and validated the Non-motor Symptoms Scale for PD (NMSS-PD) one year later. That scale has been efficiently used to assess and measure NMSs of PD and it is the most often scale used in clinical practice for assessment of NMSs in PD. NMSS scale was originally designed and validated by Chaudhuri et al. in 2007, on a total of 242 PD patients across centres in the UK, Italy, Germany, USA, and Japan.[9]

NMSS is a specific validated scale in different populations for the screening and the assessment of NMSs. It is a 30-item scale involving 9 domains: Cardiovascular, Sleep/Fatigue, Mood/Cognition, Perceptual problems, Attention/Memory, Gastrointestinal, Urinary, Sexual function and Miscellaneous domain. The items inside of every mentioned domain are assessed for severity (from 0 to 3) and frequency (from 1 to 4) and scored through the multiplication of both values (from 0 to 12). The higher result indicates higher severity and frequency of NMSs, and the maximum score is 360.[10]

The objective of this study was to evaluate the psychometric properties of the Croatian version of the NMSS, a tool to assess NMSs in PD.

Participants and methods

Participants

In this research data was analysed on 76 PD patients, which included 34 women and 42 man which underwent neurological care at Clinical Hospital Centre Osijek, Croatia. All the patients were

required to sign a statement of informed consent before we started the research.

Questionnaire procedures

Our research problem was examined using the 30-item NMSS which includes the following nine domains: Cardiovascular, Sleep/Fatigue, Mood/Cognition, Perceptual problems, Attention/Memory, Gastrointestinal, Urinary, Sexual function and Miscellaneous domain.[9] We received approval from the original author to translate the NMSS into Croatian. In the translation stage, two bilingual researchers with experience in clinical practice independently translated the original tool. In the back-translation stage, another translator who had not previously encountered the original tool translated the Croatian version back into English. Back-translation worked well in avoiding translation errors because a large part of the original language structure was retained. The translated tool was finalized in the final stage. This process required comparing the two versions, and it confirmed that there were no meaningful differences between the original and translated versions. All differences were reviewed and corrected through discussions. The consensus process was repeated to complete the translation if corrections were needed due to the accuracy of translation or cultural differences.

Statistical analysis

The data was descriptively analysed, and Cronbach's alpha coefficient assessed internal consistency. Pearson's correlation coefficient (r) was performed on the nine domains of the NMSS. The level of significance was set to $p < 0.05$.

Results

The mean age was 68.4 ± 9.6 years, and the mean disease duration was 8.7 ± 4.6 years. The highest mean score was measured for the Mood/Cognition domain, while the lowest was found for the Perceptual problems domain. The mean NMSS total score measured 110.68 ± 58.76, where the more common NMSs in PD patients were related to the following domains: mood/cognition (22.86 %), sleep/fatigue (19.74 %), sexual function (13.65 %) and urinary (11.58 %). Cronbach's alpha coefficient for the NMSS total score using the entire sample was 0.92, indicating high internal consistency. The Cronbach's alpha coefficient ranged from 0.48 for the Miscellaneous domain to 0.96 for the Urinary and Sexual function domains (Table 1).

Table 1 Descriptive statistics and internal consistency of NMSS total score and domain
Tablica 1. Deskriptivna statistika i unutarnja konzistentnost ukupnog rezultata i domene NMSS-a

NMSS	Mean (SD)	Cronbach's alpha
Cardiovascular *Kardiovaskularna*	5.26 (5.64)	0.73
Sleep/Fatigue *Spavaje/umor*	21.85 (12.46)	0.78
Mood/Cognition *Raspoloženje/ spoznaja*	25.30 (18.40)	0.93
Perceptual problems *Perceptualni problemi*	2.72 (4.75)	0.65
Attention/Memory *Pažnja/pamćenje*	9.24 (8.39)	0.77
Gastrointestinal *Gastrointestinalni*	6.57 (8.61)	0.86
Urinary/*Urinarni*	12.82 (12.34)	0.96
Sexual function *Seksualna funkcija*	15.11 (9.10)	0.96
Miscellaneous/*razno*	11.81 (7.38)	0.48
Total score *Ukupni rezultat*	110.68 (58.76)	0.92

