Revista da Sociedade Brasileira de Medicina Tropical
Journal of the Brazilian Society of Tropical Medicine
Vol.:52:e20190473: 2019
doi: 10.1590/0037-8682-0473-2019

Major Article

Comparison between the Mini-Mental State Examination and Montreal Cognitive Assessment as a Cognitive Screening Tool in Patients with Human Immunodeficiency Virus-Associated Neurocognitive Disorders

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Abstract

Introduction: The number of human immunodeficiency virus-associated neurocognitive disorders has increased, reaching more than 50% of the cases. However, there are currently no substantial data on the screening methods for this disease. This study aimed to evaluate and compare the Mini-Mental State Examination to the Montreal Cognitive Assessment in human immunodeficiency virus-infected patients. **Methods:** This was an observational study comprising 82 human immunodeficiency virus-positive individuals with and without cognitive complaints. **Results:** Positive correlation ($p<0.001$) between the Mini-Mental State Examination and the Montreal Cognitive Assessment test scores was observed, but the mean scores revealed that the Mini-Mental State Examination showed worse performance for trails ($p<0.001$), cube copying ($p<0.001$), and clock drawing ($p<0.001$) than the Montreal Cognitive Assessment. **Conclusions:** The Mini-Mental State Examination and the Montreal Cognitive Assessment tests should be used concomitantly for the assessment of human immunodeficiency virus-associated neurocognitive disorders, but visuoexecutive and visuospatial dysfunctions are better evaluated using the Montreal Cognitive Assessment test than the Mini-Mental State Examination.

Keywords: Mini-Mental State Examination. Montreal Cognitive Assessment. HIV-Associated Neurocognitive Disorder. Cognition.

INTRODUCTION

The prevalence of human immunodeficiency virus-associated neurocognitive disorder (HAND) in adults is estimated to range from 30% to more than 50%[1]. Cognitive symptoms for HAND include amnesia, decline in rational abilities, short-term memory loss, and lack of concentration[2]. The most severe HAND diagnosis, human immunodeficiency virus-associated dementia, is rare, but milder forms of impairment are common, even among those receiving combination antiretroviral therapy who have minimal comorbidities[3]. Therefore, the infectologists should properly identify patients with possible cognitive impairment to refer those patients for a detailed evaluation.

The most commonly used test for cognitive screening is the Mini-Mental State Examination (MMSE), originally described by Folstein et al.[4]. It especially evaluates some functions of the left cerebral hemisphere, such as language and memory, but it is not adequate for a more subtle global cognitive screening, such as mild cognitive impairment (MCI). On the other hand, the Montreal Cognitive Assessment (MoCA)[5] was developed to assess the visuospatial and executive functions of patients with MCI, and this test is more sensitive than the MMSE. The MoCA is a short cognitive tool with high sensitivity and specificity

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Received 16 October 2019
Accepted 31 October 2019

to detect MCI currently considered in patients who present a normal range of the MMSE cutoff points of < 26[6].

Other studies compared the sensitivity and specificity between the MMSE and the MoCA, especially in detecting MCI or dementia[7,8,9,10]. The MoCA has also been used as screening tool to evaluate cognitive changes in poststroke[11], chronic heart failure[12], chronic renal failure[13], rehabilitation program[14], and neurocognitive disorders associated with HAND[15]. However, determining a score measurement and a satisfactory cutoff point between the two tests or comparing the short HAND tests among countries, even if they have similar language, is not possible[16,17,18]. Tests including the MoCA, Isaac set test, and memory span test are considered useful options when identifying patients who require neuropsychological assessment[19]. Screening tools with good discriminant validity are necessary to ensure that screening initiatives are both effective and efficient. This study aimed to compare the MMSE with the MoCA tests in clinically stable patients with HIV-acquired immunodeficiency syndrome (HIV-AIDS).

METHODS

This was an observational study conducted from December 2015 to November 2017 at the Neurology Outpatient Clinic of Behavior and Infectious Diseases at Hospital Universitário Oswaldo Cruz (University Hospital) in Recife, Brazil. This hospital is a reference center to diagnose and treat HIV-AIDS patients. A convenience sample of individuals with HIV-AIDS aged 23 to 59 years with 8 years or more of schooling who consecutively presented at the infectious and parasitic disease outpatient clinic of Oswaldo Cruz University Hospital were included. The exclusion criteria were as follows: clinical diagnosis of stroke, delirium, psychiatric alterations, mental deficiency, traumatic brain injury, and other clinical conditions that affect cognition.

