Original Article

Neuropsychological markers of mild cognitive impairment: A clinic based study from urban India

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Abstract

Background: Mild cognitive impairment (MCI) is a transitional stage between normal aging and dementia. Persons with MCI are at higher risk to develop dementia. Identifying MCI from normal aging has become a priority area of research. Neuropsychological assessment could help to identify these high risk individuals. **Objective:** To examine clinical utility and diagnostic accuracy of neuropsychological measures in identifying MCI. **Materials and Methods:** This is a cross-sectional study of 42 participants (22 patients with MCI and 20 normal controls [NC]) between the age of 60 and 80 years. All participants were screened for dementia and later a detailed neuropsychological assessment was carried out. **Results:** Persons with MCI performed significantly poorer than NC on word list (immediate and delayed recall), story recall test, stick construction delayed recall, fluency and Go/No-Go test. Measures of episodic memory especially word list delayed recall had the highest discriminating power compared with measures of semantic memory and executive functioning. **Conclusion:** Word list learning with delayed recall component is a possible candidate for detecting MCI from normal aging.

Key Words

Cognitive marker, cognitive test, memory assessment, mild cognitive impairment

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Ann Indian Acad Neurol 2015;18:177-180

Introduction

Mild cognitive impairment (MCI) is a transitional stage between normal aging and dementia and represents an early stage of Alzheimer's disease (AD).[1,2] Common characteristic of MCI is memory impairment beyond what is considered as normal for that particular age but with other relatively intact cognitive domains.[3,4] The diagnostic criteria for MCI includes memory complaint, abnormal memory function as compared to what is expected based on age and education, preserved general cognitive function, intact activities of daily living and absence of dementia.[5]

Mild cognitive impairment is linked with an increased risk for developing AD.[4,5] Currently there is no proven treatment for persons with dementia. Hence identification of this preclinical stage of dementia namely MCI has become a priority area in dementia research. Neuropsychological assessment has proven sensitive in discriminating between normal aging and mild cognitive impairment.[6,7]

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.150566

To the best of our knowledge, there is paucity of standardized indigenous neuropsychological measures for older Indian adults. However, attempts have been made to adapt screening instruments for Indian population such as Hindi Mental State Examination,[8] and Addenbrooke's Cognitive Examination.[9] Notwithstanding these tests are screening measures and involve rather easy items which may not be sensitive for differentiating between normal aging and MCI. Ganguli *et al*., (1996) adapted "Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological Battery (CERAD-NB) for low educated Indian participants.[10] Ganguli and colleagues modified the original CERAD-NB, and eliminated and simplified several tests to suit illiterate participants. The Indian adaptation of CERAD-NB includes measures of memory and construction and could not assess several important cognitive functions like attention, working memory and executive functioning. However, despite its limitation it has been used to assess cognitive function of urban elderly people[11] and to estimate the prevalence of MCI.[12]

Recently, NIMHANS Neuropsychological Battery for the Elderly (NNB-E) has been developed and standardized for older Indian adults.[13] The clinical utility of the NNB-E for

Alzheimer dementia has been published in the recent times elsewhere.[14] The main objective of the present study was to examine usefulness of NNB-E in discriminating MCI. We were also interested in examining diagnostic accuracy/validity of different neuropsychological measures in identifying MCI.

Materials and Methods

The study sample consisted of 42 participants (22 patients with MCI and 20 normal controls [NC]) between the age range of 60 and 80 years. The two groups (MCI and NC) were matched for age and education. Patients with MCI were selected from the outpatient department of the Geriatric Services & Clinic, NIMHANS, Bangalore. All patients with MCI met the Petersen criteria[5] for MCI with clinical dementia rating (CDR) of 0.5.[15] Willing NC participants living independently in terms of their daily activities were recruited as controls. Participants were excluded if they had history of neurological/neurosurgical/psychiatric illness. A written informed consent was taken from the all participant before starting the assessment. The study was initiated after approval form ethics committee from the institute.

All participants initially were screened with Hindi Mental Status Examination and Every Day Abilities Scale for India. Later they were assessed in detail with the neuropsychological battery (NNB-E).

Hindi mental-status examination (HMSE)

Hindi mental-status examination[8] is a modified version of MMSE and is validated for Indian population. In this study, we used HMSE as a global cognitive screen.

Everyday abilities scale for India (EASI)

This is a 12-item brief measure of activities of daily living,[16] with norms, and is appropriate for use in evaluating dementia (along with other tests) in elderly people in India. This scale was used to detect difficulty in activities of daily living.

