ORIGINAL ARTICLE

Detecting Subtle Cognitive Impairment in Multiple Sclerosis with the Montreal Cognitive Assessment

Kim Charest, Alexandra Tremblay, Roxane Langlois, Élaine Roger, Pierre Duquette, Isabelle Rouleau

ABSTRACT: ***Background:*** Although cognitive deficits are frequent in multiple sclerosis (MS), screening for them with tools such as the Montreal Cognitive Assessment (MoCA) test is usually not performed unless there is a subjective complaint. The Multiple Sclerosis Neuropsychological Questionnaire (MSNQ) is among the instruments most commonly used to assess self-reported subjective complaints in MS. Nonetheless, it does not always accurately reflect cognitive status; many patients with cognitive deficits thus fail to receive appropriate referral for detailed neuropsychological evaluation. The objective of this study was to examine the validity of the MoCA test to detect the presence of objective cognitive deficits among patients with MS without subjective complaints using the Minimal Assessment of Cognitive Function in MS (MACFIMS) as the gold standard. ***Methods:*** The sample included 98 patients who were recruited from a university hospital MS clinic. The MSNQ was used to select patients without subjective cognitive complaints who also completed the MACFIMS, MoCA test and MSQOL-54. ***Results:*** 23.5% of patients without subjective cognitive complaints had evidence of objective cognitive impairment on the MACFIMS (z score < -1.5 on two or more tests). The MoCA had a sensitivity of 87% and a specificity of 68% for detecting objective cognitive impairment in this patient population using a cut-off score of 27. ***Conclusion:*** A significant proportion of patients without self-reported cognitive impairment do have evidence of cognitive deficits on more exhaustive cognitive assessment. The MoCA is a rapid screening test that could be used to target patients for whom a more detailed neuropsychological assessment would be recommended.

RÉSUMÉ : Détecter une déficience cognitive légère chez des patients atteints de sclérose en plaques au moyen de l'Évaluation cognitive de Montréal. ***Objectifs :*** Bien que des déficits cognitifs soient fréquents dans la sclérose en plaques (SEP), leur dépistage avec des outils tels que le test d'évaluation cognitive de Montréal (MoCA) n'est généralement pas effectué sauf en cas de plainte subjective. Le *Multiple Sclerosis Neuropsychological Questionnaire* (MSNQ) est l'un des instruments les plus couramment utilisés pour évaluer les plaintes subjectives auto-rapportées dans la SEP. Cependant, il ne reflète pas toujours avec précision l'état cognitif ; des patients présentant effectivement des déficits cognitifs ne sont donc pas référés en neuropsychologie pour évaluation détaillée. L'objectif de cette étude était d'examiner la validité du MoCA pour détecter, chez les patients atteints de SEP sans plaintes subjectives, la présence de déficits cognitifs objectifs en utilisant le *Minimal Assessment of Cognitive Function in MS* (MACFIMS) comme référence. ***Méthode :*** L'échantillon comprend 98 patients recrutés dans une clinique de SP d'un hôpital universitaire. Le MSNQ a été utilisé pour sélectionner des patients sans plaintes cognitives subjectives. Ils ont également complété le MACFIMS, le MoCA et le MSQOL-54. ***Résultats :*** 23,5% des patients sans plaintes cognitives présentent des déficits cognitifs objectifs au MACFIMS (score z <-1,5 à deux tests ou plus). Dans cette population de patients, le MoCA a une sensibilité de 87% et une spécificité de 68% pour détecter la présence de trouble cognitifs objectifs lorsqu'un seuil de 27/30 est utilisé. ***Conclusion :*** Une proportion significative de patients sans plaintes cognitives présente des déficits cognitifs lorsqu'une évaluation cognitive plus exhaustive est réalisée. Le MoCA est un test de dépistage rapide qui pourrait être utilisé pour cibler les patients pour lesquels une évaluation neuropsychologique plus détaillée serait recommandée.