The tools MMSE and the MoCA were used to evaluate patients' cognitive functioning. The MMSE is a short, widely used cognitive screening test that evaluates general cognitive functioning, mainly the functions that predominate in the left cerebral hemisphere classified within a range of 0 to 30 points. The MMSE cutoff point was considered 24[4]. It is composed of questions on orientation for time and space, memory, attention/calculation, call-up, language, and praxes. The MoCA used in this study had a cutoff point of 23[6,17]. The MoCA measures eight cognitive components, which are classified within a range of 0 to 30 points (with the highest score indicating better function) and is performed in 20 minutes: short-term memory with late recall, visuospatial skills (cube drawing, 1 point; clock drawing, 3 points), executive function with trail making test, language (phonemic verbal fluency and verbal abstraction), attention (concentration and working memory by cancellation, subtraction, direct and indirect span digits), appointment, repetition of sentence, and orientation to time and space. To correct the educational effects found in the original study, an additional point was given to individuals with 12 or less years of schooling, following the authors' instructions and the procedures adapted by the previous studies[5].

The MMSE and the MoCA share some common items (with small differences in format or scoring system). Compared to the MMSE, the MoCA has more tasks that assess executive functions and visuospatial skills. To evaluate depressive symptoms, the Brazilian version of the Beck's Depression Inventory[20,21] was used. The higher the subject's score, the greater the intensity of the symptoms. According to Kendall et al.[22], in a nonclinical population, scores greater than 15 and 20 points were indicative of dysphoria and depressive symptoms, respectively.

Each patient was evaluated by a neurologist utilizing a semi-structured interview, followed by the MMSE, the MoCA, and the Beck's Depression Inventory. We classified our patients as "with complaints" if they have answered "yes" to the following questions: (1) "Do you have problems with your recent and prospective memory?" (2) "Do you have difficulty planning or performing daily activities at home or at work or socially?"

Blood sample for vitamin B12 was obtained, Venereal Disease Research Laboratory (VDRL) and anti-hepatitis C virus (HCV) tests and brain computed tomography (CT) scan were performed, and CD4 cell count and HIV viral load were also assessed.

The presence of risk factors, including hypertension, dyslipidemia, smoking, and diabetes mellitus, for cardiovascular diseases was also evaluated.

Prior to performing statistical analyses, the normality of data distributions and variance homogeneity were assessed (Kolmogorov-Smirnov and Levene tests, respectively). According to these criteria, the following statistical analyses were used: For means of comparisons, for Student's t-test, and for frequency data, the Pearson chi-squared test was used. Pearson correlation was used to verify the association between the score values of the MMSE and the MoCA. An α error of 0.05 was used to reject the null hypothesis.

The study was approved by the Ethics Committee on Research involving Human Beings at the *Hospital Universitário Oswaldo Cruz* (University Hospital) under the following number: CAAE=43599015.3.0000.5192. All patients provided informed consent for inclusion in the study.

RESULTS

Eighty-two individuals with HIV-AIDS were included, aged 23 to 59 years, with 8 years or more of schooling. Thirty-two of them were women. All patients had CD4 lymphocyte count > 300 and a viral load < 50 or undetectable, with normal vitamin B12 levels; both VDRL and anti-HCV tests were negative. None of the patients had preexisting neurological diseases. Eighty patients presented with mild depressive symptoms with no value, while 2 patients had moderate depressive symptoms. More than 60% of the patients underwent CT scan with normal results.

A positive correlation ($r=0.634$, $p<0.001$) between the scores of the tests was observed (**Figure 1**).

The comparison between the mean scores of the MMSE and the MoCA (**Figure 2**) showed that the MMSE was better than

