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Sensitivity and specificity of the Mini-Mental State Examination in the Mexican population

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Abstract The Mini-Mental State Examination (MMSE) is a rapid, easy-to-administer test for the assessment of cognition functions. It is widely used in clinical practice and in applied research. In this study, we aimed to establish a standard for the Mexican population similar to the ones produced for other relevant populations. We also analysed the effects of demographic variables which regularly induce bias in responses on performance tests, and then, on the basis of the results, implemented a series of corrections to the MMSE to compensate for the usual effects of age and years of formal education. We thus generated a new scale, the adjusted MMSE (AMMSE). We established the maximum sensitivity point to discriminate between the normal population and subjects diagnosed with dementia (vascular and Alzheimer's). The study provides sensitivity and specificity estimates of this subject-standardized tool in order to reduce the probability of false positives and negatives in the Mexican population.

Keywords Mini-Mental State Examination · Mexican population · Standardization

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1 Introduction

The Mini-Mental State Examination (MMSE) (Folstein et al. 1975) is well known and widely used in clinical practice in neuropsychology (Patten and Fick 1993). In applied research, it tends to be one of a series of assessment procedures used. Several reports have used this rapid test as a baseline measure to obtain reliable diagnoses when cognitive impairment is suspected (Flaks et al. 2006; Hughes et al. 1996; Tombaugh and McIntyre 1992). The MMSE has many well-known benefits, particularly its rapid application and high sensitivity and specificity in relation to cognitive dysfunctions (Woodbury and Fillenbaum 1996). Moreover, the values reported in several psychometric studies have shown the MMSE to be a perfectly valid and reliable test (Ferrell et al. 2000; Newkirk et al. 2004; Woodbury and Fillenbaum 1996).

Consequently, in recent years, reports of standardizations for several populations have proliferated. The widespread use of inappropriate criteria has caused evident measurement biases. The normalization of this test in the Spanish population (Bird et al. 1987; Blesa et al. 2001; Cobb et al. 1993) and in other cases (for instance, research in the Brazilian population by Lourenço and Veras 2006) has allowed the empirical identification of effects related to age and years of education. Indeed, as in other performance tests, the effects of these variables are known but they are not always taken into account when calculating the final scores. In the case of the MMSE, the need for corrections has been reported elsewhere (Blesa et al. 2001; Crum et al. 1993), and indeed corrections have been introduced in the norms used for the Spanish population and for other similar populations (Jones et al. 2002; Rosselli et al. 2006; Serra and Peña 2006). However, these standards may not be appropriate in the Mexican population.

An added complication is the fact that the target populations for tests of this kind are usually elderly subjects with cultural characteristics that differ widely from country to country, even within the same geographic region. The data available suggest that the implementation of the MMSE must bear in mind specific ethnic and socio-cultural aspects of the population under consideration (Escobar et al. 1986; Rowland et al. 2006), specially those related with the bias introduced by the age distribution of the analyzed population (Ferrell et al. 2000; Pi et al. 1994; Rizzolo et al. 1991).

We hypothesize that the effect of age and years of education generates bias and error in the estimation of the MMSE score. In this paper, we intend to establish the MMSE standard for the Mexican population. That is to say, we aim to study the effect of the variables age and years-of-formal-education on the scores obtained. We then introduce corrections, in order to produce a standardized instrument for interpretation of the MMSE for the Mexican population with scores that are not biased by these variables. The new version is called the AMMSE (the Adjusted Mini-Mental State Examination). Our second aim is to study the sensitivity and specificity of the AMMSE and to establish valid cut-off points by considering its maximum ability to discriminate between normal subjects and those diagnosed with dementia (either vascular or Alzheimer's).

