Quick screening of cognitive function in Indian multiple sclerosis patients using Montreal cognitive assessment test-short version

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Abstract

Background: Cognitive impairments in multiple sclerosis (MS) are now well recognized worldwide, but unfortunately this domain has been less explored in India due to many undermining factors. The aim of this study was to evaluate cognitive impairments in Indian MS patients with visual or upper limb motor problems with the help of short version of Montreal cognitive assessment test (MoCA). **Subjects and Methods:** Thirty MS patients and 50 matched controls were recruited for the 12 points MoCA task. Receiver operating characteristic curve (ROC) analysis was performed to determine optimal sensitivity and specificity of the 12 points MoCA in differentiating cognitively impaired patients and controls. **Results:** The mean 12 points MoCA scores of the controls and MS patients were 11.56 ± 0.67 and 8.06 ± 1.99, respectively. In our study, the optimal cut-off value for 12 points MoCA to be able to differentiate patients with cognitive impairments from controls is 10/12. Accordingly, 73.3% patients fell below the cut off value. Both the groups did not have significant statistical differences with regard to age and educational years. **Conclusion:** The 12 points, short version of MoCA, is a useful brief screening tool for quick and early detection of mild cognitive impairments in subjects with MS. It can be administered to patients having visual and motor problems. It is of potential use by primary care physicians, nurses, and other allied health professionals who need a quick screening test. No formal training for administration is required. Financial and time constraints should not limit the use of the proposed instrument.

Key Words

Cognitive impairments, Indian, montreal cognitive assessment test, multiple sclerosis

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Introduction

We undertook this pilot study in response to clinical problems encountered during rehabilitation sessions with our multiple sclerosis (MS) patients in India. Most of the MS patients reported lack of concentration, difficulty to pace with their activities of daily living, and difficulty in remembering simple instructions; leading to increasing anxiety and depression among them. Also, it was noted that patients had reduced compliance with exercise regime as they forgot the exercises or the sequence of doing a particular exercise. This led to inquisitiveness to understand the underlying cerebral changes due to MS. One important domain in this aspect is cognitive impairments. We hypothesized that probably what we see in our patients is just the tip of the iceberg; this problem can be more deep rooted.

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Cognitive impairments in MS are now well-recognized worldwide ranging from 40 to 60%.[1] Unfortunately, this domain has been less explored in India due to many undermining factors. Current evidence suggests that cognitive disturbances might already occur at early stages of the disease.[2] An early detection of these impairments is clinically important and can help in determining the disability few years later.[3] While patients frequently complain about attention and memory problems or a decreased ability to cope with multiple tasks, cognitive functioning in MS still receives little attention by treating physicians.[4] Cognitive impairments in MS are dominated by a slowdown in the rate of information processing and functions with attention and memory.[5]

The cognitive dysfunction results in limitations in quality of life (QOL) of the patients, regardless of the degree of physical disability.[6] Even relatively mild symptoms can have a pretty big impact on various activities of daily living. Cognitive impairments often have a deleterious impact on someone's personal, occupational, and social functioning.[7-9] Generally,

attentional disorders and slowdown of information processing speed (IPS) may cause significant discomfort in everyday life. Impairments in processing speed may contribute to impairments in activities of everyday living in persons with MS.[10] The majority of studies clearly show an association between cognitive impairment and QOL in MS patients.

India is a low middle income country and it is not surprising that India's expenditure on healthcare is also quite low. Population-based neuroepidemiologic surveys during the last 15 years have shown the prevalence rate of neurological disorders in India to vary from 967 to 4,070 per 100,000 population.[11] There is gross mismatch of the burden of neurological disorders and the availability of trained neurologists, other essential health professionals and infrastructural facilities in developing countries as in India. The current ratio is of: One neurologist for 1,250,000 and 800 neurologists for a population of more than 1 billion people.[12,13] MS is still underdiagnosed in India. The Multiple Sclerosis International Federation World MS Atlas has projected a prevalence of 3/100,000 in Indian subcontinent.[14] The calculations based on the hospital data suggest an approximate prevalence rate of 0.17-1.33 per 100,000 of population in different parts of India.[15] The remitting and relapsing type of MS is the common mode of presentation. The relapse varies from 0.09-1.0 attacks/year.[16] Early reports on MS phenotype from different parts of the country suggested high prevalence of optic and spinal cord involvement.[17] Acute onset of motor weakness was the next common initial presentation seen in 27-31% of Indian patients.[18,19] Reported prevalence of optic neuritis in various studies from India is 23.6% from the northwest[18] and 53.3%[19] from the east of the country. This is significantly high as compared to western data. In this scenario there is a need for a neuropsychological screening tests which are quick to use, easily comprehensible to patients, and can easily be administered to those with visual and/motor problem. Also, it should be inexpensive as a widespread lack of health insurance compounds the healthcare challenges that Indian patients faces.

