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ARTICLE

Educational bias in the assessment of severe dementia: Brazilian cutoffs for severe Mini-Mental State Examination

Viés educacional na avaliação da demência grave: pontos de corte brasileiros para o Miniexame do Estado Mental grave

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ABSTRACT

Cognitive assessment in advanced stages of Alzheimer's disease (AD) is limited by the imprecision of most instruments. **Objective:** To determine objective cognitive responses in moderate and severe AD patients by way of the Severe Mini-Mental State Examination (SMMSE), and to correlate performances with Mini-Mental State Examination (MMSE) scores. **Method:** Consecutive outpatients in moderate and severe stages of AD (Clinical Dementia Rating 2.0 or 3.0) were evaluated and compared according to MMSE and SMMSE scores. **Results:** Overall 400 patients were included, 67.5% females, mean age 76.6±6.7 years-old. There was no significant impact of age or gender over MMSE or SMMSE scores. Mean schooling was 4.4±2.5 years, impacting SMMSE scores (p=0.008). Scores on MMSE and SMMSE were significantly correlated (F-ratio=690.6325, p<0.0001). **Conclusion:** The SMMSE is influenced by schooling, but not by age or gender, and is an accurate test for assessment of moderate and severe AD.

Keywords: Alzheimer disease, dementia, cognition disorders, neuropsychological tests.

RESUMO

A avaliação cognitiva na doença de Alzheimer (DA) avançada é insuficiente pela imprecisão dos instrumentos. **Objetivo:** Determinar respostas cognitivas objetivas em pacientes com DA moderada e grave por meio do Mini-Exame do Estado Mental Grave (MEEM-g) e correlacionar o seu desempenho com o Mini-Exame do Estado Mental (MEEM). **Método:** Pacientes consecutivos com DA moderada e grave (*Clinical Dementia Rating* – CDR: 2.0 e 3.0) foram avaliados e comparados conforme seus intervalos nos testes MEEM e MEEM-g. **Resultados:** Dentre 400 pacientes incluídos, 67,5% foram mulheres, com média de idade 76.6±6.7 anos. Não houve impacto significativo de gênero ou idade nas pontuações do MEEM ou MEEM-g. A escolaridade média foi de 4.4±2.5 anos, impactando nos escores do MEEM-g (p=0.008). Pontuações no MEEM e MEEM-g correlacionaram-se significativamente (F-ratio=690.6325, p<0.0001). **Conclusão:** O MEEM-g sofre influência da escolaridade, mas não de idade ou gênero, contribuindo para a precisão na avaliação da DA moderada ou grave.

Palavras-chave: doença de Alzheimer, demência, transtornos cognitivos, testes neuropsicológicos.

It has been estimated that over two thirds of community-dwelling patients diagnosed with Alzheimer's disease dementia (AD) in low-income and middle-income countries are in moderate and severe stages[1], and almost 60% of inpatients with AD have been graded at such stages[2]. Given the inevitable cognitive decline of the AD patient from mild to moderate and ultimately to severe stages of the disease, clinicians are faced not only with the challenge of defining the proper treatment regimen, but also with the need for accurate assessment of their cognitive status[3].

Several cognitive tests for patients in severe dementia stages have been developed in the past, such as the Test for Severe Impairment (TSI)[4], the Modified Ordinal Scales of Psychological Development (MOSPD)[5], the Severe Cognitive Impairment Profile (SCIP)[6] and the Severe Impairment Battery (SIB)[7]. The need for special training and specific materials notwithstanding, the impact of schooling on these scales has not been properly addressed; thus, there is a clear need for proper neuropsychological instruments for patients in late stages of AD, particularly in Brazil.

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The Severe Mini-Mental State Examination (SMMSE)[8] was designed for assessment of severe dementia. This test is based on the original Mini-Mental State Examination (MMSE)[9] ; however, it includes simpler commands and questions related to autobiographical knowledge (birth date and complete name), constructional praxis tests, phonological loop (spelling) and a semantic verbal fluency step (animal category generation). The score ranges from 0 to 30 and, like the original MMSE, it is a pencil and paper test which takes an average of 5 minutes to be completed. The SMMSE also tests receptive and expressive language skills, along with elementary executive functions and visual-spatial abilities, which are likely to be preserved in severely impaired patients.

