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Mini-Mental State Examination: psychometric characteristics in elderly outpatients

ABSTRACT

OBJECTIVE: To assess the psychometric characteristics of the Mini-Mental State Examination in elderly outpatients who seek primary health care.

METHODS: A total of 303 subjects (≥65 years) underwent comprehensive geriatric assessment with functional tools, including Mini-Mental State Examination. Sensitivity, specificity, positive predictive value, negative predictive value, and ROC curve were calculated.

RESULTS: Sensitivity, specificity, positive and negative predictive values, and area under ROC curve were 80.8%, 65.3%, 44.7%, 90.7% and 0.807 respectively (cutoff point =23/24). The best cutoff point for illiterate was 18/19 (sensitivity =73.5%; specificity =73.9%); and for literate was 24/25 (sensitivity =75%; specificity =69.7%).

CONCLUSIONS: While screening elderly outpatients for dementia, schooling must be considered in the choice of the best cutoff point in the Mini-Mental State Examination.

KEYWORDS: Aging health. Health services for the aged. Cognition, classification. Neuropsychological tests. Geriatric assessment. Sensitivity and specificity. Validity.

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INTRODUCTION

It is common to find a functional disorder with major impact on daily activities as the first manifestation, and quite often unnoticed, of disease processes in the elderly.[8] In contrast, regaining and/or maintaining the quality of life is one of the main goals for clinically approaching impaired elderly patients.

The geriatric assessment consists of combining information from conventional medical history and physical examination with those obtained from a set of specific tools. These instruments help to detect impairments, plan extended care, and assess disease severity and patient's progress.[19] Of all geriatric assessment tools, those assessing cognitive status in elderly patients are outstanding. They are essentially used in specialized settings as well as part of the semiotic evaluation in less specialized health care settings.

The Mini-Mental State Examination (MMSE), developed by Folstein et al[9] (1975), is one of the most widely used and studied instruments worldwide. Either used alone or combined with more comprehensive instruments, this test allows assessing cognitive function and screening of dementia conditions.[1,3,10,11,13,15] MMSE has been applied in clinical settings for detecting cognitive impairment, dementia progress follow-up and monitoring of treatment response. In research, it has been used in population-based studies and for the assessment of experimental drug response. This test instrument has been incorporated to a series of neuropsychological evaluation tools such as The Consortium to Establish a Registry for Alzheimer' Disease (CERAD),[16] Cambridge Examination for Mental Disorders of the Elderly (CAMDEX-R)[18] and A Structured Interview for the Diagnosis of Dementia (SIDAM).[23]

From the beginning, psychometric characteristics of the MMSE have been examined both in its original version as well as in its numerous translations/adaptations to several languages and countries.[1,4,6,10,11,15,17,20,22,24] A cutoff point of 23/24 has showed to be highly adequate to identify cognitively impaired individuals.[3,21]

In Brazil, MMSE has been studied by clinicians and researchers and has been used, though still in a small number of centers, in clinical practice and scientific investigation.[1,4,6,7,13]

The present study aimed at examining criteria validity of the MMSE Portuguese version in a sample comprising elderly subjects aged 65 attending an outpatient primary care clinic. Psychometric characteristics of MMSE were assessed for ascertaining the best cutoff point for diagnosing cognitive disorders and how schooling affected this cutoff point.

METHODS

Between April 8 and July 15, 2002, a convenience sample comprising 306 subjects was selected among those elderly patients attending an outpatient primary care clinic at a university hospital in the city of Rio de Janeiro, Southeastern Brazil. After three subjects were excluded due to missing information, the study population comprised 303 elderly patients.

The study inclusion criteria were the following: 65 years old or more; hearing and understanding abilities adequate to be involved in the study; and signing an informed consent form.

The study exclusion criteria were the following: (self- or informer) reporting of uncorrected severe eye or hearing impairment or advanced cognitive disorders and/or mental diseases impairing test understanding and completion; mother language other than Portuguese; impaired hand movement due to rheumatic or neurological diseases.

