Original Article

NIMHANS Neuropsychological Battery for Elderly in Parkinson's Disease Patients: Validation and Diagnosis using MDS PD-MCI Task Force Criteria in Indian Population

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Abstract

Introduction: Cognitive impairment is a common non-motor feature of Parkinson's Disease (PD). Diagnosis of mild cognitive impairment is challenging and routinely missed in clinical practice. Our study aimed to study the efficacy of NIMHANS Neuropsychological Battery for Elderly (NNB-E) in diagnosing subtle cognitive deficits in PD patients. **Objective:** The aim of this study is to validate NNB-E and evaluate cognitive impairment in PD patients in comparison with healthy controls. **Methods:** We recruited 31 PD patients and 31 healthy controls in the current study. We validated NNB-E using receiver operating characteristic (ROC) curve analysis, Crohnbach's alpha, principal component analysis, and Pearson product-moment correlation, and studied the cognitive impairments using NNB-E in the non-demented PD patients and controls who scored ≥24 on HMSE. **Results:** Cognitive performance of PD patients was poor compared to controls. NNB-E showed good internal consistency and construct validity with Crohnbach's alpha of 0.861 and area under the curve (AUC) of 0.878. The battery was able to detect mild cognitive impairment in 74.1% of patients and 6.4% of controls. The ROC curve showed that the overall sensitivity of the battery was 73.2% and specificity was 92.6% at an optimal cutoff score. Different cutoff values set for defining PD-MCI as per MDS task force criteria resulted in varying frequencies of MCI ranging from 25.8% to 71%. **Conclusion:** Our study established the validity of NNB-E in PD patients, and this tool was suitable for diagnosing PD-MCI and discriminating PD patients from normal controls in the Indian population. This study also showed PD-MCI at various cutoff scores with greater impairment in executive and attention domains.

Keywords: MCI, MDS task force criteria, mild cognitive impairment, NIMHANS neuropsychological battery for elderly, NNB-E, Parkinson's disease, validation

Introduction

Cognitive impairment is one of the most common non-motor aspects of Parkinson's disease (PD). The cognitive impairment in PD patients varies from mild cognitive impairment to PD dementia. PD-mild cognitive impairment (PD-MCI) is observed in around 25% to 30% of patients with PD and is not associated with impairment in everyday activities.[1] The relative risk of developing PD dementia is 39.2% in PD-MCI patients compared to PD without MCI at baseline.[2] PD dementia is reported in 24% to 31% of PD patients. PD patients may present with deficits in all cognitive domains, but the predominant impairments are seen in executive function, attention, visuospatial skills, and memory while the language domain is least impaired in PD, unlike Alzheimer's disease.[3] Diagnostic criteria for PD-MCI were standardized by the MDS task force in 2012.[4] In the PD-MCI complex, the most common type is the non-amnestic type with frequent executive and visuospatial dysfunction.

According to MDS task force criteria, cognitive impairments can be assessed at two levels using a global cognitive scale and a comprehensive neuropsychological battery validated in PD. Mini-Mental Status Examination (MMSE) is one of the most used screening tools used to assess PD dementia. As MMSE is a globally accepted screening tool, it is translated, modified, and validated in various languages including Hindi, Hindi mental status examination (HMSE). A comprehensive scale should be able to assess five cognitive domains of memory, visuospatial, attention/working memory, language, and executive functions with at least two different tests assessing each domain.[5] The main aim of the study is to find cognitive deficits in non-demented PD patients using NIMHANS Neuropsychological Battery for Elderly (NNB-E) and validation of the battery.

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NNB-E is a culture-appropriate cognitive battery developed and standardized to assess both cognitive function and decline in Indian older adults.[6] Earlier studies at our center used NNB-E in PD patients.[7-9] To the best of our knowledge, this is the first study to validate this battery in PD.

Materials and Methods

The present study was a hospital-based cross-sectional study conducted in the Departments of Neurology and Clinical Psychology. Parkinson's patients were recruited from the neurology outpatient department and movement disorder clinic that fulfilled the UKPDS Brain Bank Criteria,[10] age group of 45–65 years, subjects of either gender, right-handed, and having HMSE ≥24. Patients and controls are well-versed in Hindi.

Healthy volunteers who had normal cognition and no history of any neurodegenerative disorder after neurological examination served as controls.

The institute's ethics committee approved the research. All participants gave written informed consent, and the information was kept confidential.

The sociodemographic information, such as age, gender, and educational status, as well as a full history of medication use, including type, dose, frequency, timing, and duration of usage, were collected from the patients. The levodopa equivalent daily dosage for patients using anti-parkinsonian medicine was estimated using Tomlinson *et al*.[11] A neurological examination, as well as an OFF and ON state UPDRS assessment,[12] was performed on all patients who were enrolled.