Montreal cognitive assessment test (MoCA) is a National Institute of Neurological Diseases and Stroke and Canadian Stroke Network (NINDS-CSN) recommended test for quick screening of cognitive impairment. MoCA has been found to be reliable and sensitive test in evaluation of mild cognitive impairments[20] in stroke, MS, Alzheimer, Human immunodeficiency virus (HIV), Huntington, Parkinsonism, tremors, and epilepsy. Researchers have shown its validity in low education groups. Its modified version has been validated in blind subjects too. In a recent study by K. Waspe *et al*., modified MoCA was found to be reliable in a small cohort of 30 MS patients.[21] Lauren Krupp *et al*., showed the validity of MoCA in cognitive evaluation in MS.[22] The data is unestablished for; how will Indian MS patients perform on various standard neuropsychological tests, most of which are developed in the west. Much more information is needed pertaining to the validity of this test in longitudinal MS research, considering the multiplicity of cultures and languages.

Subjects and Methods

Patients and controls

Patients were recruited under following criteria. The inclusion 0criteria were: (1) A definite diagnosis of MS lasting >3 months as defined by Revised McDonalds 2010 criteria and (2) visual or upper limb disability due to MS. Common exclusion criteria for all subjects were: (1) Presence of coexisting medical conditions potentially affecting cognition (e.g. vitamin B12 deficiency, hypothyroidism, chronic alcoholism, and active psychiatric disorders); (2) other conditions that might affect testing (e.g., hearing impairment), and (3) patients with significant depression or other psychiatric disorders assessed by the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders were excluded from the study. Controls were relatives of the study patients, staff, or volunteers recruited from the center, matched for age and education years.

All subjects were of Indian ethnicity and studied in English medium for at least 15 years.

The study was approved by the institutional ethical committee, and written informed consent was given by each participant.

Test and study procedures

All the subjects were administered NINDS-CSN recommended 5 min 12 point MoCA (short version). This is a verbal test and does not require the patient to look into the paper or write on paper. This subtest includes a five-word immediate and delayed memory test, a six-item orientation task, and a one-letter phonemic fluency test (the letter F). Patient is given a score of 1 point on each correct response. Thus, the maximum score is of 12 points [Figure 1].

The corresponding author (DK) was responsible for training the test administrators at an investigators' meeting prior to the initiation of the study. Each training session was conducted in a small group format, with 2-5 potential testers involved. The same instructions were used for each test. There was no restriction on the professional discipline of test administrators, which ranged from research assistants, physiotherapists, and neurologists.

Statistical analysis

All statistical procedures were performed using appropriate statistical software. Demographics and neuropsychological data are compared between controls and patients using independent *t*-test. The 12 points MoCA scores were compared with age, gender, and education adjusted.

We examined the ability of the 12 points MoCA total score in differentiating cognitively impaired MS patients from controls using a receiver operating curve (ROC) analysis. We then

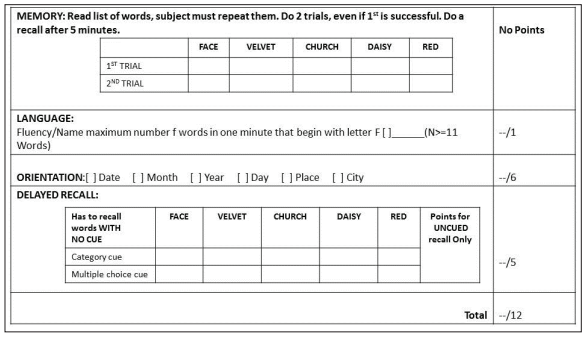

Figure 1: 12 points Montreal cognitive assessment (MoCA) test

derived a cut off score at the optimal balance of sensitivity and specificity.