NNB-E

This is a brief, comprehensive and standardized neuropsychological battery,[13,14] developed for older Indian adults. The tests are described here briefly. Episodic memory was assessed with word list and story recall test assessing immediate and delayed recall. Attention was assessed by Span task and Picture cancellation task. Constructional ability was assessed with Stick construction test. Executive functions were assessed with Digit span, Corsi block-tapping test, fluency and Go/No-Go task and Tower of Hanoi. Language abilities were assessed by picture naming test and semantic verbal fluency test.

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS 12.0). Two-tailed Student's *t* test was used to examine statistical differences between MCI and NC on each neuropsychological test variables. The T test was used to examine homogeneity of the groups for age, education and the chi square was used for gender. Receiver operating characteristics (ROC) curve analysis was used to examine diagnostic accuracy of each test.

Results

The demographic characteristics of MCI and NC are presented in Table 1. There were no significant differences between the groups in terms of years of education, age and gender ratio. All participants with MCI were fully independent for their instrumental activities for daily life.

The neuropsychological performances of the two groups are presented in Table 2. Participants with MCI performed significantly lower than NC on memory and non-memory domains of cognition. The MCI group scored significantly lower on word list immediate recall (t = 3.20, *P* =.003), word list delayed recall (t = 7.11, *P* < .001), story recall test immediate recall (t = 3.70, *P* = 0.001), story recall test delayed recall (t = 5.05, *P* < .001), fluency for animals (t = 2.51, *P* = 0.016), Go/No-Go (t = 2.16, *P = 0*.043) and stick construction test delayed recall (t = 3.79, *P* = 0.001*)*.

Table 1: Demographic characteristics of the sample

	MCI	NC	*P* value
Age Mean years (SD)	68.18 (5.70)	68.65 (6.00)	.80
Education Mean years (SD)	13.60 (3.87)	13.75 (3.30)	.88
Gender (Male)	16	15	
HMSE Mean (SD)	28.00 (2.37)	30.00 (1.00)	.01
EASI Mean	0.00	0.00	.09

Table 2: Comparison of performance between MCI and NC group

Test variable (s)	MCI	NC	*P* value
Story Recall Test (IR)	8.65 (3.09)	11.70 (2.00)	.001
Story Recall Test (DR)	6.50 (3.75)	11.47 (2.49)	.000
Digit Span (F)	5.36 (1.00)	5.85 (1.34)	.48
Digit Span (R)	3.95 (1.04)	4.05 (1.14)	.09
Corsi block-tapping test (F)	5.14 (1.06)	5.50 (1.00)	.22
Corsi block-tapping test (R)	4.14 (1.15)	4.75 (1.11)	.09
Fluency (F)	9.77 (3.29)	11.75 (3.55)	.07
Fluency (A)	12.13 (4.60)	15.20 (3.23)	.016
Fluency (V)	9.90 (4.08)	13.15 (2.92)	.006
Word List (L_1)	4.04 (1.36)	5.00 (1.89)	.095
Word List (L_2)	5.54 (1.10)	7.05 (1.74)	.002
Word List (L_3)	6.18 (1.60)	7.84 (1.42)	.001
Word List (DR)	2.77 (1.63)	6.52 (1.74)	.000
Word List (Rec)	8.86 (1.90)	9.73 (1.00)	.06
Go/No-Go	1.19 (2.40)	.05 (0.22)	.043
Attention (Total Time)	234.00 (136.56)	167.00 (25.47)	.063
Tower of Hanoi (Move^1)	3.15 (0.48)	3.00 (0.00)	.190
Tower of Hanoi (Move^2)	14.40 (8.55)	11.70 (5.39)	.288
Tower of Hanoi (Move^3)	25.41 (10.80)	26.84 (10.22)	.737
Tower of Hanoi (Time^1)	10.05 (11.18)	5.73 (1.28)	.104
Tower of Hanoi (Time^2)	87.53 (58.53)	60.00 (35.53)	.106
Tower of Hanoi (Time^3)	165.33 (114.95)	118.23 (66.11)	.217
Stick Construction (IR)	20.31 (5.70)	22.78 (4.36)	.132
Stick Construction (DR)	8.22 (7.18)	15.91 (5.61)	.001

Constant score — Stick Construction copy, agnosia, apraxia, calculation

The area under the ROC curve (AUC) indicates how well any particular test discriminates between individuals with MCI and controls. A straight line (area = 0.5) indicates that a test is doing no better than chance in classifying dementia and control group, while a perfect scale would have a ROC curve with an area of 1. Receiver operating characteristics curve analyses revealed that Word list delayed recall had the highest AUC (96%) followed by Story memory delayed recall (84%). Word list delayed recall had better discriminatory power in terms of sensitivity and specificity [Figure 1 and Table 3].

