

Value of the MoCA Test as a Screening Instrument in Multiple Sclerosis

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ABSTRACT: Objective: Since a large proportion of multiple sclerosis (MS) patients exhibit cognitive deficits, it is important to have reliable and cost-effective screening measures that can be used to follow patients effectively. The objective of this study was to evaluate the clinical value of the Montreal Cognitive Assessment (MoCA) test in detecting cognitive deficits in MS patients. **Methods:** Forty-one (70.1% women, mean age 44.51 ± 7.43) mildly impaired (EDSS: 2.26 ± 1.87) MS patients were recruited for this study. In addition to the MoCA, they were administered the MSNQ-P (patient version) and the MSNQ-I (informant version), the BDI-FS and a comprehensive neuropsychological test battery. **Results:** There were significant correlations between the MoCA test and the three factors derived from the neuropsychological evaluation (Executive/speed of processing, Learning, Delayed recall). The MoCA test was correlated with the MSNQ-I but only marginally with the MSNQ-P. In addition, there was no significant correlation between the MSNQ-P and the neuropsychological factors, whereas significant correlations were found between two of those factors (Learning and Delayed recall) and the MSNQ-I, suggesting that the informant version is more reliable than the patient version for the presence of cognitive deficits. **Conclusion:** The results obtained in the present study support the value of the MoCA test as a screening tool for the presence of cognitive dysfunction in MS patients, even in patients with mild functional disability (EDSS).

RÉSUMÉ: Valeur du test MoCA comme instrument de dépistage dans la sclérose en plaques. Objectif : Étant donné qu'une grande proportion des patients atteints de sclérose en plaques (SP) présentent des déficits cognitifs, il est important d'utiliser des mesures de dépistage fiables et économiques pour suivre ces patients efficacement. Le but de cette étude était d'évaluer la valeur clinique du MoCA pour détecter un déficit cognitif chez les patients atteints de SP. **Méthode :** Quarante et un patients atteints de SP avec déficit cognitif léger, dont 70,1% étaient des femmes et dont l'âge moyen était de $44,51 \pm 7,43$ ans, ont été inclus dans l'étude. En plus du MoCA, le MSNQ-P (version patient) et le MSNQ-I (version informateur), le BDI-FS et une batterie de tests neuropsychologiques ont été administrés aux patients. **Résultats :** Nous avons noté une corrélation significative entre le test MoCA et les trois facteurs dérivés de l'évaluation neuropsychologique (les fonctions exécutives/la vitesse du traitement de l'information, l'apprentissage, le rappel différé). Le MoCa était corrélé au MSNQ-I, mais seulement de façon marginale au MSNQ-P. De plus, il n'y avait pas de corrélation significative entre le MSNQ-P et les facteurs neuropsychologiques, alors que des corrélations significatives étaient présentes entre deux de ces facteurs (l'apprentissage et le rappel différé) et le MSNQ-I, ce qui suggère que la version informateur est plus fiable que la version patient en ce qui a trait à la présence de déficits cognitifs. **Conclusion :** Selon les résultats de cette étude, le test MoCA est un outil de dépistage utile pour mettre en évidence la présence d'une dysfonction cognitive chez les patients atteints de SP, même chez ceux qui présentent une invalidité fonctionnelle légère (EDSS).

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More than half of patients with multiple sclerosis (MS) exhibit cognitive deficits that mainly affect long-term memory, working memory, speed of information processing, attention and executive functions¹⁻⁵. Those deficits have a direct impact on MS patients' employment status and quality of life⁶. Screening for such cognitive deficits is necessary to follow patients effectively. Therefore, there is an important need for reliable and cost-effective screening tests in clinical practice.

Among the measures currently available for this purpose, the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ) appears reliable to detect cognitive impairment⁷. This is particularly true for the MSNQ that is completed by an informant (MSNQ-I)⁷⁻¹⁰, since a high score on the MSNQ completed by the patient (MSNQ-P) correlates more with the score on the Beck Depression Inventory – Fast Screen (BDI-FS)¹¹, a measure of depression, than with objective measure of cognitive functions¹². Reliability to detect cognitive deficits seems compromised when the patient presents with depressive

affect⁷. Moreover, as this is a self-reported measure, the MSNQ-P allows only subjective assessment of cognitive functioning of the patient. However, it was shown that subjective perception of patients towards their cognitive skills is not always accurate, especially when they have moderate to severe cognitive impairment¹³.