2 Method

2.1 Participants

A total of 691 subjects were evaluated in diverse aspects of the neuropsychological dimensions at the Hospital Civil of Guadalajara (Mexico) as a consequence of routine clinical examinations. After neurological diagnosis by the hospital's clinical staff; two samples were

Table 1 Description of the principal variables

Demographic variables	Normal	Dementia
Gender		
Man (%)	44.80	34.40
Woman (%)	55.20	65.60
Age		
Mean	74.240	78.75
Standard deviation	8.522	10.181
Range	50–99	62–94
Years of formal education		
Mean	3.440	1.50
Standard deviation	3.494	1.512
Range	0–17	0–4
MMSE Scores		
Mean	24.62	18.38
Standard deviation	3.893	6.413
Range	6–30	5–25

identified: a group of normal subjects or controls ($n = 344$) with no neurological deficit and another group with diagnoses of either vascular or Alzheimer's dementia ($n = 61$, with scores 4 or 5 in Reisberg's Scale). All the dementia diagnostic procedures were conducted by the hospital's neurological clinical service with neurological anamnesis and evidence from neuroimaging techniques (though the latter were not available for all participants). The sample was recruited in a clinical setting and all participants were volunteers. The remaining subjects ($n = 286$) were excluded from the study because they showed signs of other diagnoses which were irrelevant for this study. The descriptive statistics (percentages, means and standard deviation) of the two samples are shown in Table 1. The table shows statistically significant differences between the two samples in years of formal education ($t = 7.212$; $p < 0.001$) and, obviously, in the MMSE values ($t = 5.9123$; $p < 0.001$). The unilateral analysis shows higher mean values in the normal group for both variables. In accordance with the bibliography (Ostrosky et al. 2000), these results suggest that the MMSE raw score must be corrected in order to eliminate the influence of the age and, also, the years of education.

2.2 Instruments

An earlier Spanish translation of the MMSE (Blesa et al. 2001) was adapted to Mexican Spanish to reduce possible misunderstandings. To evaluate whether this process could significantly alter the contents of the test, the translation was examined by Mexican experts in psychometrics and also in neurology. No special cultural differences were found in the two versions (European Spanish and Mexican Spanish) and the agreement coefficient between the experts consulted was 0.97. Ultimately, the adaptation consisted of small, specific semantic changes (for instance, the original adjective *'quieto'* was changed to *'parado'* in the Mexican version). Each participant was assessed with this version of MMSE and the *Programa Integrado de Evaluación Neuropsicológica* (PIEN Test, Barcelona) with normalization by Peña

Table 2 Parameter estimation of the linear regression model components (Determinant Coefficient $R^2 = 0.793$)

	Non-Standardized Coefficient		t-test	Sig.
	B_i	Standard Error		
Constant	31.700	1.747	18.145	<0.001
Years of education	0.284	0.056	5.036	<0.001
Age	−0.109	0.023	−4.693	<0.001

B_i Regression coefficient, *Sig.* Significance

(2004). The complete profile of the PIEN was obtained as a neuropsychological assessment and a MMSE raw score was recorded for use in further analysis.

2.3 Procedure

Informed consent was obtained from all patients who met the inclusion criteria. PIEN and MMSE tests were conducted between January 2004 and December 2006 by an ad hoc trained psychologist in the Hospital Civil de Guadalajara (Mexico) who was not involved in the initial diagnostic procedure of normality or dementia.

Due to the academic level of the majority of the sample, the test administration was completed, for some participants, by verbally instructions and the responses were recorded by the psychologist. Finally, all statistical analyses (correlation, reliability estimation, linear regression, logistic estimation of odds ratio and ROC curve estimation) were carried out with the SPSS/PC + 15.0.

3 Results

The psychometric properties of the scale were obtained with all the study sample ($n = 405$). The evaluation of intraclass correlation yielded a value of $r = 0.88$ ($p < 0.001$), which indicated a more than acceptable internal reliability, while the correlation coefficient in cross-validation was $r = 0.92$ (confidence interval between 0.89 and 0.95 with a 94% confidence level). The internal stability of the measurements obtained was therefore satisfactory. Convergent validity could not be determined because concurrent measurements were unavailable for the dementia samples, meaning that no correlations between the tests (MMSE and PIEN) could be established. The clinical profile of the PIEN guaranteed concordance with the MMSE classification criteria for dementia but, due to the presence of missing data in the pathological sample, no statistical evidence was obtained.

As regards the standardization process, the effects of years of education and age on MMSE raw scores were analysed. Partial regression coefficients from a linear model were calculated. The model considered age and years of formal education as exogenous variables and the MMSE raw value as an endogenous variable. The results of the regression analysis are shown in Table 2.