Neuropsychological assessment: The HMSE was used to evaluate global cognition in patients and controls at the level I. Following that, all patients and controls underwent a thorough neuropsychological evaluation using the NNB-E at level II. During the assessment, adequate breaks were provided to minimize fatigue. The neuropsychological tests in patients were administered during the on-state between 9 and 11 am.

NNB-E is a brief battery developed, standardized, and validated (by Tripathi, Kumar, Bharath and Marimuthu) for assessment of cognitive functions in Indian adults.[13] The NNB-E exclusively evaluates the main cognitive domains such as attention, memory, visuospatial abilities, executive functions, language, and parietal focal signs. The battery takes about 45 to 60 min to administer. Visuospatial abilities are assessed on stick construction tests (copy condition), verbal and visual learning and memory are assessed on the word list, and story recall (verbal passage) and recall of stick construction on immediate and delayed recall trials. Executive functions are tested by category fluency test (generating names of animal, vegetable, and fruits in 1 min each), go no go test, digit span backward and corsi block test backward. Category fluency test was used to assess language and cognitive switch while visual and verbal working memory were tested by Corsi block test backward and digit span test backward respectively. Response inhibition is assessed by the Go/No-Go test. Picture cancellation test, Digit span, and Corsi span forward conditions were used to assess the attention. The details of the neuropsychological tests conducted for patients and controls are provided in [Table 1].

Using MDS task force level II criteria, PD-MCI is diagnosed when there is an impairment of at least two tests, either in a single domain or different domains. The performance is assessed between 1 and 2 SD below the appropriate normative mean. The task force proposed two tests in each cognitive domain, a minimum of 10 tests for addressing all domains equally to increase the sensitivity of the battery.[14]

Statistical analysis

SPSS version 23.0 (IBM, Armonk, NY) was used for statistical analysis, with a significance level of 5%. To compare demographic and clinical data of Parkinson's patients and controls, independent sample t-tests for normally distributed continuous data and $\chi 2$ tests or Fisher's exact tests for categorical data were used as appropriate. Analysis of covariance with *post hoc* Bonferroni correction was done to adjust for age, gender, education, and HAM-D scores.

Receiver operating characteristic (ROC) curve analyses with the area under the curve (AUC) were used to define how well the cognitive impairment in NNB-E differentiated Parkinson's patients from controls. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for various cutoff scores. Optimal, screening, and diagnostic cutoffs were calculated for the subtests that were significant between patients and controls. Principal component factor analysis (PCFA) with varimax rotation was used to assess construct validity for the NNB-E. A minimal eigenvalue of 1 was used to determine factor extraction. Internal consistency was determined using Cronbach's alpha coefficient.

Intergroup analysis was performed using *t*-test and Mann–Whitney U-test. Analysis of covariance was employed to determine the differences in cognitive impairment by adjusting for covariates. The NNB-E was compared between the PD patients and healthy control by ANCOVA with age, gender, years of education, HAM-D, and disease severity as covariates and Bonferroni correction for multiple comparisons, with an adjusted α-value of $p \leq 0.01$

Raw scores of each component in the NNB-E were converted to a standardized z-score. Then, according to the MDS criteria, the z-scores of the neuropsychological subtests were further divided into groups of MCI, MCI -1, -1.5, and -2 standard deviations below the mean. The sensitivity and specificity for the NNB-E in predicting MCI in PD patients were calculated for the obtained z-score.

Results

Sociodemographic variable

Thirty-one patients with PD and an equal number of controls were recruited and underwent cognitive assessment by NNB-E. The mean age of the patients and controls included in the study