It therefore seems important to perform testing using objective measures such as the Montreal Cognitive Assessment

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(MoCA)¹⁴ or the Mini-Mental State Exam (MMSE)¹⁵ which are frequently used to screen for mild cognitive impairment (MCI) in the elderly. In this population, the MoCA is known for its high specificity and sensitivity for distinguishing MCI from Alzheimer's disease (AD)^{14,16}. Conversely, the MMSE appears to be less sensitive to cognitive impairment in the elderly, possibly also in MS patients, because this measure does not include the attentional and executive functions which are areas most commonly affected by these conditions^{8,17}. Thus, whereas the MoCA seems to be a promising avenue as a cognitive screening measure in MS, it remains to be examined. To our knowledge, no studies have been conducted to assess the value of this test within this population.

The objective of this study is to evaluate the clinical value of the MoCA in detecting cognitive deficits in MS patients. Results of the MoCA will be examined in relation to the scores obtained in a comprehensive neuropsychological assessment. In addition, scores on the MoCA will also be analyzed as a function of the scores obtained on the MSNQ to determine the consistency of findings obtained by objective (MoCA) and subjective (MSNQ) screening measures. It is expected that scores on the MoCA will be consistent with those obtained in the neuropsychological assessment, that is, patients with cognitive deficits will show lower scores on the MoCA. Moreover, it is expected that MoCA scores will show a higher correlation with MSNQ-I than with MSNQ-P, the former being more reliable to assess the presence of cognitive impairment in MS patients.

METHODS

Participants

Forty-one patients with MS were recruited from the Multiple Sclerosis Clinic of Notre-Dame Hospital (CHUM). This study was approved by CHUM ethics committee and all patients signed an informed consent form. The demographic data and disease characteristics are presented in Table 1.

To be included in the project, patients had to meet the following criteria: (1) be suffering from multiple sclerosis (relapsing-remitting or secondary progressive) according to 2005 Revisions to the McDonald Diagnostic Criteria¹⁸; (2) aged between 18 and 55 years; (3) have French as their first language, or be fluent in that language; (4) have completed at least a high school degree; (5) be able to provide informed consent; (6) medications, such as stimulants (Modafinil, methylphenidate, Amantadine), acetylcholinesterase inhibitors, antidepressants with stimulant effects, benzodiazepines (regular use), were tolerated as long as the prescribed dose had been stable for at least one month prior to the study. Patients were excluded from the study if they had: (1) a history of neurological disorders other than MS, psychiatric or other serious medical conditions that may affect the neuropsychological performance (eg, traumatic brain injury, stroke); (2) a BDI-FS score greater than 4, indicating possible depression¹; (3) a score on the EDSS (Expanded Disability Status Scale) greater than 7.5; (4) a history of developmental disorders (eg, ADD / ADHD, learning disabilities); (5) a history of alcohol or drug abuse; (6) sensory

or motor deficits that may interfere with neuropsychological assessment; (7) experienced a MS relapse in the month prior to enrollment, or between screening and neuropsychological testing; (8) use of corticosteroids during the last 30 days, or use of analgesics which could interfere with cognitive performance.

Procedures

All evaluations took place at the Notre-Dame Hospital (CHUM). Patients were recruited from the MS Clinic during follow-up visits with their neurologist. All patients complaining of memory problems were referred to a research assistant. If they met inclusion criteria, the study was explained to them and written consent was obtained for participation. The MoCA test was then administered and the BDI-FS was completed during this assessment to screen for depression. If all inclusion and exclusion criteria were met, patients were scheduled for a comprehensive neuropsychological evaluation with a neuropsychologist. Patients were handed questionnaires to be completed at home and brought back at the time of neuropsychological assessment.

On the day of the neuropsychological assessment, the patient met with the research assistant who reviewed all questionnaires to ensure completion. The Timed 25-Foot Walk Test was performed and patients were asked to complete the MSNQ-P

Table 1: Participants demographic data and disease characteristics

	MS Patients
Gender	
Women : N (%)	29 (70.1%)
Men : N (%)	12 (29.9%)
Age	
M (SD)	44.51 (7.43)
Education	
High School (12th grade); N (%)	12 (29.3%)
College: N (%)	8 (19.5%)
University: N (%)	21 (51.2%)
EDSS	
M (SD)*	2.26 (1.87)
MS Course	
Relapsing-remitting: N (%)	35 (85.4%)
Secondary Progressive: N (%)	6 (14.6%)
Disease Duration (years)	
M (SD)	13.49 (6.79)
Delay since last relapse (years)	
M (SD)	2.84 (2.69)
Treatment	
Immunosuppressant : N (%)	33 (80.5%)
Untreated : N (%)	8 (19.5%)

*Mean score with standard deviations in parenthesis; EDSS=Expanded Disability Status Scale; N=number of patients; SD=standard deviation

¹Four out of 41 patients had a BDI-FS score above 4. Following a clinical diagnostic assessment, they were found not to be depressed and were included in the study.