NMSS: Non-Motor Symptoms Scale; SD: standard deviation *NMSS: Ljestvica nemotornih simptoma; SD: standardna devijacija*

The total NMSS score was highly correlated with each of the nine domains, the Pearson's correlation coefficient ranged from 0.45 to 0.82, indicating a strong association with the related construct. The highest correlation was measured for the Attention/Memory domain, while the lowest one was found for the Cardiovascular domain (Table 2).

Table 2 The domains-total NMSS score correlation
Tablica 2. Korelacija domena i ukupnog NMSS rezultata

NMSS	*r*
Cardiovascular/*Kardiovaskularna*	0.45*
Sleep/Fatigue *Spavaje/umor*	0.71*
Mood/Cognition *Raspoloženje/spoznaja*	0.76*
Perceptual problems *Perceptualni problemi*	0.47*
Attention/Memory *Pažnja/pamćenje*	0.82*
Gastrointestinal *Gastrointestinalni*	0.67*
Urinary/*Urinarni*	0.76*
Sexual function/ *Seksualna funkcija*	0.74*
Miscellaneous/*Razno*	0.64*

NMSS: Non-Motor Symptoms Scale; * - statistically significant at $p < 0.05$ *NMSS: Ljestvica nemotoričkih simptoma; * - statistički značajno pri p < 0,05*

Discussion

The aim of this study was to evaluate the psychometric properties of the Croatian version of the NMSS, a tool to assess NMSs in PD patients. The Croatian version of NMSS was earlier translated but it had not been psychometrically validated by Bago Roznakovic et al. in 2017 year on a total of 71 PD patients and 60 healthy participants.[11] To the best of our knowledge, this is the second study in Croatia which investigated NMSs for patients with PD in which Croatian version of the NMSS was used for NMSs assessment.

We found most necessary and important to investigate the NMSs of patients suffering from PD because of the mentioned and proved statement that NMSs associated with PD are often very prevalent and severe but for now, they are sadly often under-recognized and remain untreated in early stages of disease.[7] The secure the right and early treatment of NMSs in patients with PD, it is first necessary to make as complete and as high-quality assessment of their severity and prevalence as possible.

The reason why we chose to translate and validate the Croatian version of the NMSS for the purpose of assessing NMSs of patients suffering from PD rather than use already translated and clinically used questionnaires in Croatia is mainly because the NMSS is the rating scale, it is specifically designed to provide a quick screen for problematic NMSs for clinical management and it can be used for the evaluation of the effect of treatment.[9] The results of this paper were discussed in connection with published literature in NMSs of patients suffering from PD domain from around 20 years ago until today.

The earlier mentioned translation of the Croatian version of NMSS[11], after its original validation by Chaudhuri et al. in 2007[9] the NMSS was also translated and validated on PD patients from various countries and regions.[10,12-21]

Back in 2007, Chaudhuri et al. made the first and original validation of NMSS on a total of 242 PD patients across centers in the UK, Italy, Germany, USA, and Japan. The total NMSS score was almost two times lower than the one in our research, measuring 56.46 (40.66). The same result as ours was found in terms of the lowest domain mean score which was measured for the Perceptual problems domain - 1.71 (4.03). The highest score was found for the Sleep/Fatigue domain measuring 12.60 (10.35). In terms of correlation of NMSS domains with a total NMSS score, the correlation coefficient (r) ranged from 0.45 for the Cardiovascular domain to 0.96 for the Mood/Cognition domain. In our research, the lowest correlation with total NMSS score was also found for the Cardiovascular domain measuring also 0.45, while the highest correlation was found for the Attention/Memory domain (r = 0.82). Four domains (Mood/Cognition, Attention/Memory, Urinary, and Sexual function) showed Cronbach's alpha coefficient higher than 0.70 (from 0.71 for the Urinary domain to 0.85 for the Mood/Cognition domain). The other two, the Sleep/Fatigue and Perceptual problems domains reached values around 0.60 and the remaining domains had Cronbach's alpha under the limit, while mean Cronbach's alpha was 0.61.[9] Those Cronbach's alpha results indicate lower internal consistency reliability than one in our research.