Keywords: Multiple sclerosis, Cognition, Cognitive impairment, Neuropsychology

doi:10.1017/cjn.2020.97 Can J Neurol Sci. 2020; 47: 620–626

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease affecting the central nervous system that predominantly attacks myelin in the brain and spinal cord.[1] About 40 to 65% of patients with MS have cognitive deficits.[1] These cognitive deficits are associated with poor functional status,[2] as well as decreased quality of life[3] and productivity.[4,5] The functions predominantly affected in MS are episodic memory,[6,7] working memory,[8] information processing speed,[9–12] attention,[13] executive functions[14] and visuospatial functions.[15]

Although many patients are aware of their cognitive deficits and report these difficulties to their health professionals, patients' assessments of their own cognitive status are not always accurate.[16–20] Whereas the Multiple Sclerosis Neuropsychological

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Received October 15, 2019. Final Revisions Submitted April 29, 2020. Date of Acceptance May 15, 2020.
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Questionnaire (MSNQ) is used frequently, the results obtained by the self-reported measures (MSNQ-P [patient form]) do not always accurately reflect objective cognitive functioning in patients with MS.[16,21,22] It is, therefore, possible that a patient without any subjective complaint on the MSNQ-P would nonetheless present clinically significant objective cognitive deficits on a more in-depth assessment. Unfortunately, in the absence of subjective complaints on the MSNQ-P, many patients with cognitive deficits thus fail to receive appropriate referral for comprehensive neuropsychological evaluation. This has important clinical implications given the known impact of cognitive dysfunctions on personal and professional life.[2–5]

Over the years, a number of neuropsychological test batteries have been developed specifically to evaluate patients with MS' cognitive abilities by assessing the functions that are preferentially affected in MS.[23] Many of these tests, such as the Brief Repeatable Battery of Neuropsychological Tests (BRBN)[24] and the Minimal Assessment of Cognitive Function in MS (MACFIMS),[25] show good sensitivity but are too time-consuming for more widespread administration.

Because it is neither realistic nor appropriate to perform an exhaustive neuropsychological evaluation of all patients with MS, clinicians need a short, sensitive and reliable screening test that could rapidly detect the presence of cognitive impairment and lead to referral for a more complete neuropsychological evaluation. To reduce testing time, researchers have developed the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS),[26] a short version of the MACFIMS. While the validity of the BICAMS has been demonstrated, the lack of executive function assessment has been criticised[27] since executive deficits have been reported in at least half of patients with MS regardless of their level of cognitive impairment.[28] To compensate for these limitations, a shortened version of the MACFIMS battery was studied by Gromisch and his team.[29] In this version, called aMACFIMS, only some trials of the original tests are administered. It achieved higher specificity but lower sensitivity than the BICAMS. However, the tests which are shortened lose their psychometric properties and, especially for memory tests (CVLT-II and BVMT-R), can no longer be used with the tested patients because of familiarity with the material (e.g. same words, same geometric figures) and practice effects.

Many clinicians and researchers use the Symbol Digit Modalities Test (SDMT)[30] as a screening test. Its quick administration time (5 minutes) and its high sensitivity to the cognitive deficits experienced by patients with MS[31] explain its widespread use. However, it only assesses the speed of information processing, which is often but not always affected in MS. Some use the Mini Mental State Examination (MMSE),[32] but it does not include items to assess executive and attentional functions, which makes it less appropriate as a screening tool for MS.[33,34]

In contrast, the MoCA test is particularly adapted to cognitive screening[35] of patients with MS since it evaluates many of the cognitive functions known to be preferentially affected in MS.[22,36] In addition, the MoCA test is very accessible since it is free of charge and available in more than 30 languages. Since September 2019, a certification is mandatory to administer the MoCA, except for students, residents, fellows and neuropsychologists. Administration time is less than 10 minutes, an advantage for patients with MS, who often report fatigue. Studies have already shown that MoCA scores are significantly lower in patients with MS compared to healthy controls[37,38] and that the test is sensitive to the type of cognitive impairment noted in MS.[22] However, no study to date has investigated the use of the MoCA in patients with MS without subjective complaints.

The aim of this study was to fill this gap in the literature by assessing the efficacity of the MoCA test in detecting the presence of subtle objective cognitive deficits among patients without subjective complaints, given the fact that a significant proportion of these patients do show cognitive deficits upon objective testing. To achieve this aim, patients without subjective cognitive impairment – as reported by the MSNQ-P – were screened for cognitive impairment with the MoCA and their scores were compared with their results on the MACFIMS neuropsychological test – the gold standard for this study. We hypothesised that the MoCA test score would be a valid screening tool to discriminate cognitively impaired from cognitively intact patients and indicate who should be referred for detailed neuropsychological evaluation.