According to earlier Brazilian studies, educational levels impact MMSE scoring[10,11] ; therefore, it would be important to evaluate the impact of education over SMMSE scores as well. The aim of this study was to determine objective cognitive responses in moderate and severe AD patients by way of the SMMSE, and to correlate performances with MMSE scores, providing cutoff ranges for accurate assessment and monitoring of these patients.

METHOD

Participants

According to Clinical Dementia Rating (CDR)[12,13] scores, four hundred outpatients (N=400) with moderate and severe AD were consecutively recruited from the Departamento de Medicina Comportamental of the *Universidade Federal de São Paulo*, in Sao Paulo, Brazil, between November 2008 and February 2013. All patients met Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[14] diagnostic criteria for probable Alzheimer's disease. On all occasions, a written explanation of the research design was read to the patient by the main researcher or the primary family caregiver and additional explanations were given when necessary, after which an informed consent was signed. All proceedings were approved by the Ethics Committee of *Hospital São Paulo, Universidade Federal de São Paulo* (registration no. 1298/03).

This was a cross-sectional study and, in order to avoid biases or inter-rater variations, the same appropriately trained neuropsychologist (JRW) and clinical neurologist (FFO) were responsible for conducting all cognitive tests in all included patients. An analysis of internal consistency among raters was not carried out, considering that the reliability had already been established in the original study with correlation between scores of 0.99, or $p<0.0001$ [8]. In parallel, functional aspects of staging were evaluated by associated medical staff in an attempt to keep cognitive raters blind to the functional status of patients, and vice-versa. We did not include patients who did not spend time with the same caregiver at least four days per week, patients who had uncorrected visual or auditory deficits that could affect their evaluation (inadequate or unsuited prostheses), and patients with history of cerebrovascular events (ischemic or hemorrhagic strokes) in the 12 months preceding the neuropsychological assessment.

Procedures

With regard to the cognitive evaluation, all participants were assessed by way of MMSE and SMMSE, along with the CDR. Sessions were always conducted in the same room, by the same interviewers and without outside interference. For adaptation of the SMMSE to the Brazilian Portuguese language, standard methods of translation, back translation and adaptation by bilingual clinical staff were adopted. More information about this project and its preliminary results can be found in the original article related to standardization of the SMMSE for the Brazilian Portuguese language[15].

Despite the briefness of each individual assessment (about 50 minutes), whenever fatigue, anxiety or nervousness were noticed the test was interrupted until the subject was relieved, and the testing proceeded only after the subject calmed down, also considering the possibility of postponing the end of the assessment up until the next visit.

Data Analysis

A descriptive analysis was employed for all subjects with regard to gender, age at examination, schooling, MMSE scores and SMMSE scores, according to CDR scores 2.0 or 3.0. A simple linear regression was used for comparisons between MMSE and SMMSE scores. An adjusted linear regression was employed for MMSE and SMMSE scores (dependent variables) in relation to gender (0 for men and 1 for women), age at examination and schooling as independent variables.

Additionally, we performed the t-test to investigate whether there were differences regarding age, schooling, MMSE scores or SMMSE scores between genders, and also if there were schooling or age differences between CDR scores (2.0 or 3.0). The Chi-square test was employed for evaluation of differences between genders among moderately and severely impaired patients. The threshold of significance was set at $p<0.05$.

RESULTS

Demographic and clinical data

For all patients (N=400), mean age at examination was 76.68±6.7 years-old (range 60-95), mean schooling was 4.4 ±2.5 years (range 0-11), mean MMSE score was 10.49±3.9 (range 1-18), and mean SMMSE score was 23.07±5.5 (range 8-30). Table 1 discriminates subjects according to

Table 1. Results according to Clinical Dementia Rating (CDR) scores.