Results

Characteristics of the study subjects

The study was conducted on 30 MS patients with visual/upper limb motor disability and 50 healthy controls. The mean age and duration of education for the patients group was 40.13 ± 9.54 and 15.9 ± 2.00 years, respectively. A total of 18 males and 12 females were recruited.

For healthy control group, mean age was 40.13 ± 9.54 years and they underwent 15.9 ± 2.00 years of education. This group had 28 males and 22 females.

No differences were found among groups regarding age ($P < 0.0001$), gender ($P < 0.0001$), and mean number of years of education ($P < 0.0001$). Demographic information and 12 points MoCA scores for the two groups are shown in Table 1. MS patients were correctly matched to healthy controls according to gender ($P < 0.0001$), age ($P < 0.0001$), and mean number of years of education ($P < 0.0001$).

Group performances on 12 points MoCA

The average score by MS patients on 12 points MoCA was 8.06 ± 1.99. This was lower than the mean score by healthy controls who scored 11.56 ± 0.67. For both the groups the average administration time for 12 points MoCA was <7 min.

Group differences on each subtest of 12 points MoCA

Significant differences were found between both the groups on three subtests. The MS patients scored 60% less than healthy controls in the test of language. Even in orientation testing, the MS patients scored 51.86% less and in delayed recall domain they scored 8.83% less than healthy controls. Performance of both the groups is shown in Table 2.

Cut off score determination

The cut off score for 12 point MoCA was considered at 10 (1.5 of standard deviation in healthy controls). Also around the cut off score of 10.50 there was excellent sensitivity (96.67%) and specificity (90%) for detecting patients with cognitive impairments as shown in Table 3. ROC analysis for cognitive impairments in MS patients versus healthy controls is shown in Table 4 and Figure 2. Accordingly a total of 73.33% of MS patients (30) performed less than healthy controls.

Discussion

To the best of our knowledge, this is the first study to evaluate cognitive impairments in visually impaired or MS patients having upper extremity disability and also the first study to use short version of 12 points in this category of patients. Our results show that 12 points MoCA is a good recognition tool for cognitive impairments in Indian MS patients.

Time is money. The early recognition and subsequent intervention is one of the key steps in rehabilitation of MS patients. It is a challenge to make rapid assessment and subsequent management in these patients. Thus early

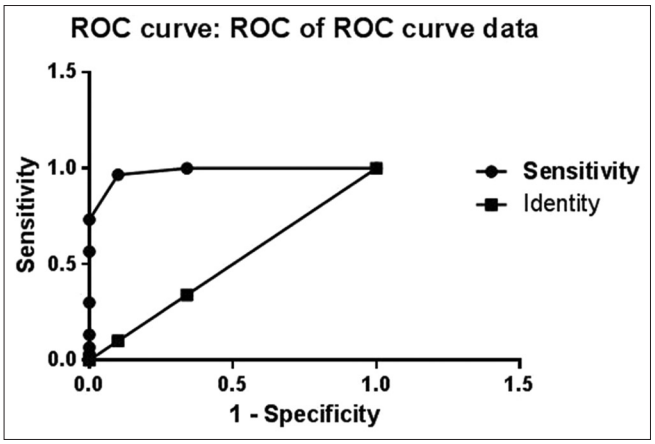

Figure 2: Receiver operating curve (ROC) curve depicting the ability of 12 points MoCA in differentiating patients with cognitive impairments from controls

Table 1: Demographic data and clinical features of the study subjects

	Controls *N*=50	MS patients *N*=30	*P* value
Age*	41.6±10.49	40.13±9.54	0.5323
Gender	28M: 22F	18M: 12F	-
MS duration*	NA	8.47±1.92	-
Education years*	16.2±2.32	15.9±2.00	0.5577
12 points MoCA*	11.56±0.67	8.06±1.99	<0.0001

*Mean±standard deviation. MoCA=Montreal cognitive assessment, M=male, F=female, MS=Multiple sclerosis, NA=???