Methods

Participants

This study used data from a previous investigation[39] on the effect of the beta-interferon medication Rebif® on clinical evolution (work status and quality of life) in treated vs. untreated patients with MS. In that study, 111 patients treated with Rebif exclusively for at least 2 years and up to 18 years were compared to 185 patients, matched in age, gender, education level, age at disease onset and disease duration, who never received disease-modifying drugs. Among the 296 patients with MS, a subgroup of 121 patients (52 treated and 69 untreated) agreed to complete the MACFIMS. Since there was no effect of treatment group on cognitive functions observed, the two groups were combined for the present study. All participants were recruited from the MS Clinic of the Centre Hospitalier de l'Université de Montréal (CHUM). The CHUM ethics committee approved this study and every participant signed an informed consent form.

Among the initial sample of 121 patients who completed the MACFIMS, only those without subjective cognitive complaints were selected, that is, those who scored below 24 on the MSNQ-P,[21,40] leaving a final sample of 98 patients (19 men and 79 women) with MS. To be included in the project, patients had to meet the following criteria: (1) diagnosed with MS (clinically isolated syndrome, relapsing–remitting or secondary progressive) according to the 2005 Revision of the McDonald Diagnosis Criteria (Polman et al., 2005); (2) followed at the CHUM's MS Clinic within the last 2 years; (3) aged 18 years or over; (4) EDSS $\leq$ 5.5; (5) able to read and write in French. Patients were excluded from the study if they met any of the following criteria: (1) had a history of drug abuse, neurological or developmental disorders, or psychiatric or other medical conditions that could affect their neuropsychological performance (e.g. traumatic brain injury, stroke); (2) were unwilling or unable to consent; (3) or were diagnosed with primary progressive MS.

Measures

Screening Tests

The MoCA and the MSNQ were used as screening tests for cognitive impairment.[23,24] In addition to the total score (/30), the

https://doi.org/10.1017/cjn.2020.97 Published online by Cambridge University Press

MoCA includes the following sub-scores: (1) visuospatial and executive functioning, (2) naming, (3) attention (e.g. simple attention, working memory, vigilance), (4) language (e.g. repetition, phonemic fluency), (5) abstraction, (6) delayed free recall and (7) orientation. The MSNQ was completed by the patient (MSNQ-P) and a close relative (MSNQ-I). The MSNQ-P score was used to confirm the absence of subjective cognitive complaint by the participants. A score under 24 met this criterion.[21,40]

Exhaustive Neuropsychological Testing

Exhaustive neuropsychological assessment was conducted using the MACFIMS. Normative data available for each test (see below) were used to compare our sample to healthy controls. Impairment on each measure was defined as a cut-off z score of −1.5. The presence of objective cognitive impairment was defined as failure of two or more tests on the MACFIMS battery.

Verbal fluency was evaluated with the French version of the Controlled Oral Word Association Test (COWAT) with the letters P–F–L.[41] This task measures oral production of words beginning with a specific letter in a limited period of time, excluding proper nouns, numbers and the same word with a different suffix.[42] Normative data of French-speaking Quebec adults adjusted for age and education were used for this version of the COWAT.[43] Visuospatial functioning was assessed by the Judgment of Line Orientation Test (JLO),[44] which evaluates the ability to visually match 30 pairs of angled lines. Original norms of the JLO were used.[44] Information processing speed was measured using the SDMT[45] and the Paced Auditory Serial Addition Test (PASAT-3).[46] For the SDMT, participants must orally pair specific numbers with given geometric symbols as quickly and accurately as possible. On the PASAT-3, participants must add 60 pairs of randomised digits by adding each new digit to the one heard immediately prior to it. Normative data from a study by Centofanti[47] were used for SDMT, and norms from Rao[48] were utilized for PASAT-3. Executive functions were evaluated by the Sorting Test, a subtest of the D-KEFS, and normative data from the D-KEFS examiners' manual were used.[49] In this subtest, participants are asked to sort cards that share either perceptual or verbal features to form and explain as many categories as possible. The Brief Visual Memory Test (BVMT-R) was used as a measure of visuospatial memory and original norms were used for scoring.[50] In this task, participants have 10 seconds to observe six geometric stimuli presented visually, and then must draw as many stimuli as they remember in the correct location. Verbal memory was assessed by the California Verbal Learning Test (Second Edition) (CVLT-II) and normative data from the CVLT manual were used.[51] This task evaluates recall and recognition of verbal material using a 5-trial presentation of a 16-word list (list A) and a single presentation of an interference list (list B). At each trial, examiners read the entire list and participants are asked to recall as many words as possible.