A modified translated version of the MMSE, proposed by Bertolucci et al[4] and Almeida,[1] was used in the study. Some items were adapted making sure the originally MMSE developed by Folstein et al[9] was preserved in order to improve their appropriateness to specific characteristics of Brazilian culture (Table 1).

The proposed modifications were as follows:
1) in the "Space Orientation" section, the original items "State, County, Town, Hospital, Floor" were translated/adapted to "state, city, district, building where the interview is taking place and floor;" when interviewees did not know the district, they could name a nearby street or the city's area where the health unit was located;
2) original objects in "registration and naming" (Apple, Penny, Table) were replaced with "car, vase, ball";
3) in the "Attention and Calculation" section, "serial 7s subtraction" and "spelling the word world" were asked and the highest score test were recorded.

The sampling process consisted of inviting to participate in the study those patients showing up at the clinic's reception desk to make an appointment in the Internal Medicine Division. They were then asked to read and sign an informed consent form. Invitations did not follow a random sequence; all individu-

Table 1 - Mini-Mental State Examination. Back translation of the translated instrument (with modifications) proposed by Bertolucci et al.[4]

TIME ORIENTATION
What is the year? What is the season? What is the month? What is the day of the week? What is the day of the month?

SPACE ORIENTATION
What state are we? What city are we? What district are we? What building are we? What floor are we?

REGISTRATION
Now listen carefully. I'll say three words and you will name them after I have said them. Ok? The words are: CAR [pause], VASE [pause], BALL [pause]. Now you name them. [Allow 5 trials but give points only to the first one.]

ATTENTION AND CALCULATION [Serial 7s]
Now I would like you to subtract 7 from 100 and then subtract 7 from the result. Then continue to subtract 7 until I tell you to stop. Did you understand? [pause] Let's start, how much is 100 minus 7? [Give one point for each correct answer]. If the maximum score is not reached, ask: spell the word WORLD. Correct any spelling mistakes and then ask: Now, spell the word WORLD backwards. [Give one point for each letter at the correct position. Record the best result.]

RECALL MEMORY
Ask: What are the three words I asked you to memorize? [Do not give any clues.]

LANGUAGE
[Point to the pencil and watch and ask:] What is it? (pencil) What is it? (watch)
Now I'll ask you to repeat what I will say. Right? Then repeat the following: "NOT HERE, NOT THERE, NOT ANYWHERE".
Now listen carefully because I'm going to ask you to perform a task: [pause] Take this paper with your right hand [pause], then with both your hands fold it in half once [pause] and then throw it on the floor.
Please read it and do what is written in the paper. Show the examinee the paper with the following command: CLOSE YOUR EYES.
Ask: Please write a sentence. If the patient does not answer, ask: Write about the weather. [Put a blank paper and a pencil or pen in front of the patient.]
Ask: Please copy a design. [Show the page with intersecting pentagons.]

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als aged 65 or more who showed up at the front desk were asked to participate. The number of individuals enrolled each day varied according to their agreement to participate and the research team's enrollment capacity. Those who refused to participate in the study were referred back to clinic's routine care. Reasons for refusal and the characteristics of those who refused to participate in the study were not documented.

The study team consisted of two high-level research assistants (RA1) who were trained in the use of functional and cognitive assessment tools and administered the MMSE and other functional assessment tools.[12,14] In addition, subjects were evaluated by two geriatricians (RA2) who administered a structured clinical interview for diagnosing dementia that is included in CAMDEX-R[18] section A, and by two neuropsychologists (RA3) who administered the cognitive section of CAMCOG-R.[18] Since there are no studies on CAMCOG-R making recommendations on the applicable cutoff points for low schooling populations, an informal translation of this tool was used as a guide for evaluating subjects' performance and each specialist produced a report on that.

The study geriatricians had at least two-year formal training in both internal medicine and geriatrics. Also, they regularly cared for patients diagnosed with neuropsychiatric conditions in the geriatrics outpatient clinic.