Table 1: NNB- E cognitive test results in PD patients and Controls

Domain & Cognitive test	Patient ($n=31$)	Control ($n=31$)	*t*	*p*
	Mean (SD)			
Language				
Verbal fluency animals	11.61 (3.39)	12.85 (3.46)	-1.443	0.154
Memory				
Story memory test dr	5.49 (2.15)	10.52 (2.42)	-8.983	<0.001*
Word list learning trial 1	4.46 (1.78)	5.78 (1.69)	-3.040	0.003*
Word list learning trial 2	6.2 (1.91)	7.52 (1.55)	-2.999	0.004*
Domain & cognitive test	**Patient ($n=31$)**	**Control ($n=31$)**	***U***	***p***
	Median (Q1, Q3)			
Attention/working memory				
Digit forward	5 (4,6.5)	8 (6,10)	209.500	<0.001*
Picture cancellation time taken	3.15 (2.46,3.5)	2.4 (2.07,3.03)	266.500	<0.001*
Picture cancellation total cancelled	112 (108.5,114.5)	114 (113,115)	365.000	0.016*
Picture cancellation omission	3 (0,6.5)	1 (0,2)	393.500	0.041*
Picture cancellation commission	1 (0,1)	0 (0,0)	288.000	<0.001*
Corsi block tapping forward	6 (3,7)	6 (4,7)	459.500	0.338
Executive function				
Digit backward	4 (3,6)	5 (3,9)	404.500	0.058
Corsi block tapping backward	4 (4,6)	5 (4,7)	416.000	0.215
Go no go test hits	16 (15,17)	17 (17,17)	278.500	<0.001*
Go no go test misses	1 (0,2)	0 (0,0)	231.000	<0.001*
Language				
Verbal fluency fruits	9 (8,10)	11 (9,12)	306.500	0.003*
Verbal fluency vegetables	9 (7,11)	14 (10.75,17)	195.000	<0.001*
Memory				
Word list learning trial 3	7 (5,8)	9 (8,10)	184.000	<0.001*
Word list learning total learning	18 (13,20)	23 (21,24)	208.000	. <0.001*
Word list learning delayed recall	7 (4.5,7.5)	7 (6,9)	357.500	0.013*
Word list learning recognition hits	9 (8,10)	10 (10,10)	267.500	<0.001*
Word list learning recognition miss	1 (0.5,2)	0 (0,0)	223.500	<0.001*
Story memory test - ir	7 (4.5,8.5)	11 (9,13)	116.000	<0.001*
Visuospatial ability/visual learning & memory				
Stick construction	22 (19.5,24)	24 (24,24)	242.000	<0.001*
Stick construction - ir	15 (10,20)	19 (11,21)	429.000	0.117
Stick construction- dr	8 (5,14)	20 (10,23)	226.500	<0.001*

*This value is significant

was 56.22 ± 5.2 and 53.74 ± 5.95 years, respectively. The mean duration of the disease was 3.84 ± 2.67 (0.5 to 10 years) in patients. The male and female gender ratio of the patients and controls was 24:7 and 17:14, respectively. The median value of education in patients and controls was secondary education. Patients and controls did not differ in age, educational status, and HAM D values but there was a significant difference in gender distribution (Fisher test, $p = 0.001$).

Clinical details of the patients were provided in the Table 2. The mean HAM-A score was 0.89 ± 1.11, HAM-D was 1.00 ± 1.56, and HMSE was 26.05 ± 5.06 in PD patients. The first motor symptom in most of the patients at the onset of the disease was a tremor of the upper limb seen in 19 (61.29%) patients. Subjective memory complaints were reported by 12 (38.7%) patients and three (9.6%) controls. Hallucinations were seen in six (19.4%) patients and one (3.2%) control.

Construct validity of NNB-E

To validate NNB-E, construct validation was done by ROC curve [Figure 1]. The AUC of the ROC curve for predicting cognitive impairment in PD patients was highest with Story Memory Test Delayed Recall (AUC = 0.949; 95% CI, 0.9–0.998) followed by story memory test immediate recall (0.909; 95% CI, 0.841–0.942), word list total learning (0.843; 95% CI, 0.736–0.951), word list Learning Trial 3 (0.84; 95% CI, 0.738–0.941), verbal fluency vegetables (0.836, 95% CI; 0.728–0.945), digit forward (0.805, 95% CI; 0.688–0.923), stick construction delayed recall (0.802; 95% CI, 0.686–0.918) [Table 3].

Component analysis

PCFA: According to Bartlett's test of sphericity (χ^2 1385.59, df 300, and $P < 0.001$) and Kaiser–Meyer–Olkin measure of sampling adequacy (0.79), the data were appropriate for