Procedures

All evaluations took place at the CHUM and participants were recruited at the MS clinic at a follow-up visit with their neurologist. If the patient met the criteria for inclusion, informed written consent was obtained, and the patient was scheduled for a neuropsychological evaluation.

A neuropsychology graduate student, under the supervision of a certified neuropsychologist, performed the evaluation. First, the patient was questioned about the psychosocial background, including education, family status and occupation/employment. They were then given the MSNQ-P to complete. Following administration of the neuropsychological test battery, the patient was given a number of questionnaires to complete at home, including the Multiple Sclerosis Quality of Life (MSQOL)-54, which contains questions pertaining to mood (emotional well-being scale), pain and fatigue (energy scale) and the MSNQ-I to be given to a relative. The examination also included an assessment of the level of the patient's disability according to the Expanded Disability Status Scale (EDSS).[52]

Table 1: Patients' sociodemographic profile and disease characteristics

	Cognitively intact N = 75	Cognitively impaired N = 23	Failure (%) z score ≤ -1.5 t or $\chi 2$
Gender			
Women, N (%)	61 (81.3)	18 (78.3)	$p = 0.767$
Men, N (%)	14 (18.7)	5 (21.5)	
Age			
Mean (SD)	49.4 (11.8)	50.3 (10.4)	$p = 0.601$
Education			
Mean (SD)	14.8 (2.3)	14.3 (3.8)	$p = 0.440$
Disease duration (Years)			
Mean (SD)	10.5 (7.7)	9.9 (6.7)	$p = 0.730$
MS course			
CIS N (%)	6 (8.0)	1 (4.3)	
RRMS N (%)	58 (77.3)	18 (78.3)	$p = 0.812$
SPMS N (%)	11 (14.7)	4 (17.4)	
Last EDSS score			
Mean (SD)	1.7 (1.9)	2.1 (2.2)	$p = 0.391$

Statistical Analysis

To make a direct comparison between MoCA test scores and performance on the MACFIMS possible, a global MACFIMS score was calculated by averaging each standardised z score obtained for the various tests included in the MACFIMS. Direct comparisons between patients with MS who are cognitively intact and those who are cognitively impaired (2 or more tests < −1.5 SD on the MACFIMS battery)[53] were performed by computing t tests on total MoCA test scores and on the results obtained on the different sections of the MoCA test. A hierarchical multiple regression analysis was carried out with the global score on MACFIMS as the dependent variable. Demographic, MSQOL variables and MoCA subtests were added gradually in three blocks as independent variables. This allowed us to examine what percentage of variance in the MACFIMS global score could be explained by these variables.

https://doi.org/10.1017/cjn.2020.97 Published online by Cambridge University Press

Table 2: Performance on the MACFIMS: frequency of failures (%)

	Failure (%) z score ≤ -1.5
Symbol Digit Modality Test _90s (SDMT)	10.2
Judgment of Line Orientation Test (JOL)	10.2
California Verbal Learning Test (CVLT-II) Total recall	6.7
Short-delay free recall	4.1
Long-delay free recall	11.2
Recognition	7.1
Paced Auditory Serial Addition Test-3 (PASAT-3)	29.6
Brief Visual Memory Test – Revised (BVMT-R)	
Total recall	13.3
Delayed free recall	8.2
Delis–Kaplan Executive Function System (D–KEFS)	
Free sorting test	0
Controlled Oral Word Association Test (COWAT)	
Total score	24.5

Finally, to validate the clinical use of MoCA as a screening test, ROC curves were generated for the total MoCA score and scores obtained on its different subsections to determine the best cut-off to separate cognitively impaired from cognitively intact patients.