All study procedures were developed and standardized by one of the authors (RAL). The study team training was divided in three steps. First, the investigator met with all research assistants to explain and discuss in details the study routine procedures.

Second, the investigator met with each RA individually for providing training in specific procedures. This same investigator trained RA1s in the administration of MMSE and activities of daily life evaluation tools.[12,14] Patient visits conducted by RA2s and all criteria of dementia syndrome used were standardized. CAMCOG-R routine procedures were standardized in a sub-sample of 10 subjects during 10 sessions.

The third step involved a three-month data collection where the main purpose was to monitor quality and standardization of interviews and evaluation tools. When there were any deviations, the case was discussed with the RA and advice on the correct procedure was provided.

No reliability test was performed to compare the level of agreement between evaluators. A reliability test-retest was carried out and will be published timely.

All test procedures were carried out in one shift and, upon completion, RA2s and RA3s would meet for discussing and establishing each subject's diagnosis (case/non-case). Therefore, the "reference test" for diagnosis of dementia syndrome was the specialists' opinion (RA2) based on their structured clinical evaluations and patient's performance in the neuropsychological test according to DSM-IV[2] and Interna-

Table 2 - Socioeconomic characteristics according to DSM-IV diagnosis of dementia (n=303). Rio de Janeiro, Brazil, 2002.

|	Total n (%)	Dementia (%)	p-value
Gender			
Male	86 (28.4)	22.1	0.360
Female	217 (71.6)	27.2	
Age group (years)			
65-69	97 (32.0)	18.6	0.039
70-74	119 (39.3)	24.4	
75-79	51 (16.8)	31.4	
≥80	36 (11.9)	41.7	
Schooling*			
Illiterate	80 (26.5)	42.5	0.000
1-4 years	139 (46.0)	26.6	
5-8 years	71 (23.5)	8.5	
≥9 years	12 (3.9)	8.3	
Marital status**			
Married	109 (36.9)	23.9	0.874
Single	29 (9.8)	27.6	
Widow	122 (41.4)	27.9	
Separated	35 (11.9)	22.9	
Retired***			
Yes	202 (69.2)	23.8	0.186
No	90 (30.8)	31.1	
Income**** (R$)			
0-200	78 (26.9)	37.2	0.001
201-600	165 (57.1)	24.8	
>600	46 (15.9)	8.7	

*1 case unknown
**8 cases unknown
***11 cases unknown
****14 cases unknown

tional Classification of Diseases (ICD-10) criteria.

MMSE results were kept in a sealed envelope to prevent the knowledge of subject's performance to affect RA2's diagnostic decision.
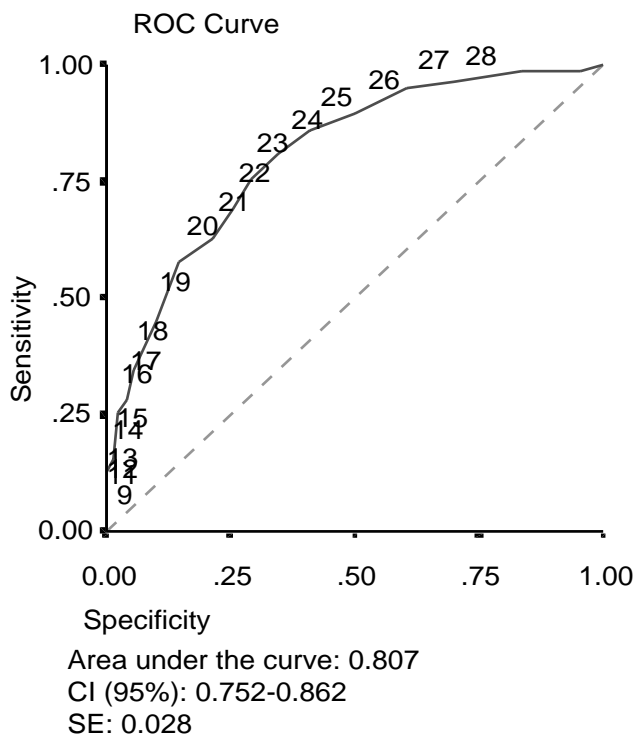
Figure - The ROC curve of Mini-Mental State Examination total scores and dementia diagnosis - DSM-IV (n=303). Rio de Janeiro, Brazil, 2002.