(self) questionnaire and have a close family member or friend complete the MSNQ-I (informant) questionnaire.

The neuropsychological evaluation was administered in the morning. Cognitive tests were divided into two blocks and the order of administration was counterbalanced among the participants who were randomly assigned to each block. The order of motor testing (Purdue and 9-holes) was also reversed for half the subjects in order to reduce the effect of practice and fatigue.

Measures

Screening tests and questionnaires

Two measures commonly used as screening tests for cognitive deficits were examined: the MSNQ and the MoCA. The MSNQ was completed by the patient (MSNQ-P) and by one of his relatives (MSNQ-I). The MoCA test is a paper-and-pencil test freely available on the web for clinical and research purposes (www.mocatest.org) that can be administered in less than ten minutes (min) by health professionals and by trained non-medical personal. Questionnaires assessing the patient's psychological state (anxiety, depression, and fatigue), health status or functioning at work were also handed. These included the Work Role Functioning Questionnaire (WRFQ)¹⁹, the Modified Fatigue Impact Scale (MFIS)²⁰, the Pittsburgh Sleep Quality Index (PSQI)²¹, the Epworth Sleepiness Scale²², the Hospital Anxiety and Depression Scale (HADS)²³ and the SF-36 Health survey questionnaire.

Neuropsychological tests

Our neuropsychological test battery included tests most often used in the assessment of MS patients²⁴⁻²⁶. Detailed descriptions of those tests can be found in Lezak et al²⁷. Perceptual and visuo-constructional functions were evaluated using Benton Judgment of Line Orientation and copy of the Rey-Osterrieth Complex Figure (ROCF). Verbal memory was assessed with the Rey Auditory Verbal Learning Test (RAVLT) and two subtests of the Wechsler Memory Scale-III (logical stories and paired associates) while the ROCF immediate recall and delayed recall, the Brief Visual Memory Test (BVM-T-R) and the 10/36 Spatial Recall Test were used as measures of visuospatial memory. Speed of information processing was assessed using the Conners Continuous Performance Test (CPT-II), the Symbol Digit Modalities Test (SDMT), and the Paced Auditory Serial Addition Test (PASAT). Executive functions were measured by the Trail Making Test (lines A and B), the verbal fluency task (phonemic: P, semantic: animals, alternating: vegetables-musical instruments) and by two subtests of the D-KEFS, the Color-Word Interference Test and the Sorting Test. Finally, motor function and visuo-motor coordination were assessed by the Nine-Hole Peg Test and the Purdue pegboard.

Statistical Strategy

To reduce the number of cognitive measures, neuropsychological tests results were grouped into factors. Factor analyses were first performed to determine the cognitive variables included in each factor. Reliability analyses (Cronbach's alpha: α) were conducted to determine the internal

Table 2: List of the variables contributing to each cognitive factor

Factor	Variables
Executive/Speed of information processing	Trail B (time), Stroop inhibition (time) and flexibility (time), PASAT (2 seconds and 3 seconds), SDMT (60 and 90 seconds),
Learning	RAVLT (total), paired associates (total), Logical memory (story A + story B, 2 nd trial), Rey-O complex figure (immediate recall), BVM-T-R (total), Spatial recall 10/36 (total).
Delayed recall	Delayed recall of the following tests: RAVLT, paired associates, Logocam memory : Stories A and B, Rey-O complex figure, BVM-T-R and Spatial recall 10/36.

PASAT: Paced Auditory Serial Addition Task; SDMT: Symbol Digit Modalities Test; RAVLT: Rey Auditory Verbal Learning Test; BVM-T-R: Brief Visual Memory Test-Revised

validity of each factor. Three factors were obtained: (1) Executive/Speed of information processing ($\alpha = .87$), (2) Learning ($\alpha = .79$) and (3) Delayed recall ($\alpha = .81$). The variables included in each factor are listed in Table 2. Subsequently, correlation coefficients (Pearson) were performed between (1) MoCA (total score) and MSNQ-I and MSNQ-P, (2) the total score BDI-FS vs. MoCA (total score) and MSNQ-I and MSNQ-P and (3) the result of each cognitive factors (Executive, learning, delayed recall) vs. the MoCA (total score and scores for sub-sections) and MSNQ-I and MSNQ-P.