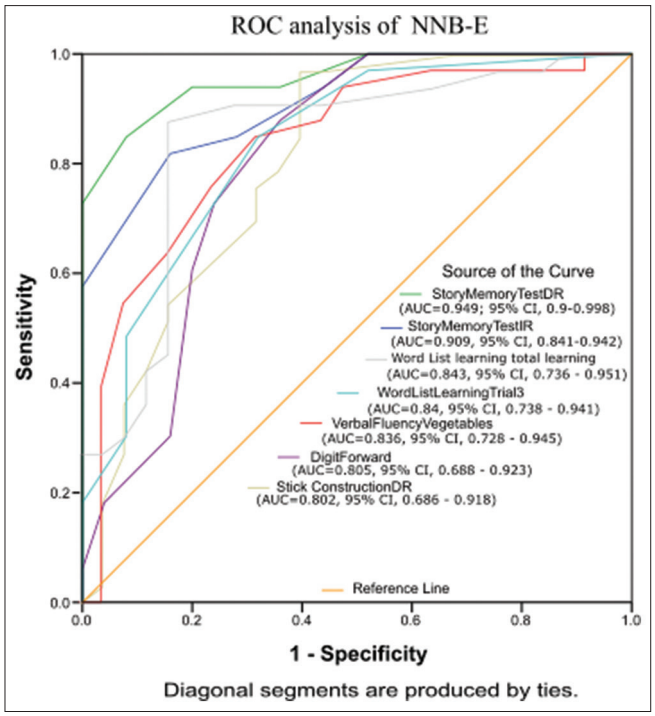

Figure 1: Receiver operating characteristic curves

Table 2: Clinical findings in Parkinson's patients

	Minimum	Maximum	Mean	Std. Deviation
Age	45	65	56.22	5.2
Duration (in years)	0.50	10.00	3.83	2.67
LEDD	193.00	1050.00	562.45	180.49
Subjective Response to Levodopa	15.00	95.00	69.74	17.13
UPDRS Off	14	64	37.97	14.42
UPDRS On	3	45	19.41	10.44
Hoehn and Yahr	1	4	1.63	0.70
Schwab and England	40	100	72.37	16.35
HAM A	0	4	0.89	1.11
HAM D	0	5	1.00	1.560
HMSE	25	31	26.05	5.057

principal component analysis. This was further explained through the diagonal values of the anti-image correlation matrix (>0.5). Based on the significant break in the scree plot and eigenvalue criterion, a seven-component solution was yielded by PCA [Figure 2]. The seven factors explained 78.2% of the variance. The following was the content of the various components: component 1 explains verbal learning, memory, and language functions; component 2 mainly focused on visuospatial, memory, attention, and executive functions; component 3 is about memory; component 4 is attention; component 5 is executive function; component 6 is memory; and component 7 is language and attention. Results of the rotated component matrix results are shown in the Supplementary Table 1 (values >0.5 are significant).

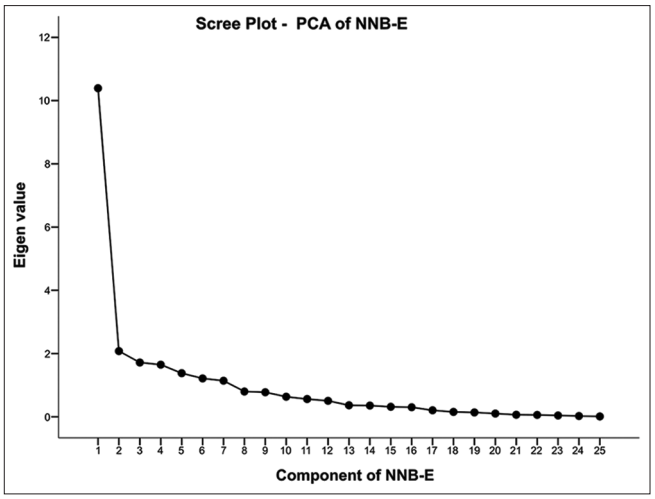

Figure 2: Figure showing eigen values of principal component factor analysis

Poor composite scores of factor 1 (verbal learning, memory, and executive function and language), factor 2 (visuospatial, memory, attention, and executive functions), factor 3 (memory), factory 6 (memory), and factor 7 (language, executive function, and attention) were associated with MCI status.

Internal consistency and reliability

Cronbach's alpha, a measure of the internal consistency of the test, revealed an overall reliability coefficient of 0.861 indicating a strong correlation between the individual components of the battery. Cronbach's alpha value did not change much when one of the test items was deleted. Pearson product–moment correlations between total cognitive score and individual component scores ranged from 0.808 (word list total learning) to 0.413 (picture cancellation time) [Supplementary Table 2]. The strongest correlations were present in Word List total learning, Stick construction test DR, and Story Memory Test.

Comparative analysis of scores obtained from NNB-E between Parkinson's patients and controls

The cognitive scores on different tests of the NNB-E were detailed in the Table 1. PD patients had shown significantly poorer performance compared to controls in Story Memory Test immediate and delayed recall, Digit Forward Test, Stick Construction Test–Copying and delayed recall, Word List Learning Trial 1, Word List Learning Trial 2, Word List Learning Trial 3, Word List Total Learning, Word List delayed Recall, Word List Recognition Hits, Word List Recognition Miss, Verbal Fluency Fruits, Verbal Fluency Vegetables, Attention Trial Time Taken, Attention Trial Total Cancelled, Attention Trial Omission, and Go/No-Go Test. In other tests such as digit backward test, stick construction immediate recall, Verbal fluency Animals, and Corsi Block Tapping Forward and Backward tests did not establish statistical significance between patient and control groups.