Table 3 - Preexisting diseases in elderly population (n=303). Rio de Janeiro, Brazil, 2002.

Diseases	Frequency	%
Systemic arterial hypertension	181	59.7
Diabetes Mellitus	57	18.8
Stroke	20	6.6
Myocardial infarction	12	4
Depression	57	18.8
Cancer	7	2.3
Parkinson disease	4	1.3

Data were entered in the Epi Info software program, version 6.04. Comparisons of frequency between categorical variables were performed using Chi-square test and mean comparison between two groups were carried out through variance analysis. For comparing means of variables with a non-normal distribution a non-parametric Kruskal-Wallis test was used. SPSS statistical package, version 9.0, was used to calculate the ROC curve, sensitivity (sen) and specificity (spe) for all the instrument's cutoff points. Positive predictive value (PV_{pos}) and negative predictive value (PV_{neg}) were estimated based on contingency tables.

The study was approved by the Institutional Ethics Committee of Pedro Ernesto University Hospital, Universidade Estadual do Rio de Janeiro.

RESULTS

Of 303 subjects studied, 217 (71.6%) were female; their mean age was 73 years (SD±5.3), median age was 72 years and mode age was 65 years. Nearly all subjects were in older age groups and almost 70% were 70 years old or more. Most of them (more than 60%) had no partners, and only 36% reported being married. Only 4.3% reported having more than eight years of schooling, and 26.4% were illiterate. Nearly 70% were retired and only 13.2% reported to be engaged in an occupation. More than 80% had a monthly income of less than three minimum wages (Table 2). No significant gender difference was found in the distribution of diagnosis of dementia (χ^2=0.8367; p=0.36).

In dementia subjects, the mean MMSE total score ± SD was 19.2±4.5 and median total score was 19.0. In non-dementia subjects, mean MMSE total score ± SD was 24.5±4.0 and median total score was 25.0. As this variable is likely to have a non-normal distribution, the Kruskal-Wallis test was used and showed significant difference between these two groups (p-value=0.000).

Table 4 - Sensitivity and specificity of the Mini-Mental State Examination at distinct cutoff points (n=303). Rio de Janeiro, Brazil, 2002.

Cutoff points	Sensitivity			Specificity		
	Total	Schooling		Total	Schooling	
		Yes	No		Yes	No
17/18	0.346	0.205	0.529	0.9417	0.966	0.870
18/19	0.449	0.227	0.735	0.902	0.944	0.739
19/20	0.577	0.341	0.882	0.853	0.927	0.565
20/21	0.628	0.432	0.882	0.787	0.882	0.413
21/22	0.692	0.523	0.912	0.747	0.854	0.326
22/23	0.756	0.568	1	0.711	0.826	0.261
23/24	0.808	0.659	1	0.653	0.764	0.217
24/25	0.859	0.750	1	0.591	0.697	0.174
25/26	0.897	0.818	1	0.498	0.590	0.130

Schooling in dementia and non-dementia subjects had a median of 1 and 4, and a mean of 1.89±2.48 and 3.75±3.13 respectively (F=22.739; p-value=0,000). Table 2 shows the statistical values of other variables in these two groups.

Table 3 shows the frequencies of reported preexisting diseases. Prevalences of dementia syndrome in the study sample according to DSM-IV[2] and ICD-10 criteria were 25.7% and 15.2% respectively.

The Figure illustrates MMSE sensitivity and specificity at different cutoff points. The estimated ROC curve had an area under the curve of 0.807 (95% CI: 0.752-0.862).