Croatian authors Bago Roznakovic et al. conducted a research about NMSs in de novo PD comparing to normal aging while using the NMSS score. A total of 71 PD patients and 60 healthy participants (control group) completed their study. Significantly higher frequency of NMSs in PD patients was found in Cardiovascular, Sleep/Fatigue, Mood/Cognition, Hallucinations and Attention/Memory when comparing to control group. Most PD patients in their research suffered from sleep/fatigue (97.2 %), mood/cognition (98.6 %) and attention/memory (97.2 %) NMSs. The highest NMSS score was present in the Mood/Cognition domain in PD patients' group (median 14.0), the same as the highest score in our study which was also found for the Mood/Cognition domain measuring 25.30 (18.40). The total NMSS score was higher in the PD group than in the control group indicating that NMS were more serious and frequent among PD patients (median PD 38,00 vs. controls 8,00; $p < 0.001$).[11] Both PD patients and the control group total NMSS scores were lower than the one in our research that measured 110.68 (58.76). When investigating the correlation between the total NMSS score and NMSS domains, the highest correlation with total NMSS score was found for the Mood/Cognition domain (r = 0.785) and the lowest for the Hallucinations domain (r = 0.311). For comparison, the highest correlation with a total NMSS score in our research was found for the Attention/Memory domain (r = 0.82), while the second highest was found for the Urinary domain (r = 0.76) and also the Mood/Cognition domain (r = 0.76). On the other hand, the lowest correlation was found for the Cardiovascular domain (r = 0.45).

Martinez-Martin et al. conducted an international study on the psychometric attributes of the NMSS for PD on 411 PD patients 12 centres across 10 countries in America, Asia, and Europe. The total NMSS score measured 57.1 (44.0) was almost two times lower than the one in our study which was measured on

110.68 (58.76). The same as in our research, the highest mean value was measured for the Mood/Cognition domain - 11.2 (14.3) while the lowest was measured for the Cardiovascular domain - 1.8 (3.2), which was the second lowest domain measured in our study. The intraclass correlation coefficient ranged from 0.67 for the Sexual function domain to 0.91 for the Mood/Cognition domain, which is higher correlation with a total NMSS than ours where it ranged from 0.45 to 0.82. In terms of internal consistency reliability, Cronbach's alpha ranged from 0.44 for the Miscellaneous domain to 0.85 for the Mood/Cognition domain.[10] Similar results for Cronbach's alpha are measured in our study (from 0.48 to 0.96), especially for the lowest which was also found for the Miscellaneous domain measuring 0.48.

The validation of the Chinese NMSS for PD was made on a total of 126 PD patients in a study conducted by Wang et al. The highest mean value was measured for the Mood/Cognition domain, the same as in our research, with a result of 8.26 (11.23) while the lowest was measured for the Cardiovascular domain with a result of 0.60 (1.44). The total NMSS score was measured on 31.06 (30.88), which is more than 3 times lower than our total NMSS score. Cronbach's alpha coefficient for the total NMSS was 0.89, which is slightly lower than the one in our research. The Cronbach's alpha coefficients for the 9 NMSS subscales were 0.23, 0.68, 0.90, 0.55, 0.85, 0.54, 0.85, 0.89, and 0.36, respectively. Significant coefficients ($rS > 0.19$, $P < 0.05$) were found for all 30 items of 9 NMSS domains except item 2 (fainting) in the item–total (corrected) correlation analysis of the NMSS.[12]