Table 2: Comparison of performance in each subtest for 12 points MoCA

Category	30 MS patients	50 healthy controls	*P* value
Language	0.4	1	<0.001
Orientation	2.33	4.84	<0.001
Delayed recall	5.47	6	<0.001

MoCA=Montreal cognitive assessment, MS=Multiple sclerosis

Table 3: Sensitivity and specificity at various cut offs

Cut off	Sensitivity %	Specificity %
<2.500	3.333	100.0
<4.500	6.667	100.0
<6.500	13.33	100.0
<7.500	30.00	100.0
<8.500	56.67	100.0
<9.500	73.33	100.0
<10.50	96.67	90.00
<11.50	100.0	66.00

Table 4: ROC analysis for MS patients versus controls

Area under the ROC curve	
Area	0.9810
Standard error	0.01144
P value	<0.0001

ROC=Receiver operating curve, MS=Multiple sclerosis

recognition, through quick screening batteries holds a pivotal place in patients who are visually impaired/having upper extremity motor problems. Since these categories of patients are usually excluded while administering commonly used cognitive test batteries, the task of recognizing impairments in them becomes necessary.

One of the important finding of this study is the prevalence of cognitive impairments in this category of Indian MS patients. Our results extend the findings in the existing literature by providing a quantitative data on the magnitude[20,21] of cognitive problems in MS patients.

The tool used in this study is a short version of MoCA, which was recommended by NINDS-CSN for a minimum, common, clinical, and research standards for the description and study of vascular cognitive impairment.[22] Due to its simplicity, this tool can be easily used by physicians/therapists to recognize cognitive impairments.

This short version of MoCA was considered superior to mini mental state examination (MMSE) as the latter lacks efficacy to detect executive function disorders.[23] MoCA has been shown superior to MMSE by many researchers. Dong Y *et al*., showed that 30 points MoCA has more discriminatory ability than MMSE and can help in detection of patients with cognitive impairment at higher risk for incident dementia.[24] Pendlebury *et al*., in their comparative study using various neuropsychological tests, showed 1 year after transient ischemic attack and stroke, MoCA had good sensitivity and specificity; whereas the MMSE showed a ceiling effect.[25] Also the MMSE may not adequately identify neuropsychological abnormalities associated with etiologies that preferentially involve frontal or frontal-subcortical circuits.[26,27]

Current evidence suggests the similarities between subcortical vascular cognitive impairment and MS.[28] According to Schmidt *et al*., subcortical vascular cognitive impairment is caused by lacunae and widespread ischemic white matter damage which closely resembles white matter abnormalities seen in MS. Recent evidence suggests that the progression rate of ischemic white matter lesions on magnetic resonance imaging (MRI) is very similar to that observed in MS. The cognitive consequences of both diseases are strikingly similar which is at least partly caused by damage to frontal-subcortical circuits. Involvement of these common functional anatomical structures has now led to common interventional approaches. The full MoCA has been shown as an effective screening tool for screening of cognitive functions in vascular cognitive impairments.

This brief screening instrument provides an objective and cost effective means of determining the need for further evaluation of cognitive problems for Indian MS patients. Considering that all the subjects fall in high educational group, there may be a floor effect in low education group/those who are not fluent in English. This is also the first study to directly examine the cognitive impairments in Indian MS patients. Due to paucity of normative data from Indian population on various validated MS specific neuropsychological tests, this study holds an important place in highlighting the need for the same.

Our study is limited by the single center setting and use of a single cognitive test battery. There is a grave paucity of studies on validation/normalization of standard neuropsychological tests for MS in Indian population. So this pilot study was undertaken with a single tool. However, authors recommend further comparative studies with tests validated in Indian population. The 12 points MoCA can miss out on patients with mild to moderate cognitive impairments, as some of the MS specific cognitive domain testing is missing and also the local language translation may yield different results in same population.

Our data suggest that future studies of large cohorts are warranted to conduct these analyses and ensure that the 12 points MoCA has optimal psychometric properties for routine clinical use in MS. It should also be noted that our sample size was sufficient to identify significant group differences.

In summary, the present study provides information regarding the utility of the 12 points MoCA as an efficient diagnostic tool, in quick screening of cognitive impairments in MS. Further studies are needed on large cohort with local translated version of the test. Also, English proficiency can be evaluated (e.g. National Adult Reading Test), before administrating English version of cognitive tests in the population where English is not the first language. The findings by 12 points MoCA can be further substantiated with use of neuroimagery.

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