RESULTS

According to the EDSS scores (Table 1) this population is rather mildly impaired by MS. Mean scores for the BDI-FS, the MoCA test and the MSNQs are presented in Table 3. Correlations obtained between MoCA, MSNQ, BDI-FS and the neuropsychological factors (Executive/Speed of processing, Learning, Delayed recall) are presented in Table 4.

Relationship MSNQ-MoCA

Even though there was a significant and moderate correlation between MSNQ-I and MSNQ-P ($r = .482$, $p = .001$), only the MSNQ-I correlated significantly with the MoCA total score ($r = -.390$, $p = .012$), although there was a tendency for MSNQ-P to correlate with the MoCA test ($r = -.300$, $p = .056$). The negative correlations observed suggest that the higher the score on the MoCA, the lower the score on the MSNQ. Informant perception of the patient's cognitive functioning appears to be more accurate than the patient's own perception.

Table 3: Mean scores obtained in the BDI-FS, the MoCA and the MSNQ

MS Patients	
BDI-FS	
M (SD)*	1.66 (1.71)
Range of scores (Min – Max)	0 – 7
MoCA (total score)	
M (SD)	26.02 (2.30)
Range of scores (Min – Max)	21 – 30
MSNQ	
MSNQ-P, M (SD)	21.20 (10.13)
Range of scores (Min – Max)	1 – 48
MSNQ-I, M (SD)	17.28 (11.79)
Range of scores (Min – Max)	0 – 42

*Mean score with standard deviations in parenthesis

Relationship with the BDI-FS

Since the scores obtained on screening tests may be influenced by the patient's depressive affect, especially on self-reported measures such as the MSNQ-P^{11,28}, we first analyzed the relationship between BDI-FS and MSNQ-P. No significant correlation was found ($r = -.031$, $p = .847$). Moreover, no significant correlation was obtained between the BDI-FS and the MSNQ-I ($r = .084$, $p = .601$) or with the total score on the MoCA test ($r = .231$, $p = .146$), in the present study. However, it should be taken into account that the average BDI-FS scores was very low ($M = 1.66$, $SD = 1.71$), indicating that the majority of patients reported no or very little depressive affect.

Relationship between the MSNQ, the MoCA and the neuropsychological evaluation

None of the three cognitive factors (Executive/Speed of information processing, Learning and Delayed recall) correlated

significantly with the MSNQ-P, indicating that the patient's perception of his cognitive functioning did not necessarily reflect the cognitive profile obtained through an objective evaluation. In contrast, significant and moderate correlations were obtained between the MSNQ-I and the Delayed recall factor ($r = -.463$, $p = .002$) and the Learning factor ($r = -.484$, $p = .001$). Thus, patients who obtained lower performances on memory testing were rated by their informant as presenting more cognitive deficits. Contrary to expectation, there was no correlation between the MSNQ-I and the Executive/Speed of information processing factor ($r = -.240$, $p = .165$). Thus, the MSNQ-I appears more sensitive to memory deficits than to executive and speed of information processing dysfunctions. Significant and moderate to high correlations were obtained between the MoCA total scores and the three cognitive factors: Learning ($r = .686$, $p < .001$), Delayed recall ($r = .636$, $p < .001$) and Executive/Speed of information processing factor ($r = .367$, $p = .030$). In addition, the score obtained on the memory section of the MoCA significantly and moderately correlated with the score obtained on the Learning factor ($r = .419$, $p = .006$), and on the Delayed recall factor ($r = .419$, $p = .006$) while the score obtained on the Visuospatial/Executive section of the MoCA was significantly and moderately related to the performance on the Executive/Speed of information processing factor ($r = .394$, $p = .019$). These results support the construct validity of these sections of the MoCA.

Finally, MS patients were classified as cognitively intact or cognitively impaired based on the same general procedure described by Rao et al⁶. We calculated the percentage of MS patients who performed at or below 1.5 s.d. (or 7th percentile or scaled score ≤ 5) of age-appropriate norms (Table 5). Patients were classified as "cognitively intact" if they had two or less failed measures and "cognitively impaired" if they failed on three or more measures. In our sample, 27 patients were considered "cognitively intact" and 14 were considered "cognitively impaired". There was a significant difference between the groups (intact vs. impaired) on EDSS scores ($F [1,40] = 7.447$, $p = .009$, $\eta^2 = .16$) and on MSNQ-I ($F [1,40] = 4.143$, $p = .049$, $\eta^2 = .096$), but not on MSNQ-P ($F [1,40] = 0.350$, $p = .557$). The difference between the groups on the MoCA test was highly significant ($F [1,40] = 17.084$, $p < .001$, $\eta^2 = .305$).