The validation of the Korean version of the NMSS for PD was made by Koh et al. on a total of 102 PD patients. The total NMSS score in their research was measured at 43.87 (42.35) with the highest value again for the Mood/Cognition domain - 10.54 (13.41) and the lowest for the Perceptual problems domain - 0.69 (1.99). Those results in terms of the highest and the lowest measured mean value are the same as in our study, but the total NMSS score in our research is still noticeably higher. Cronbach's alpha coefficient for the total NMSS score was 0.742 and each of the nine NMSS domains gave Cronbach's alpha coefficients of ≥ 0.70. That result is better than the one measured in our study in which the Perceptual problems and Miscellaneous domains did not reach Cronbach's alpha higher than 0.70. Furthermore, the correlations between each domain with the total NMSS score were statistically significant - Spearman's rank correlation coefficient (rS) ranged from 0.376 for the Cardiovascular domain to 0.806 for the Attention/memory domain.[13] The results for the best and the worst correlation with total NMSS score was measured for the same NMSS domains in our research.

Carod-Artal and Martinez-Martin made a research on the independent validation of the NMSS for PD in a total of 150 Brazilian patients with PD. The highest measured NMSS domain in their research was also the Mood/Cognition domain - 11.2 (13.7) and the lowest score was measured for the Cardiovascular domain - 1.5 (2.5). The total NMSS score measured 48.9 (36.3)[14] which is still lower than the total NMSS score in our research. Same result for the highest and the lowest value was earlier found in an international [10] and Chinese study.[12] The mean Cronbach's alpha of the NMSS Brazilian version was 0.60, and four domains (Mood/Cognition, Attention/Memory, and Urinary and Sexual function) showed a satisfactory internal consistency and reached a Cronbach's alpha over the standard 0.70.[14] These results are equivalent to those in the original study of validation[9], and still lower than those from our study.

The evaluation of an Arabic version of the NMSS for PD was made in the research of Sellami et al. on 62 Tunisian PD patients. The mean NMSS score was 82.29 (55.76) which is still lower than the total score in our research. The mean Cronbach's alpha of the NMSS Arabic version was measured at 0.87[15], indicating a high internal consistency reliability, the same as in our study.

Cova et al. made validation of the Italian version of the NMSS for PD on a total of 71 PD patients from Rome (43 patients) and Milano (28 patients). The total NMSS score was 39.76 (31.90), and the highest mean score was measured for the Urinary domain - 7.87 (8.70), which was not the case in earlier research. The lowest mean value was found for the Perceptual problems domain, the same as in the NMSS original validation study[9], Korean study[13], and in our study, measuring 0.90 (1.86). In terms of NMSS domains AND total NMSS score correlation, all domains, except the Sexual function domain, showed a statistically significant correlation with the total NMSS score. Internal consistency reliability was adequate, as the Cronbach's alpha coefficient resulted in 0.72 for the total NMSS scale which is slightly worse than in our study (0.79). The Cronbach's alpha coefficients for the 9 NMSS subscales were measured at 0.72, 0.64, 0.68, 0.73, 0.69, 0.69, 0.68, 0.73 and 0.71.[16]

Furthermore, two review articles were made on the assessment and use of NMSS for PD, the first back in 2017. by Sauerbier et al.[17] specifically for the Asian population, and the second by Wamelen et al. in 2020.[18] Except earlier mentioned and discussed

studies, Sauerbier et al.[17] in their review additionally included seven studies from China[22-28], three from Korea[29-31], one from Singapore[32] and one from India[33] in which NMSS was used. Three years later, Wamelen et al.[18] additionally included three studies[34-36] in their review. Both reviews[17,18] concluded that the NMSS provided a roadmap for clinical quantification of the NMSs in PD patients and that the NMSS has been validated with acceptable psychometric properties as a reliable and reproducible outcome measures.