CDR scores (gender)	n	Age at examination (years)			Schooling (years)			Mini-Mental State Examination scores			Severe Mini-Mental State Examination scores		
		Mean	SD*	Range	Mean	SD*	Range	Mean	SD*	Range	Mean	SD*	Range
2.0 (all subjects)	254	76.62	6.6	60-95	4.32	2.4	0-11	12.55	2.7	2-18	25.96	3.5	12-30
2.0 (females)	166	77.36	6.6	61-95	3.95	2.3	0-11	12.54	2.9	2-18	25.89	3.6	12-30
2.0 (males)	88	75.23	6.4	60-88	5.02	2.6	0-11	12.57	2.2	7-18	26.11	3.3	16-30
3.0 (all subjects)	146	76.78	6.9	60-90	4.54	2.7	0-11	6.90	2.9	1-17	18.05	4.7	8-30
3.0 (females)	104	77.07	6.8	60-90	4.59	2.8	0-11	6.86	2.9	1-17	17.82	4.5	8-30
3.0 (males)	42	76.07	7.0	60-90	4.43	2.5	0-11	7.02	2.8	2-14	18.60	5.2	8-29

*SD=standard deviation.

Clinical Dementia Rating scores (2.0 or 3.0) with regard to gender, age at examination, schooling, MMSE scores, and SMMSE scores.

Overall, female patients were older than male patients (p=0.0156), but males had higher schooling than females (p=0.0205). Nevertheless, there were no differences regarding age (p=0.0816) or schooling (p=0.4111) between moderately and severely impaired patients. Likewise, there were no differences regarding MMSE scores (p=0.3003) or SMMSE scores (p=0.1265) between genders. There were no differences between proportions of males and females according to CDR scores 2.0 or 3.0 (X^2=1.46; p=0.227).

Neuropsychological data

Results from the adjusted linear regression for each of the listed dependent variables (MMSE and SMMSE) in relation to gender, age at examination and schooling are presented in Table 2. The regression was significant for the SMMSE (p=0.009) regarding education (p=0.008), translating into an increase of 0.29 points in the SMMSE for each increase of one year in schooling; results were also marginally significant for age at examination (p=0.075). Also on the SMMSE model, gender, age and education explained 2.2% of the variation in the test (adjusted squared multiple R=0.022). The regression was not significant for the MMSE (p=0.364); therefore, gender, age and education did not interfere in the MMSE scores.

A scatterplot (Figure) was elaborated for correlations between MMSE and SMMSE scores. A simple linear regression was significant for such correlations (F-ratio=690.6325, p<0.0001): variability in each test explained 63.4% of the variability in the other (squared multiple R=0.634).

DISCUSSION

Our results have shown that the SMMSE is strongly influenced by schooling; the same result was demonstrated for the MMSE in previous studies[16]. Furthermore, our results suggest that patients in moderate and severe stages of AD keep displaying objective cognitive responses in test performance. In view of the simplicity of the SMMSE, health professionals may be easily trained to use it in combination with the MMSE for cognitive assessment up until the time when patients become more severely affected.

The relevance of these results relies on the fact that about two-thirds of all patients with dementia live in the

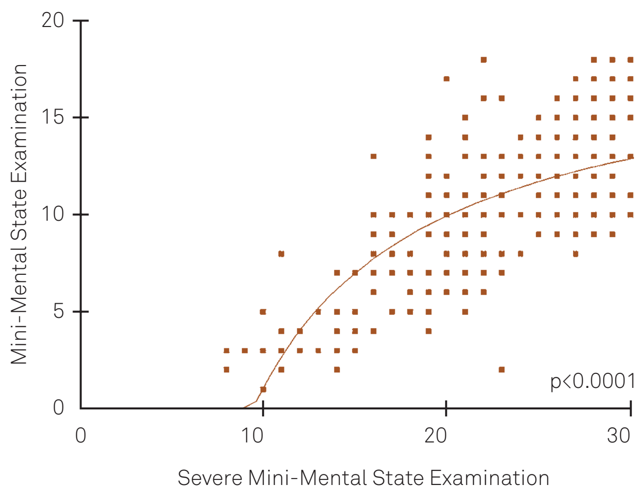

Figure. Correlations between Mini-Mental State Examination and Severe Mini-Mental State Examination scores.

Table 2. Results from the adjusted linear regression*.