Results

There was no statistical difference between patients with MS who completed the MACFIMS (N = 121) and those who did not (N = 175) in terms of age (t [294] = 1.07, p = .089), education (χ^2 [3, N = 296] = 6.61, p =.086), gender (χ^2 [1, N = 296] = 0.044, p = .834), duration of the disease (t [275] = 1.31, p = .190), MS course (χ^2 [2, N = 296] = 0.513, p =.774) and EDSS score (t [294] = 0.902, p = .368).

Among the 121 patients who completed the MACFIMS, 98 did score below 24 on the MSNQ-P, confirming the absence of cognitive complaints in this patient group. This final sample included 19 men and 79 women, aged 26 to 71 years (*Mean* = 49.57; *SD* = 11.40) who had completed between 8 and 18 years of education (*Mean* = 14.56; *SD* = 2.77). Duration of the disease ranged from 4 months to 35 years (*Mean (years)* = 10.75; *SD* = 7.61). Data on the sociodemographic situation, patient status and duration of illness are presented in Table 1. Despite the absence of cognitive complaints according to the MSNQ-P, 23 out of the 98 patients were classified as cognitively impaired (23.5% of the sample), having failed at least 2 tests on the MACFIMS battery. Table 2 shows the frequency of failures for each of the MACFIMS subtests that support this classification. It is worth mentioning that only 10.2% (10/98) of the sample was found to be impaired on SDMT while a higher proportion of patients were impaired on COWAT, BVMTR and CVLT-II, which suggests that some patients are intact on the SDMT although they have impaired memory and executive functions. Indeed, in our sample, among the 23 patients classified as impaired on the MACFIMS (2 or more tests < -1.5 SD), only 8 (34.8%) were impaired on the SDMT. The results of the cognitive screening tests are presented in Table 3.

Table 3: Results of cognitive testing

	Cognitively intact N= 75	Cognitively impaired N = 23	t or $\chi 2$
Montreal Cognitive Assessment (MOCA) total score			
Mean (SD)	27.8 (1.7)	25.4 (2.2)	p < .001
Visuospatial/executive			
Mean (SD)	4.4 (0.7)	3.6 (1.2)	p < .001
Naming			
Mean (SD)	3.0 (0.2)	2.8 (0.4)	p = 0.123
Attention			
Mean (SD)	5.7 (0.5)	5.5 (0.9)	p = 0.158
Language			
Verbal fluency			
%Failure (< 11 words)	28.0%	69.6%	p = .001
Number of words			
Mean (SD)	12.4 (3.5)	8.8 (3.6)	p < .001
Sentence repetition			
Mean (SD)	1.88 (0.3)	1.87 (0.3)	p = 0.895
Abstraction			
Mean (SD)	1.8 (0.4)	1.7 (0.4)	p = 0.295
Delayed free recall			
Mean (SD)	4.1 (1.0)	3.3 (1.1)	p < .001
Orientation			
Mean (SD)	5.9 (0.3)	5.9 (0.2)	p = 0.787
Multiple Sclerosis Neuropsychological Questionnaire (MSNQ)			
Informant form			
Mean (SD)	10.5 (0.2)	17.6 (7.7)	p < .001
Patient Form			
Mean (SD)	14.4 (6.2)	14.8 (4.9)	p = 0.767
Global score on Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS)			
Mean (SD)	.31 (0.57)	-0.64 (0,48)	p < .001

Relationship Between the MSNQ-P and MACFIMS Scores

There was no significant correlation between the MSNQ-P score and the result of the neuropsychological evaluation including the MoCA test (total score and sub-sections), the scores obtained on all the tests on the MACFIMS battery, or the global score on the MACFIMS.

https://doi.org/10.1017/cjn.2020.97 Published online by Cambridge University Press

Table 4: Summary of hierarchical regression analyses

	R2	*ΔR2*	*ΔF*
Model 1 Age, duration of illness, last EDSS score	.031	.081	1.615
Model 2 Multiple Sclerosis Quality of Life Questionnaire (MSQoL-54): pain, emotional well-being and energy	.043	.041	1.394
Model 3 Montreal Cognitive Assessment (MoCA): attention, orientation, visuospatial/executive, verbal fluency and free delayed recall	.426	.381	12.880***