Natadidjaja et al. made a validation of the Indonesian version of the NMSS for PD on a total of 70 PD patients in 2023. The mean NMSS total score was 51.86 (44.02) which is still more than two times lower score than the total NMSS score in our research. In terms of correlation of each NMSS domain with total score, all domains were significantly correlated with total score, the same as in our study with the correlation coefficient (r) ranging from 0.506 for the Miscellaneous domain to 0.805 for the Mood/Cognition domain. Cronbach's alpha coefficient for the NMSS total score was 0.853 and Cronbach's alpha coefficients for the 9 NMSS domains were 0.274, 0.565, 0.702, 0.534, 0.806, 0.666, 0.701, 0.814, and 0.146.[19] That result of internal consistency reliability is lower than the one that we measured in our research.

In 2023, Eghlidos et al. made a research on the validation of the Persian version of the NMSS for PD on a total of 186 PD patients from Iran. The total NMSS score was measured on 52.01 (38.54) or also two times lower than the total NMSS score in our study. The lowest mean values were measured for the Perceptual problems domain - 1.30 (4.22), and the highest mean value was measured for the Mood/Cognition domain - 11.77 (12.01)[20], same as in the Korean[13] and our study. The correlation between the NMSS total score and NMSS subscales ranged from the Perceptual problems/Hallucinations domain (r = 0.40) to Mood/Cognition domain (r = 0.79). The overall Cronbach's alpha of the Persian version of NMSS was 0.84. Three domains (Mood/Cognition, Attention/Memory, and Urinary domain) had good internal consistency (more than 0.7), and two domains (Sleep/Fatigue and Perceptual problems/Hallucinations) showed acceptable value (more than 0.6). The rest of the NMSS domains had values of Cronbach's alpha lower than 0.6.[20] Considering those results, the intercorrelation between the total NMSS score and NMSS domains, as well as internal consistency validity is slightly lower than in our study.

Also, in year 2023, Hamdan et al. tested the validity and reliability of NMSS for PD on a total of 35 PD patients in Dr. Soetomo General Hospital, Surabaya, Indonesia. Internal consistency reliability was performed using Cronbach's alpha coefficient value of > 0.7 for the reliability of the total NMSS score (0.836). Cronbach's alpha coefficients ranged from 0.489 to 0.985, and the highest Cronbach's alpha was measured for the Sexual function domain which was 0.985.[21] This is similar to the results in the Brazilian[14] and Italian[16] versions of the validation studies, in which Cronbach's alpha coefficient of a total NMSS score was measured on 0.60 and 0.72, with the reliability value of each item ranging from 0.37 and 0.82 and from 0.64 to 0.71, whereas in a study conducted by Martinez et al.[10], the Cronbach's alpha coefficients ranged from 0.44 to 0.85.

Differences and variations of results in earlier cited studies are probably caused by a wide clinical picture and various clinical manifestations of PD, including NMSs. There is no reported data about the significant influence of culture or territorial area on NMSs in PD[37], meaning that they are likely triggered by different pathology of PD. Since our results of internal consistency reliability and intercorrelation between separate dimensions of NMSS are pretty high when compared to the ones from cited studies, we think that the differences in the results of those studies have no consequences on the interpretation of the Croatian version of the NMSS in Croatian-speaking PD patients.

Conclusion

According to our results, the total score of NMSS for our participants, and therefore PD symptom severity, was self-estimated at 110.68 (58.76) which is higher than all the total NMSS scores in studies from relevant literature included and discussed in this paper. The highest mean value was measured for Mood/Cognition, while on the other hand, the lowest values were measured for the Perceptual problems domain. Cronbach's alpha ranged from 0.48 to 0.93 and a statistically significant correlation was found between all NMSS domains and the total score when Pearson correlations were performed. Therefore, when looking at the results of internal consistency reliability and intercorrelation between separate dimensions of NMSS, and when comparing them with the relevant studies and relevant literature from this research domain, it can be concluded that the Croatian version of the NMSS can be considered a comprehensive and helpful measure for NMSs in Croatian-speaking PD patients.

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