Performance assessment in the MMSE showed the following values at cutoff point of 23/24: sen=80.8%, spe=65.3%, PV_{pos}=44.7% and PV_{neg}=90.7%. However, in the general population, the best equilibrium cutoff point would be of 22/23, where sen=75.6%, spe=71.1%, PV_{pos}=47.6% and PV_{neg}=89.4% (Table 4).

Stratification by levels of schooling revealed that, of those 78 subjects diagnosed with dementia, only seven had more than five years of schooling (n=6, five to eight years; and n=1, nine years or more). Because of that, the sample was divided in two subgroups: illiterate and educated. The best cutoff point detecting cognitive disorders in illiterate subjects was 18/19; and in those educated, the best cutoff point was 24/25 (Table 4).

When ICD-10 was used as a criterion, at the cutoff point of 23/24, sensitivity was 80.8%, specificity was 60.3% and the area under the ROC curve was 0.816 (95% CI: 0.753-0.879).

DISCUSSION

MMSE has been widely studied throughout its 30 years of existence. Its structure and psychometric characteristics have been extensively reviewed and many translations and cultural adaptations have been produced as well.

In Brazil, investigators[1,4] have suggested literally translating most MMSE items, such as those assessing time orientation (except for "season of the year"), attention and calculation, object naming, understanding of spoken and written commands as well as those assessing writing and visual-spatial abilities. But these authors had also suggested that other items be adapted as they were not appropriate to cultural characteristics of Brazilian population. Nevertheless, some of these suggestions are still being discussed: How assessment of time and space orientation can be improved? What are the most adequate words for registration and recall? What is the best sentence to be repeated?

In the present study the translated tool by Bertolucci et al[4] and approved by Almeida[1] was found to be largely appropriate but some modifications were needed. On one hand, it was more consistent with Folstein et al's[9] original propositions; for instance, the choice of widely used simple two-syllable words for learning and recall. On the other hand, a few inadequate choices were changed such as the use of "semester" instead for time orientation. This division of the year is basically part of the collective school learning and so it is not familiar to most individuals seen at public health services, as those selected to participate in this study.

A negative aspect of the present study was that the evaluation tool, informally translated/adapted by the before mentioned authors,[1,4] has been accepted. The fact no study has so far addressed the important issue of using adequate methodology for transculturally adapting this instrument perpetuates a number of issues concerning informal adaptations. Also, as the present study did not include these issues in its objectives, they are still untackled.

Various Brazilian authors have studied psychometric characteristics of the MMSE. To assess cognitive performance of those seeking care in a hospital's medical triage service, Bertolucci et al[4] administered the

MMSE to 530 patients. There were found distinct cutoff points for diagnosis of cognitive impairment according to schooling: 13 for illiterate, 18 for low to intermediate schooling and 26 for high schooling, with 82.4%, 75.6%, and 80% sensitivity and 97.5%, 96.6%, and 95.6% specificity respectively. These cutoff points have been widely accepted by some authors and services. However, methodology issues related to the study design showed their main findings needed to be reviewed.

These issues were summarized by Almeida[1] as follows: a) it was not possible to establish whether some individuals out of 530 assessed in the screening had dementia; b) 70 out of 94 controls for cognitive impairment were diagnosed with delirium but not dementia; c) most interviewees aged less than 60 years; d) study controls were not psychically assessed.

Similarly, aiming at exploring the best cutoff point in MMSE for the elderly and the impact of age and schooling on this population's scores, Almeida[1] (1998) studied 211 subjects aged 60 years or more seen in a mental health outpatient clinic. They were systematically assessed using SRQ-20, MMSE and a clinical interview for diagnosis of dementia according to ICD-10 criteria. After comparing scores of dementia and non-dementia patients, Almeida[1] concluded that distinct cutoff points according to patient's past school experience were required. A cutoff point of 19/20 (80.0% sensitivity and 70.9% specificity) for those elderly without schooling and a cutoff point of 23/24 (77.8% sensitivity and 75.4% specificity) for those with past school experience proved to be more adequate. Almeida[1] also concluded that "... it would be advisable to replicate the study findings in other groups of (non-psychiatric) patients and in those living in the community as well".