Table 4: Correlations observed between MoCA, MSNQ, BDI-FS and neuropsychological factors

	MSNQ-P	MSNQ-I	BDI-FS	Executive factor	Learning factor	Delayed recall factor
MoCA (total score)	-.300 (.056)	-.390* (.012)	.231 (.146)	.367* (.030)	.686*** ($<.001$)	.636*** ($<.001$)
MSNQ-P	-	.482** (.001)	-.031 (.847)	-.223 (.197)	-.025 (.875)	-.069 (.668)
MSNQ-I	-	-	.084 (.601)	-.240 (.165)	-.484** (.001)	-.463** (.002)
BDI-FS	-	-	-	.050 (.777)	.031 (.845)	.053 (.740)

* $p < .05$, ** $p < .01$, *** $p < .001$

Table 5: Results on the neuropsychological tests used to classify patients as cognitively intact or cognitively impaired

	Mean (s.d.)	range	% with deficit*
RAVLT			
- Total (trials 1-5)	48.15 (8.19)	30-59	22.0%
- Delayed recall	9.07 (2.94)	1-14	14.6%
Rey-O figure			
-Immediate recall	17.87 (5.88)	5-30	24.4%
-Delayed recall	17.63 (5.81)	6-32	26.8%
10/36 Spatial Recall Test			
- Total (trials 1-3)	19.00 (4.33)	9-27	24.4%
- Delayed recall	6.37 (2.30)	2-10	34.1%
PASAT total score -3 sec. (N= 38)*	42.74 (12.62)	22-66	29.3%
Trail B (time)	78.19 (35.5)	32-213	36.6%
SDMT(90 sec.)	50.17 (10.03)	27-79	9.8%
Verbal fluency (animals 90 sec.)	22.80 (4.98)	14-36	22.0%
Sorting task (correct sorts)	7.94 (4.98)	2-12	19.5%

*with ≤ 1.5 s.d. or scaled score ≤ 5 according to age-appropriate norms; **some patients were unable to perform the task, mean and s.d. based on those who completed the task, % with deficit includes those who did not complete the task. RAVLT: Rey Auditory Verbal Learning Test; PASAT: Paced Auditory Serial Addition Task; SDMT: Symbol Digit Modalities Test.

DISCUSSION

The results obtained in the present study support the value of the MoCA test as a screening tool for the presence of cognitive dysfunction in MS patients, even in patients with mild functional disability (EDSS). These findings are consistent with the current literature on the MoCA test. Indeed, while its original purpose was to detect mild cognitive impairment (MCI) in elderly patients, the greater sensitivity of the MoCA test, compared to the MMSE, has been reported in other clinical populations such as patients with Huntington's disease²⁹, Parkinson's disease^{30,31}, stroke, ruptured aneurysm^{32,33}, chronic heart failure³⁴ and Rapid Eye Movement (REM) Sleep Behavior Disorder³⁵. In the present study, the value of the MoCA test as an objective screening tool in MS patients was confirmed by the highly significant difference observed in MoCA total score between cognitively intact and cognitively impaired patients. It was further supported by the significant correlations obtained between scores on specific sections of the MoCA test and the corresponding factors derived from the comprehensive neuropsychological evaluation, including executive functions.

The weak correlation between the MSNQ-P and the results of the neuropsychological testing has previously been reported^{7,10}. In our study, the MSNQ-P was not correlated with the presence of depression (assessed by the BDI-FS) as it is often reported^{7,36}. However, this might be due to the absence or the very low level of depression in our sample. Nevertheless, our patients' self-estimation of their cognitive deficits was only marginally correlated with an objective measure of their cognitive functioning. This is not specific to the MSNQ-P since we recently reported¹³ important discrepancies between objective and subjective assessment of cognitive functioning using the Prospective and Retrospective Memory Questionnaire²². In contrast, there was a strong correlation between the results obtained on the neuropsychological tests, at least for memory functioning, and the score on the MSNQ-I. These results are

consistent with what has previously been reported^{7,36}. The lack of correlation with executive functions was somewhat surprising since it is a domain frequently affected in MS. Since an informant is not always available, the use of an objective screening measure of cognitive functioning such as the MoCA appears a valuable clinical tool that can be used to select patients for a comprehensive neuropsychological evaluation.

The main limitation of our study is the small sample size and the small range of MoCA test scores. To further confirm the value of the MoCA as a clinically useful screening tool, the next step is to study its psychometric characteristics (cut-off score with measures of sensitivity and specificity) in a large sample of thoroughly investigated MS patients who would also be administered a neuropsychological battery sensitive to MS, such as the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS)²⁶ or the Brief Repeatable Battery of Neuropsychological Tests (BRB-N)²⁵.

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