An analysis of covariance was performed for each variable of the NNB-E by keeping age, gender, education, and HAM-D as

Table 3: Table showing area under curve values of neuropsychological tests in NNB-E and various cutoff values at different specificity and sensitivity levels

Neuropsychological test	Optimal Cutoff Score	Diagnostic Cutoff Score	Screening Cutoff score	Specificity	Sensitivity	NPV%	PPV%	Area Under Curve*
Story Memory Test IR	8			0.846	0.756	77.6	83.1	0.909 (0.841–0.942)
		7		1.00	0.536	68.3	100	
			13	0.153	1.00	100	54.1	
Story Memory Test DR	7			0.889	0.829	83.9	88.2	0.949 (0.891–0.99)
		6		1.00	0.68	75.8	100	
			10	0.44	1.00	100	64.1	
Stick Construction	23			0.926	0.659	73.1	89.9	0.78 (0.685–0.878)
		16		1.00	0.171	54.7	100	
			23	0.926	0.658	73	89.9	
Stick Construction DR	12			0.704	0.707	70.6	70.5	0.802 (0.686–0.918)
		4		0.962	0.170	53.7	81.7	
			18	0.555	0.951	91.9	68.1	
Digit Forward	6			0.741	0.756	75.2	74.5	0.805 (0.688–0.923)
		2		1.00	0.048	51.2	100	
			8	0.444	1.00	100	64.3	
Picture cancellation (Total Cancelled)	112			0.778	0.537	62.7	70.8	0.67 (0.545–0.795)
		103		1.00	0.048	51.2	100	
			114	0.333	0.756	57.7	53.1	
Picture cancellation Time taken	2.55			0.667	0.732	71.3	68.7	0.763 (0.638–0.881)
		5.57		1.00	0.024	50.6	100	
			2.17	0.370	1.00	100	61.3	
Verbal Fluency Fruits	10			0.577	0.805	74.7	65.6	0.715 (0.585–0.84)
		6		1.00	0.122	53.2	100	
			12	0.15	1.00	100	54.1	
Verbal Fluency Vegetables	11			0.692	0.780	75.9	71.7	0.836 (0.728–0.945)
		5		0.962	0.170	53.7	81.7	
			21	0.038	1.00	100	51	
Word List Learning Trial 1	5			0.630	0.683	66.5	64.9	0.766 (0.641–0.884
		1		1.00	0.048	51.2	100	
			9	0.037	1.00	100	50.9	
Word List Learning Trial 3	8			0.704	0.854	82.8	74.3	0.84 (0.738–0.941
		3		1.00	0.024	50.6	100	
			9	0.444	0.975	94.7	0.637	
Word List Learning Total Learning	20			0.815	0.829	82.7	81.8	0.843 (0.736–0.951)
		12	26	1.00	0.24	56.8	100	
				0.111	1.00	100	52.9	
Word List Learning Recognition Hits	9			0.778	0.683	71.1	75.5	0.722 (0.652–0.864)
		8		0.963	0.439	63.2	92.2	
			9	0.778	0.683	71.1	75.5	
Go/No-Go Test	16			0.815	0.659	70.5	78.1	0.767 (0.642–0.854)
		5		1.00	0.024	50.6	100	
			16	0.815	0.659	70.5	78.1	
Total score (Composite average z-score)	−0.027			0.926	0.732	77.6	90.8	0.878 (0.794–0.962)
		−0.68		1.000	0.219	56.1	100	
			0.585	0.407	1.000	100	62.8	

*Area under curve, 0.7–0.8=Acceptable, 0.8–0.9=Excellent, >0.9=Outstanding. Optimal cutoff was the intersection value of sensitivity and specificity. Screening cutoff was obtained by taking value having >80% sensitivity and negative predictive value (NPV) while diagnostic cutoff is obtained by taking value having >80% specificity and positive predictive value

confounders. After *post hoc* Bonferroni adjustments for multiple comparisons, all the subtest variables which had a significant difference between patients and controls in univariate analysis were found to have a statistical significance except for Word List Learning Trial 2 and Word List Delayed Recall.

Diagnosis of MCI using MDS task force cutoff criteria

For each neuropsychological test, z-scores were calculated from the mean and standard deviation. We tested the differences in cognitive impairments using different cutoff scores of -1 SD, -1.5 SD, and -2 SD below the z-scores for each test.