***p < .001.

Table 5: Regression coefficients of each predictor of the global score on MACFIMS

Component	*B*	β	r_s
Age	−.004	−.068	−.116
Duration of illness	.014	.158	.076
Last EDSS score	−.059	−.172	−.194
Gender	.046	.027	.106
Education	−.001	−.004	.100
MSQoL-54: energy	.000	−.011	.110
MSQoL-54: emotional well-being	.006	.142	.191
MSQoL-54: pain	−.003	−.111	.172
MoCA: attention	−.047	−.069	.105
MoCA: orientation	.061	.095	.123
MoCA: visuospatial/executive	.150	.228*	.432
MoCA: verbal fluency	.288	.406***	.469
MoCA: free delayed recall	.213	.297 **	.439

*p < .05; ** p < .01 ***p < .001.

However, the MSNQ-I was significantly correlated with the MoCA total score (r = -0.246, $p = 0.017$) and the global score on the MACFIMS (r = -0.278, $p = 0.007$). As shown in Table 3, no difference was found between cognitively impaired and cognitively intact patients on the MSNQ-P (t[96] =-0.297, $p = 0.767$), whereas these two subgroups were statistically different on the MSNQ-I (t[92] = -3.720, p <.001).

Relationship Between the MoCA and MACFIMS Scores

As shown in Table 3, a *t* test reveals that patients who were classified as cognitively impaired had a lower MoCA score than those who were considered cognitively intact (t[96] = 5.6, p <.001). In addition, the results obtained in three sub-sections of the MoCA: visuospatial/executive (t[96] = 5.61, p < .001), verbal fluency (χ^2 [1, N = 98] = 12.94, p < .001) and delayed recall (t [98] = 3.35, p = .001) were significantly different between the two groups, whereas scores obtained in naming, attention, orientation, abstraction and sentence repetition were not statistically different.

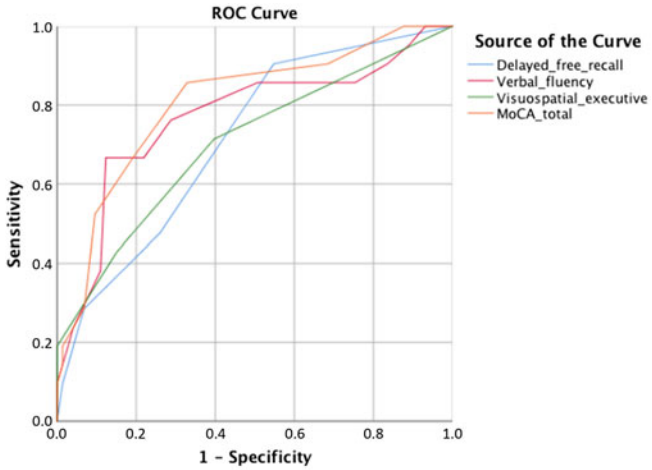

Figure 1: *Results of the ROC curve for the Montreal Cognitive Assessment in patients with multiple sclerosis without cognitive complaints*

In light of these results, hierarchical multiple regression analyses were performed with the global score on MACFIMS as the dependent variable. A summary of the results is shown in Table 4. Age, duration of illness, EDSS score, sex and education did not significantly explain the variance of the global score on MACFIMS (p =.191). The inclusion of depression and fatigue also did not explain an additional portion of the variance (p =.102). MoCA test scores significantly explain 42.6% of the variance in the global score on MACFIMS. Examination of the regression coefficients (see Table 5) shows that only the visuospatial/executive score, verbal fluency and delayed free recall were significantly related to the global score on MACFIMS (visuospatial executive: β = .228, $p = 0.021$; verbal fluency: β = .406, p <.001; delayed free recall: β = .297, $p = 0.002$), and not the orientation and attention scores.