Variable	Coefficient	Coefficient for age at examination	Coefficient for schooling	Coefficient for female gender	Adjusted squared multiple R	F-ratio	p-value for the regression
Mini-Mental State Examination	7.525 (p=0.001)	0.042 (p=0.147)	0.010 (p=0.897)	-0.497 (p=0.235)	<0.001	1.065	0.364
Severe Mini-Mental State Examination	16.727 (p<0.001)	0.074 (p=0.075)	0.290 (p=0.008)	-0.847 (p=0.151)	0.022	3.946	0.009

*Adjusted linear regression for each of the listed dependent variables (Mini-Mental State Examination or Severe Mini-Mental State Examination) in relation to the following factors: gender (male=0, female=1), age at examination (years-old) and schooling (years).

developing world, mostly part of populations with low schooling[17]. Nonetheless, most cognitive measures were designed for people with high educational levels. Thus, there is a need for cultural adaptations in many low and middle income countries in order to compensate for the educational and cultural biases of the original versions[16,18]. In accordance with this situation, several studies have demonstrated that cognitive performance in screening tests is directly influenced by sociodemographic variables such as age and education[19-21]. To the best of our knowledge, this is the first study to analyze the SMMSE in a Brazilian population with low schooling and, taking into account the considerable sample size, our results emphasized the need for culturally adapted tests to be used in this setting.

Considering correlations between scores and demographic variables, schooling had no impact over MMSE scores. Several factors might have contributed to this difference. The main reason for this finding is possibly the fact that we included only patients in moderate and severe stages of dementia, situations in which the cognitive performance does not depend on factors like previous formal education, but on functional aspects. In this regard, the influence of schooling over MMSE scores may be better understood by a phenomenon known as "floor effect" (extremely low performance or, in this case, nearing zero). Moreover, our sample differed from the original[8] and previous SMMSE articles with regard to sample size. No published studies correlating both tools, MMSE and SMMSE, had ever included more than two hundred patients. On the other hand, an explanation for the significant correlation between SMMSE and schooling may also be due to the extent of scores (8-30, while the amplitude of the MMSE was 1-18), demonstrating that patients reached the highest SMMSE scores while not reaching higher MMSE scores, and implying greater sensitivity of the SMMSE for moderate and severe AD stages.

Different mechanisms have been proposed to explain the possible relationship between low education and cognitive decline, such as the lower brain reserve hypothesis, the lack of occupational activities leading to lower intellectual demands, and low cognitive stimulation throughout life[22]. An alternative proposal for enhancement of our results would be to conduct the same assessment over time in a more representative cohort to yield more reliable evidence of subject profiles, besides considering other social and demographic features which might be typical of developing countries[23].

Previous studies on the relationship between education and neuropsychological performance in Brazilian elderly suggest the need of using specific cutoff scores, which should be adjusted for each level of schooling. For instance, brief cognitive tests such as the category fluency (CF test)[24] and the Cambridge Cognitive Examination (CAMCOG)[25] are widely used for dementia screening, but may require new cutoff values for patients with low schooling. Both studies included wide samples, but none of them included severely impaired AD patients.

Bearing in mind the increase in life expectancy of the elderly in developing countries such as Brazil, the escalating survival of dementia patients, and the advent of new therapeutic trials, the need for proper instruments of dementia assessment will be increasingly crucial. In this perspective, our findings suggest that, together with the traditional MMSE, the SMMSE may be a valid instrument for assessing patients in later stages of dementia, taking into account its advantages over other batteries, particularly its briefness and ease of application.

Some limitations of this research require mentioning. First, while the CDR was employed for staging of dementia severity, there are other scales that serve the same purpose, and results could be different with these other tools. However, given the initial purpose to discriminate between moderate and severe stages, the chosen scale proved to be a proper measure for patient staging. In addition, taking into account the heterogeneity of the Brazilian population (especially in a city like Sao Paulo, with continental proportions), even considering the wide diversity in levels of schooling, our findings may not be generalizable to the whole population of Sao Paulo. In this sense, similar studies should be coordinated by specialized and referenced teams intending to corroborate such data.

In conclusion, in the same way that the MMSE is a proper instrument for evaluation of mildly impaired patients, we found the SMMSE to be an adequate alternative to assess AD patients in moderate and severe stages, even considering variations in their educational levels. Further studies are required to determine which particular items on the SMMSE are more specific and sensitive to cognitive change during AD progression, as well as to compare its scores with other cognitive protocols and functional scales[26], and also to rate the influence of neuropsychiatric symptoms[27] over its scoring system, a particular aspect that might favor more objective therapeutic strategies[28].

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