Discussion

The main finding of the present study is that patients with MCI performed poorly on episodic memory, semantic memory and executive functioning. In the present study, we were able to demonstrate that NNB-E could discriminate between MCI and NC. Recent studies suggest that patients with MCI show deficits in multiple domains including memory,[17,18] semantic memory[19-21] and executive functioning.[17,22,23] This study also confirmed that patients with MCI have deficits in several domains including memory. Consistent with our observation, in the last decade, MCI is considered a heterogeneous group and therefore construct of MCI has expanded to include impairments in other cognitive domains.[4,5] MCI is divided into two subtypes: Amnestic MCI (single/multiple) and non-amnestic MCI (single/multiple). In our study, all participants met the criteria of amnestic MCI. It has been argued that participants with amnestic MCI are likely to develop AD and represents an early stage of AD.[1] The patients with MCI in this study need to be followed up to confirm it.

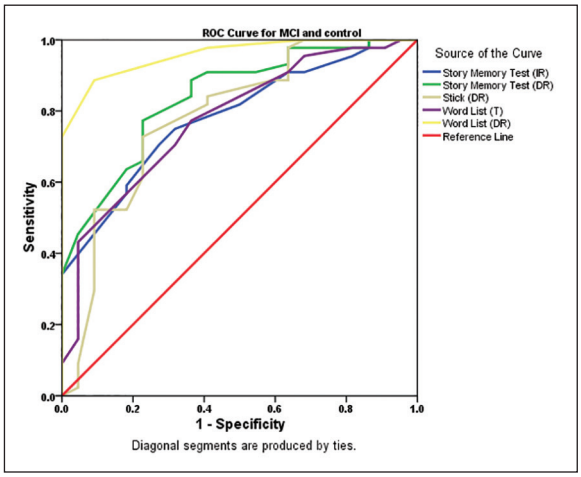

Figure 1: ROC curves of normal *vs* MCI

Our results indicate that the delayed recall on the Word list had the highest diagnostic accuracy in terms of sensitivity and specificity for discriminating between MCI cases and controls. Story recall test and Stick construction delayed recall had lesser discriminatory capacity (sensitivity and specificity). The results from the present study are consistent with other studies from West, indicating that measures of delayed recall were considerably more effective for detecting MCI than were measures of non-memory domains such as semantic fluency, executive functions or construction.[6,7, 24]

In our study, Word list was more sensitive than the other test of verbal learning and memory (Story recall test). These findings are consistent with the previous research, which indicates that Word list paradigm is more useful for examining verbal memory function compared with the story recall test.[10,25,26] It is well known that Word list involves several learning trials, which could result in better encoding and recall whereas story recall test involves a single learning trial that requires more active and effortful processing.[26] Therefore, better performance on story recall depends on several factors including executive functioning, processing speed and education.[25-27] Further research is needed to understand the role of executive functions and demographic variables clearly as well as their interactions in influencing performance on verbal learning measures.

Neuropsychological assessment is considered as gold standard tools for MCI. There are few culturally valid neuropsychological measures in India and none of the test has been validated for MCI. Based on our findings we suggest that NNB could be used as a sensitive tool for MCI.

There are several limitations of the present study. Our MCI sample was very small and future research is required on a larger sample to confirm the findings. We could have compared performance on NNB-E with other existing cognitive tests. However, there was lack of similar indigenous measure for older Indian participants. In our study, all participants met the criteria for amnestic MCI. Hence findings of the present study could not be generalized to non-amnestic MCI. Usefulness of NNB-E for other MCI groups should be examined in future research.

In conclusion, this is the first Indian study, which examined diagnostic accuracy of different neuropsychological measures using participants with MCI. We found that participants with MCI showed deficits in memory and executive functioning. However, measures of episodic memory and word list more specifically emerged as sensitive tool to identify MCI and could be potential cognitive marker for MCI.

Table 3: Area Under the Curve for NC and MCI

Test Result Variable(s)	AUC	Std. Error	*P* value	Cut-off	Sensitivity	Specificity
Word List (Delayed Recall)	.958	.021	.000	4	0.88	0.91
Story Recall Test (Delayed Recall)	.842	.049	.000	9	0.77	0.78
Story Recall Test (Immediate Recall)	.782	.056	.000	10	0.75	0.69
Word List Learning (Total)	.779	.059	.000	17	0.71	0.69
Sick Construction (Delayed Recall)	.770	.065	.000	11	0.71	0.78

AUC = Area under the curve

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How to cite this article: Tripathi R, Kumar K, Balachandar R, Marimuthu P, Varghese M, Bharath S. Neuropsychological markers of mild cognitive impairment: A clinic based study from urban India. Ann Indian Acad Neurol 2015;18:177-80.

Received: 12-02-14, **Revised:** 09-03-14, **Accepted:** 08-05-14

Source of Support: Nil, **Conflict of Interest:** None declared.