Patients with impairment of two tests per domain or one test each in two different domains were considered as mild cognitive impairment as per the task force criteria. PD patients who have scored within 1 SD are considered normal. According to Level 2 MDS PD-MCI criteria, three MCI groups were determined. MCI-1SD which includes patients with 1 SD below the normative value (70.9%); MCI 1.5 SD was determined by taking 1.5 SD below normative values (41.9%) and MCI-2 SD was calculated by 2 SD below the normative value (25.8%). Sensitivity and specificity were calculated for each cutoff score. MCI 1 SD was found to have sensitivity (71%), specificity (80%), positive predictive value (78.6%), and negative predictive value (73.5%), while with MCI-1.5 SD, NNB-E had sensitivity (41.9%), specificity (93.5%), positive predictive value (86.7%), and negative predictive value (61.7%). Further with MCI-2 SD, the accuracy of NNB-E was sensitivity (25.8%), specificity (100%), positive predictive value (100%), and negative predictive value (57.4%). In addition, cognitive impairment was determined by the AUC of the composite average of the calculated z-score. NNB-E was able to detect MCI in 74.1% of patients and 6.4% of controls. We found 92.6% specificity and 73.2% sensitivity calculated by AUC. For -1 SD, -1.5 SD, -2SD cutoff scores, and cognitive deficits in various domains were represented in Table 4a and 4b.

Discussion

Our study revealed that NNB-E was able to differentiate cognitive impairments between PD patients and controls. It was proven to be an effective battery for distinguishing cognitive deficits between Alzheimer's patients and healthy older adults.[6]

Various neuropsychological batteries were recommended for use in PD patients for global cognitive assessment such as Montreal Cognitive Assessment, the Mattis Dementia Rating Scale 2, and the Parkinson's Disease-Cognitive Rating Scale.[15] MMSE and Montreal cognitive assessment (MoCA) battery are the most used screening tools for dementia in PD patients. However, MMSE has its demerits in its inability to test all cognitive domains. MoCA is a comparatively better screening tool than MMSE in PD MCI.[16] For level II assessments, comprehensive batteries such as International Parkinson and Movement Disorder Society (MDS) neuropsychological battery (NB) and The Consortium to Establish a Registry for Alzheimer's disease (CERAD) neuropsychological battery were used.[17,18]

NNB-E (level II assessment) established a satisfactory discriminative power to diagnose MCI in PD. Of all the subtests, Story Memory Test Delayed Recall was observed to be the most accurate test to differentiate between PD MCI patients and healthy controls. Other subtests that reached an adequate discriminability to diagnose MCI in PD patients were Story memory test immediate recall, Word list total learning, Word list Learning Trial 3, Verbal fluency vegetables, Digit Forward, Stick construction Delayed recall followed by stick construction, go no go test, word list trial 1, picture cancellation time taken, and verbal fluency fruits. Previous studies validated other neuropsychological batteries, and the AUC of these batteries was comparable to the present study. AUC obtained by using the average composite z-score for NNB-E was 0.878 in the current research, while in other studies, PD had shown an AUC of 0.913 for MoCA and 0.733 for fluid object memory evaluation.[19] Another study reported an AUC of 0.75 for MoCA, MMSE, and ACE-R in PD patients. AUC was 0.71 for MoCA, 0.72 for SCOPA-Cog, and 0.68 for MMSE in a study conducted by Marras *et al.*[20] AUC for Mattis dementia rating scale 2 in a study conducted by Matteau *et al*. was 0.82 with a sensitivity and specificity of 0.86 and 0.54 at optimal cutoff while that of CERAD battery was 0.989.[17,21]

PCFA was done to lower the redundancy of the neuropsychological subtests. We derived factor structures. The first 2 factors had most of the factor loadings and had multiple cognitive domains supporting the predominant multi-domain nature of the PD-MCI. Memory domain is loaded on more than one factor (factors 1, 2, 3, and 6). This may be due to attention deficits seen in the majority of the PD patients, which may influence posterior-mediated cognitive functions leading to memory deficits. A study by Cholerton *et al*. yielded seven factors and a variance of 72%.[22]

Table 4a: The frequency of amnestic and non-amnestic domains in PD with MCI

	PD MCI total	Amnestic Single domain (%)	Amnestic Multiple domains (%)	Non amnestic single domain (%)	Non amnestic multiple domain (%)
z < −1 SD	22	4.5	54.5	9.09	50
z < −1.5 SD	13	23.07	15.38	23.07	61.5
z < −2 SD	8	0	25	25	37.5