Sensitivity and Specificity of the MoCA Test

With a cut-off score of 27, ROC curve analysis (AUC = 0.815, 95% CI, .714 -.916, p < .001) yielded a sensitivity of 87% and a specificity of 68% for the total score on the MoCA test. The best sensitivity/specificity ratio was obtained with the complete MoCA test (Youden index [YJ][54] = 0.550). The three sub-scores that were significant in the regression analysis (executive/visuospatial, verbal fluency, delayed recall) demonstrated a potential value for classifying patients, but their Youden indices were not as high as that achieved with the complete MoCA scale (Figure 1).

Discussion

The important contribution of this study is that it assesses cognitive impairment in patients without subjective cognitive complaints. Despite the absence of cognitive complaints as assessed by the MSNQ-P, the results of this study demonstrate the relevance of performing objective cognitive screening tests in patients with MS with the MoCA, especially in light of the known impact of cognitive deficits on professional and personal life.

https://doi.org/10.1017/cjn.2020.97 Published online by Cambridge University Press

Although the informant version of the MSNQ (MSNQ-I) appears to be more accurate than the patient version (MSNQ-P) in assessing the presence of cognitive deficits, it is not as precise as objective testing and is often not available in a clinical context. Indeed, many patients, particularly those with a low level of disability (low EDSS score), do not come to a medical appointment accompanied by a person who knows them well enough to give an accurate account of their daily functioning and cognitive status as required by the MSNQ-I.

Our study found evidence of subtle cognitive deficits in patients with no subjective complaints and demonstrated the validity of the MoCA test in detecting such subtle cognitive impairment. In addition to being strongly correlated with the overall MACFIMS score, its ability to classify patients as cognitively intact or not, with acceptable sensitivity (87%) and specificity (68%), justifies its clinical use. None of the scores obtained for the individual sub-sections reached such levels of sensitivity and specificity.

The MoCA test has a number of advantages: it is rapid, reliable and valid, and addresses many domains highly relevant to MS such as verbal memory and executive functions. These domains can be affected in some individuals who do not show impaired speed of information processing as assessed by the SDMT. Moreover, the MoCA test can easily be administered by most health professionals, is free of charge (although certification is now required, except for students, residents, fellows and neuropsychologists) and available in numerous languages directly through the Internet.

The multiple regression model demonstrates the importance of assessing executive functions, verbal fluency and verbal memory, as these were the functions that most effectively predicted the impairment revealed by the MACFIMS. These results are consistent with prior work[30] that showed that executive functions and verbal memory are the two aspects initially affected in MS and that they should be examined even in patients with a very low level of disability (EDSS $\leq$ 1.5).

These results also concur with those obtained by Vogel *et al.*,[55] which showed that the visuospatial/executive, memory, attention and language domains of the MoCA test adequately reflected constructs similar to those measured by an exhaustive neuropsychological evaluation in a clinic specialised in neurodegenerative disease. The MoCA, which evaluates these functions, is, therefore, a more appropriate tool for screening in MS than other screening tests that do not evaluate these functions, such as the SDMT.

Our study has some limitations. It was conducted with rather young and educated patients and the range of MoCA test results observed was relatively limited (from 21 to 30). For improved generalisability, this study should be replicated among less educated and older patients, especially given the significant impact of these factors on cognition.[56–58]

Using the MACFIMS as the gold standard, the MoCA test could accurately identify the presence of cognitive impairment in patients with MS without subjective cognitive complaints. This study suggests that the MoCA should be used more systematically in follow-up clinical appointments. Considering the impact of cognitive impairment on personal and professional life, this rapid screening test could be used to identify patients for whom a more detailed neuropsychological assessment would be recommended.

Acknowledgements

The authors would like to thank the patients who participated in this study. A special thanks to Hugues Leduc for his suggestion regarding the statistical analyses and to Karen Grislis for manuscript editing.

Disclosures

Dr Duquette has served on editorial boards, has been supported to attend meetings by EMDSerono, Biogen-Idec, Novartis, Genzyme, and TEVANeuroscience and received grants from CHIR and MS Society of Canada. The remaining authors have no conflicts of interest.

Statement of Authorship

KC: data analysis, manuscript writing and submission of the manuscript; AT: testing, statistical analyses and editing of the manuscript; RL: recruitment and testing. ER: study design and recruitment. PD: study design, recruitment and data analysis; IR: study design, recruitment and testing, data analysis, editing and submission of the manuscript.

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