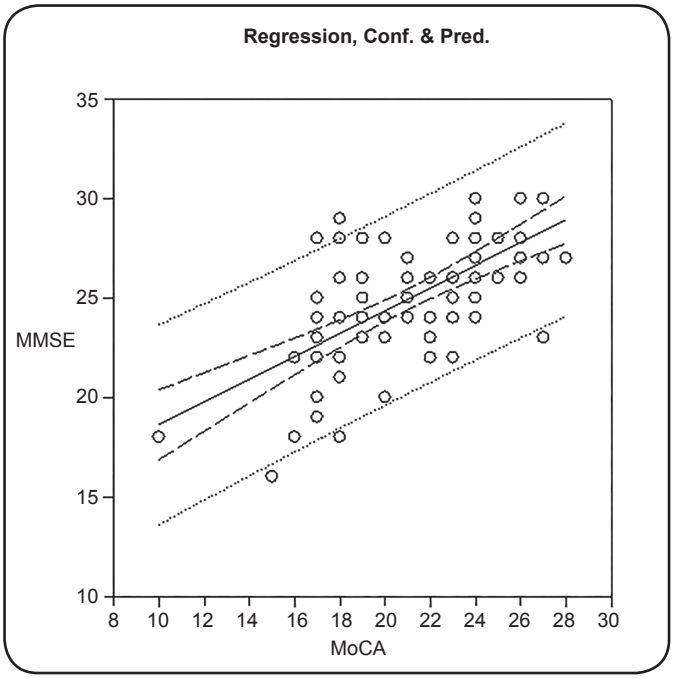

FIGURE 1: Linear regression between the MMSE and MoCA scores in 82 individuals with human immunodeficiency virus-acquired immunodeficiency syndrome. **MoCA**: Montreal Cognitive Assessment; **MMSE**: Mini-Mental State Examination.

MMSE		MoCA		Value p
$\bar{X}$ ±	Dp	$\bar{X}$ ±	Dp	
24.93	3.07	21.01	3.46	< 0.001

Comparisons: Student's t-test.

MoCA: Montreal Cognitive Assessment; **MMSE:** Mini-Mental State Examination

FIGURE 2: Mean values of the MMSE and MoCA scores in 82 individuals with human immunodeficiency virus-acquired immunodeficiency syndrome.

the MoCA ($p<0.001$). Regarding the proportion of individuals with scores over the cutoff point in each test, the MMSE had a higher proportion (45.1%) than the MoCA (26.8%) ($p<0.001$).

When comparing the pentagon of the MMSE and each of the three MoCA subtests (**Table 1**), the trails, the cube copying, and the clock drawing, the performance in the pentagon was better than that in the trail ($p<0.001$), in the cube ($p<0.001$), and in the clock ($p<0.001$).

When comparing the orientation sub-item in the MMSE and MoCA (**Table 2**), a statistical difference was observed between the two tools ($p<0.001$).

We classified 34 patients as "with complaints." The complainants and the no complaints individuals with scores above the cutoff point of the MMSE (40%) and the MoCA (50%) had no statistically significant difference.

Individuals with and without cardiovascular risk factors with scores within the cutoff points of the MMSE and the MoCA had no statistically significant difference.

DISCUSSION

This is a study that compared two tests, the MMSE and the MoCA, to determine which of these would be the best screening tool when identifying HAND. A positive correlation between the scores with each test was verified. This correlation could be partially explained by the presence of subtests involving similar questions about memory and orientation in both tests. On the contrary, there was a significantly higher value of means scores

TABLE 1: Proportion of 82 individuals with human immunodeficiency virus-acquired immunodeficiency syndrome according to the scores obtained in the visuoconstructive subtests of MoCA and MMSE, respectively.

Cut-off	MoCA Trail n (%)	MMSE Pentagon n (%)	x	*p*	MoCA Cube n (%)	MMSE Pentagon n (%)	x	*p*	MoCA Clock n (%)	MMSE Pentagon n (%)	x	*p*
Above	47 (57.3)	65 (73.9)	13.6	0.001	30 (36.5)	65 (73.9)	28.9	0.001	37(45.1)	65 (73.9)	18.9	0.001
Below	35 (42.7)	17 (26.1)			52 (63.5)	17 (26.1)			45 (54.9)	17 (26.1)		
	82 (100)	82 (100)			82 (100)	82 (100)			82 (100)	82 (100)		

Comparisons: Pearson's chi-squared test (Yates). **MoCA**: Montreal Cognitive Assessment; **MMSE**: Mini-Mental State Examination.

TABLE 2: Proportion of 82 individuals with human immunodeficiency virus-acquired immunodeficiency syndrome according to the scores obtained from the orientation sub-item in the MMSE and MoCA, considering the cutoff points of 10 and 6, respectively.

Cut-off	MMSE		MoCA		X^2	*p*
	n	%	n	%		
maximum	27	33	57	69.5	20.4	< 0.001
below	55	67	25	30.5		
	82	100	82	100		

Comparisons: Pearson's chi-squared test (Yates). **MoCA:** Montreal Cognitive Assessment; **MMSE:** Mini-Mental State Examination.

in the MMSE than in the MoCA, and this could be explained by the difference among the items in the respective subtests. In fact, the MoCA is composed of 5 items for evocation memory, while the MMSE has 3 items for immediate memory and 3 items for evocation memory. In this study, the maximum memory items hit rate in the MoCA was zero, while in the MMSE, it was 13%. Memory is an item of fundamental importance in cognition, especially in patients with HIV-AIDS who have asymptomatic cognitive impairment as observed by Muniyandi et al.[23] in 69% of the cases. The item memory is important in the evaluation of the tests, especially recent and prospective memory. During the performance of daily life tasks, both memories are used, and their change usually causes problems easily perceived by patients, such as unemployment in HIV-AIDS patients[24]. Regardless of whether individuals present complaints or not, this fact suggests that the memory item is clinically relevant in the final count in both tests.