Table 4b: The frequency of cognitive domains in PD with MCI

Two tests in each domain	PD MCI total	Attention deficits (%)	Execution deficits (%)	Memory deficits (%)	Visuospatial deficit (%)	Language deficit (%)
z < −1 SD	22	27	36	18	18	9
z < −1.5 SD	13	23.07	23.07	7.6	7.6	0
z < −2 SD	8	12.5	12.5	0	12.5	0

We found MCI in 25.8%, 41.9%, and 70.9% of the PD patients in the current study as per level II criteria taking cutoff values below -1 SD, -1.5 SD, and -2 SD. AUC composite average optimal cutoff diagnosed MCI in 74.2% of PD patients with a specificity of 92.6% and sensitivity of 73.2%. In previous neuropsychological validation studies of MDS task force PD-MCI criteria, the prevalence of PD-MCI ranged from 33% to 62%.[23,24] Scarfone *et al*. showed that 9.9% of patients were in the MCI group when cutoff value was below 2 SD while 92.1% of patients were in the MCI group when liberal cutoff of below 1 SD was considered.[25]

Sensitivity and specificity of 81.3% and 85.7% were found in a study with the usage of a 10-test battery for diagnosing PD-MCI by level II criteria at cutoff below -2 SD.[5] In our study, the sensitivity and specificity were highest with AUC optimal cutoff and at below -1 SD. However, the sensitivity decreased when stringent cutoffs were taken.

Multiple domain impairments are more frequent compared to single domain impairments (94.5%, 84.6%, and 62.5%) in the current study. A study by Goldman *et al*. reported multiple domain impairment in 93% of PD MCI patients.[5] Approximately 93.4% had multi-domain impairment in another study.[24] This is supported by a recent Indian study, which reported predominant multi-domain MCI in PD patients.[26]

Previous studies reported executive dysfunction with deficits in other cognitive domains such as verbal, visuospatial function, and memory deficits in PD patients.[24,27] Deficits in attention/working memory and executive function were predominantly noticed in our study followed by memory and visuospatial functions. The language domain is the least affected. This finding is in acceptance by other studies.

Impairment of cognitive domains

Visuospatial Ability, Visual Learning and Memory: Visuospatial skills include several cognitive abilities such as pattern recognition, constructional ability, spatial analysis, and color recognition.[28] We tested pattern recognition (picture cancellation), constructional ability, and spatial analysis in our study. We found significant impairment of visuospatial ability, visual learning, and memory in Parkinson's patients. Previous studies have reported poor visuospatial function in PD patients. Deficits have been published on the judgment of line orientation, form discrimination, reasoning, and figure copy.[29]

Memory

Significant impairment in verbal memory was reported in our patients—word list learning and story recall IR and DR. Several studies described clearly that both verbal and non-verbal memory could be disrupted in PD patients without dementia. Impairments in both immediate and delayed story recall have been reported in patients with PD.[30–33]

Executive function and attention

The prefrontal cortex (along with the parietal lobe including the executive network) regulates a person's attention to one event and exclusion of other events and switching between the events.[34] PD patients have decreased deactivation of the cortex with a disrupted activation and deactivation pattern leading to poor performance during executive tasks. Executive functions include cognitive features such as planning, monitoring, cognitive flexibility, response inhibition, information processing, and retrieval from declarative memory.[35] Executive functions control the patient's quality of life.[36] PD patients show executive function deficits even in the early stages of the disease.[37] Elgh and colleagues reported executive function deficits in 30% of PD patients. They showed lower scores in the cognitive switch or inhibitory control in previous studies similar to the current study.[38]

Attention: In our study group, impairment was found by the tests of attention including digit span forward and Picture cancellation test (complex attention cloud also includes working memory). Few studies reported simple attention deficits.[31,32] Other studies documented deficits in complex attention in PD.[30,39,40] However, many studies failed to find deficits in simple attention in PD patients.[39,41] The impairment of complex attention is troublesome.

Acquisition/learning of information in both verbal and visual modalities along with impaired delayed recall and lower scores on recognition (Story memory, memory for the word list, and visual construction IR and visual memory DR) were observed in PD patients compared to controls in our study. The initial encoding could be due to impaired attention, as reflected by relatively lower scores on symbol cancellation in terms of both increased time and the total number of symbols canceled.

The current study is in concordance with the previous studies concerning relatively more inadequate attention in PD patients corroborated by digit span forward condition. Go/no-go test (hits and misses) indicates impaired response inhibition and lesser category fluency scores in PD patients showing relatively poorer executive functions as well.