Brucki et al[6] (2002) made recommendations for the use of MMSE in Brazil. They assessed 433 subjects, of which 289 were escorts of patients attending a neurology outpatient clinic in a general hospital and 144 were randomly selected from a sample of an epidemiological study carried out in the city of Catanduva, Southeastern Brazil; 222 subjects had 65 or more years. Once more it was found schooling was a major factor affecting performance. Bruck et al[6] suggested that those subjects with MMSE scores lower than 20, 25, 27, 28 and 29 – in illiterate, 1 to 4, 5 to 8, 9 to 11, and 12 or more years of schooling respectively –, should undergo a more in-depth cognitive and functional assessment.

As it was said before, psychometric characteristics of the MMSE in Brazil have been assessed thus far in mental health outpatients or patients from various

health care services.[1,4,6] Yet, given its characteristics, MMSE can be a valuable tool mostly for cognitive screening of elderly populations without a prior diagnosis of cognitive disorders, i.e., those seeking care in primary care outpatient clinics.

In this sense, the performance examination of patients seen in primary care outpatient offices and clinics, together with methodological considerations and Almeida's findings[1] (1998), indicate a need for studying psychometric characteristics of the MMSE in this particular population group.

Table 4 clearly shows the impact of schooling on distinct MMSE cutoff points. Although not reported, when schooling was divided into more subgroups (for example, four-year subgroups), sensitivity and specificity remained the same, and sometimes even greatly affected by the small number of "cases" identified. Accordingly, specific cutoff points for two age groups, very close to those found by Almeida,[1] also showed to be adequate in this outpatient sample studied.

Major socioeconomic differences were found between those with dementia and those with no cognitive impairment, concerning the variables age group, schooling and income. As for age group, aging is likely the major risk factor for dementiating diseases and for that reason it is well recognized and explored in the international literature.[21] Similarly, it is recognized the relationship between dementia, income and schooling, all variables interrelated in a complex manner. Years of schooling have been seen as a neuronal protection factor as well as a misdiagnosis factor since the performance of individuals assessed through cognitive assessment instruments is highly affected by schooling. In contrast, behaviors that are risk factors for dementiating diseases are often seen among those individuals with lower schooling, lower income and poor access to goods and services.[20-22]

In regard to diagnostic approaches of dementia syndrome, CAMCOG has been a neuropsychological evaluation tool increasingly used in some Brazilian centers and its administration guidelines and validity have been discussed. Although efforts have been made for CAMCOG validation in Brazil,[5] there are no standard data available for its consistent use as a reference evaluation tool for diagnosis of dementia.

Hence, CAMCOG-R cutoff points, set for different realities than that of Brazil, could not be applied. But the perception of individual's performance in the evaluation test has added to clinical data a set of key information for making a diagnosis according to set criteria.

During case discussions, those providers involved in establishing the diagnosis exchanged their impressions and this could be further investigated as a valid model for diagnostic management.

The confirmation of existing cognitive, behavioral, functional and occupational disorders by a reliable informer (caregiver, relative, friend or others) is part of diagnostic criteria proposed by several international organizations, including that of the present study.[2] Not having this procedure in the present study is certainly a limitation and might have resulted in diagnostic misclassification.

However, the "gold standard" will be a broad geriatric assessment and mid- and long-term follow-up of these individuals for diagnostic confirmation. An interview with a close informer, providing new information and validating that reported in the initial interview, is key for clinical follow-up. It is thus suggested that current results be reviewed within reasonable time, long enough to allow for diagnostic confirmation but making sure preliminary results are not affected by new cases.

In conclusion, the present study recommends that, for cognitive screening of elderly populations in outpatient primary care units, MMSE should be used at the cutoff points of 18/19 and 24/25 according to having or not prior formal education respectively.

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