Moreover, the orientation item for both tests was also analyzed in this study and showed a significant difference. Hence, it is possible to suggest that despite the differences between the two tests, they still have a positive correlation. However, other items such as trails, cube copying, and clock drawing are different to that of pentagon, justifying the different results between the tests. The trail making test is a subtest of the MoCA that can increase the diagnostic accuracy of HAND. According to Mai et al.[25], all three MoCA visuoexecutive subtests, including trails, cube copying, and clock drawing, detect more abnormalities than the MMSE pentagon copying and thus contributes to over 10-fold superiority to detect visuoexecutive dysfunction. When comparing each MoCA visuospatial item with the MMSE pentagon design, a significant difference in each comparison was observed. Hence, the difficulty in performing the MoCA visuospatial items may depend on the individual's ability to draw object shapes and the gender of the individual[26]. Although the results of the MMSE are relatively consistent with that of the MoCA, a more elaborated test in relation to some aspects of cognition, such as executive and visuospatial functions, penetrates more in the functions of the right hemisphere than in the MMSE[4,27]. On the contrary, the MoCA is questioned because it represents two different situations in its results, categories and diagnosis: several individuals meeting the criteria for HAND had better cognitive ability as measured by the quantitative MoCA than individuals classified as normal[15]. It is well known that individuals have natural difficulties in drawing figures and remembering them later. The question is whether this fact is because of a memory failure or if there is a natural inability to draw object shapes. Moreover, especially in developing countries, the degree of education acquired does not generally correspond to the content of what should be learned. This discordance arises from an important difference in the approaches taken to diagnose neurocognitive disorders on one hand and to measure cognition on the other hand[15,28].

When comparing the tests, the MMSE and the MoCA, in clinically compensated HIV-AIDS patients, the results showed that the MMSE and the MoCA are not able to detect any cognitive differences among the complainants and non-complainants groups. Several screening tools are limited with regard to detecting mild HAND (either symptomatic or asymptomatic). This might be the reason why the signal from less severe disease is significantly weak for brief tests to measure. The MoCA has good sensitivity for any or symptomatic HAND, but it has a poor specificity[18]. Cardiovascular risk factors may be associated to individuals with HIV-AIDS and can be considered a confounding factor. The MoCA is a valid

screening tool to assess post-stroke cognitive impairment; it is more sensitive but less specific than the MMSE. Contrary to the prevailing view, the MMSE also exhibited acceptable validity in this setting[11]. Both tests, assessing cognitive impairment in patients with heart failure, showed that the MoCA, a screening tool for MCI, identified subtle but potentially clinically relevant cognitive dysfunctions with greater frequency than the MMSE[12]. In this HIV-positive population, when we compared the tests in individuals with and without cardiovascular risk factors such as arterial hypertension, diabetes mellitus, dyslipidemia, and smoking, we observed that the MMSE and the MoCA showed no differences. The MoCA appeared to be a reasonable screening tool to detect cognitive impairment in HIV-positive patients, and although it is not sufficient to diagnose HAND, it has the potential to provide significant clinical data[29,30,31].

This study has limitations. First, the study includes individuals with higher schooling who were not matched with the control group. Second, the study was conducted in a single center without using a gold standard test. However, it is performed in a reference center, reducing classification error.

In conclusion, our study has added to the body of evidence encouraging the use of a screening tool in the real clinical scenario of HAND management. We suggest that the MoCA is more sensitive than the MMSE test when evaluating individuals with HAND; however, some of the categorical aspects of the MoCA can be questioned such as the diagnostic result and can be better used as an assessment of cognitive capacity[31]. Visuospatial perception and ability can be considered individual factors, which make it difficult to achieve results even in schooling individuals[28]. To assess individual aptitudes in each patient, the clinical use of the MMSE combined with the MoCA may provide better information for the diagnosis of HAND than one of the isolated tests[32]. Regardless if the MoCA could be used as a sole instrument in detecting cognitive changes in HAND[33], further investigations to better understand how a combination of cognitive tests might represent a viable alternative to a single screening tool to diagnose HAND are required.

Conflict of Interest

The authors declare that they have no conflict of interest.

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