Despite having a methodological strength, there were limitations in terms of the small sample size and nature of the study design (cross-sectional). Validation of NNB-E with the inclusion of other neuropsychological batteries for comparison could provide us with better knowledge of determining MCI at level II cognitive assessment. Future research should focus on longitudinal studies to understand the onset and progression of cognitive impairment. Consequently, studies should explore various other factors influencing cognitive impairment in PD patients such as sleep, medications, psychosis, and metabolic markers. Further studies should also focus on the combined effect of these factors in the causation of mild cognitive impairment. Although differences in the number of patients having MCI are noticed at various cutoff values, the clinician's role in correlating the scores with the clinical observations helps in setting an optimal cutoff that helps in correct diagnosis.

Conclusion

The present research concludes that NNB-E is a valid tool for assessing MCI in PD patients with a good discriminative power to differentiate between patients and controls. It also extends support to the existing MDS task force criteria in diagnosing PD MCI in the Indian population, which helps in early diagnosis and management to improve the quality of life.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Table showing Rotated Component Matrix values of the Principal component analysis

	Component						
	1	2	3	4	5	6	7
Story Memory Test IR			0.619				
Story Memory Test DR			0.604				
Stick Construction		0.631					
Stick Construction IR		0.704					
Stick Construction DR		0.641					
Digit Forward		0.653					
Digit Backward		0.643					
Corsi Block Tapping Forward		0.697					
Corsi Block Tapping Backward		0.781					
Verbal Fluency Fruits							0.727
Verbal Fluency Animals							0.554
Verbal Fluency Vegetables	0.520						
Picture Cancellation Time Taken							-0.638
Picture Cancellation Total Cancelled				0.920			
Picture Cancellation Omission				-0.913			
Picture Cancellation Commission			-0.817				
Word List Learning Trial 1	0.861						
Word List Learning Trial 2	0.813						
Word List Learning Trial 3	0.698						
Word List Learning Total Learning	0.830						
Word List Learning Delayed Recall	0.722						
Word List Learning Recognition Hits						0.807	
Word List Learning Recognition Miss						-0.768	
Go/No-Go Test Hits					0.911		
Go/No-Go Test Misses					-0.861		

Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization. a. Rotation converged in 7 iterations

Supplementary Table 2: Pearson's product–moment correlation (Component—global score correlation NNB-E)

Variable	Patient ($n=31$)		Control ($n=31$)		PD and controls (62)	
	r	*P*	*r*	*P*	*r*	*P*
Story Memory Test–IR	0.581	<0.001*	0.524	0.00602	0.738	<0.001*
Story Memory Test–DR	0.588	<0.001*	0.73	<0.001*	0.787	<0.001*
Stick Construction	0.64	<0.001*	0.451	0.0181	0.664	<0.001*
Stick Construction–IR	0.753	<0.001*	0.796	<0.001*	0.718	<0.001*
Stick Construction–DR	0.747	<0.001*	0.73	<0.001*	0.805	<0.001*
Digit Forward	0.594	<0.001*	0.379	0.0512	0.652	<0.001*
Digit Backward	0.526	<0.001*	0.649	<0.001*	0.614	<0.001*
Corsi Block Tapping Forward	0.693	<0.001*	0.595	<0.001*	0.613	<0.001*
Corsi Block Tapping Backward	0.624	<0.001*	0.583	<0.001*	0.586	<0.001*
Verbal Fluency Animals	0.605	<0.001*	0.235	0.248	0.476	<0.001*
Verbal Fluency Fruits	0.177	0.267	0.518	<0.001*	0.468	<0.001*
Verbal Fluency Vegetables	0.419	<0.001*	0.454	0.0198	0.606	<0.001*
Attention Trial Time Taken	−0.259	0.102	−0.22	0.271	−0.413	<0.001*
Attention Trial Total Cancelled	0.522	<0.001*	0.34	0.0827	0.555	<0.001*
Word List Learning Trial 1	0.63	<0.001*	0.492	<0.001*	0.646	<0.001*
Word List Learning Trial 2	0.716	<0.001*	0.624	<0.001*	0.723	<0.001*
Word List Learning Trial 3	0.769	<0.001*	0.594	<0.001*	0.804	<0.001*
Word List Learning Total Learning	0.752	<0.001*	0.692	<0.001*	0.808	<0.001*
Word List Learning Delayed Recall	0.661	<0.001*	0.574	<0.001*	0.676	<0.001*
Word List Learning Recognition Hits	0.587	<0.001*	0.464	0.0148	0.637	<0.001*
Word List Learning Recognition Miss	−0.545	<0.001*	−0.464	0.0148	−0.636	<0.001*
Go/No-Go Test Hits	0.567	<0.001*	−0.0637	0.752	0.491	<0.001*
Go/No-Go Test Misses	−0.57	<0.001*	−0.338	0.0843	−0.599	<0.001*

*The value is significant