In accordance with the results presented by Ostrosky et al. (2000) in a Spanish sample, our results indicate an evident effect of age and years of education on the MMSE score. Nevertheless, our study is based on the original form of the MMSE with no new items on the scale (only items adapted for linguistic reasons, from Blesa et al. 2001), unlike other versions of MMSE applied to Mexican samples. The sampling technique used here was applied exclusively to the clinical population. In fact, the general aim of this paper is not strictly a

Table 3 Corrected Coefficients derived from the regression parameters in order to obtain the AMMSE score

	Age ≤ 59	60 to 69	70 to 79	80 to 89	Age ≥ 90
Up to 6 years in school	0	1	2	3	3
More than 6 years in school	0	0	1	2	3

AMMSE Adjusted Mini-Mental State Examination

Table 4 Descriptive indicators of the groups in AMMSE

Diagnosis	n	Mean	SD	SEM
Control	344	27.17	3.645	0.197
Dementia	61	19.79	5.625	0.720

n Sample size, *SD* Standard Deviation, *SEM* Standard Error of Mean

psychometric assessment of the MMSE, since we also intended to provide clinicians with an objective screening scale that is free of measurement error.

The differences between the two groups (normal and demented participants) in relation to the years of formal education suggest that the low educational level of the demented group may be confounded with their poor performance on the MMSE. In order to separate these two effects, we carried out independent estimation procedures for each variable. With this statistical technique, we made sure that we would obtain a direct estimation of the two effects.

The comparison between the coefficients in Table 2 and the ones obtained by Blesa et al. (2001) following the same statistical procedure indicates that the correction factors are different for the two populations. To correct the effect of age and years of education in the Mexican sample, coefficient values (B_i) for these two variables without considering the coefficient for the constant term) were used to estimate the odds ratios for each effect according to the procedure derived from the logistic regression model. In fact, these values explain how a change in a unity in either age or years of education affects the raw MMSE score. In our samples, the odds ratios were $OR_{AGE} = 1/0.284$ for the age variable, and $OR_{EDUCATION} = 1/-0.109$ for years of education. Since the coefficients have opposite signs and are in accordance with their direction, we established that the variables presented opposite effects on the MMSE scores (age presented a negative effect, whereas years of education showed a positive effect). With the estimated odds ratios, and combining the positive effect of education and the negative effect of age, we derived the corrective coefficients for the MMSE raw score. These values for the correction are shown in Table 3; each cell shows the value that we must add to the MMSE raw score in order to obtain the corrected AMMSE score.

Using the above table, we obtained corrected MMSE scores for age and years-of-education effects. This new Adjusted Mini-Mental State Examination (AMMSE) score was distributed with a positive bias (mean = 26.81, SD = 4.087, Kolmogorov-Smirnov test with $p = 0.001$) and showed a high correlation with the original values (r = 0.891, $p < 0.001$). This last result suggests that the AMMSE retained the psychometric properties of the MMSE. Statistically significant differences in the AMMSE mean values ($t = 66.194$; $p = 0.001$; effect size r = 0.64—derived from Cohen's d) were obtained between the normal and dementia groups (see Table 4).

The intensity of the effect (r = 0.64) indicated a substantial discrimination capacity between the normal and dementia groups. To assess the effect's relevance, we considered the estimation of a cut-off point of the original value in the clinical diagnosis of the patients and

Table 5 Values of sensitivity and specificity of MMSE and AMMSE in order to obtain the cut-off point

	MMSE Sensitivity	MMSE Specificity	AMMSE Sensitivity	AMMSE Specificity
20/21	0.302	0.897	0.310	0.868
21/22	0.307	0.877	0.316	0.871
22/23	0.437	0.861	0.423	0.858
23/24	0.608	0.851	0.628	0.849
24/25	0.823	0.849	0.843	0.831
25/26	0.868	0.802	0.901	0.780
26/27	0.975	0.799	0.907	0.745
27/28	0.981	0.684	0.989	0.712

MMSE Mini-Mental State Examination, *AMMSE* Adjusted Mini-Mental State Examination

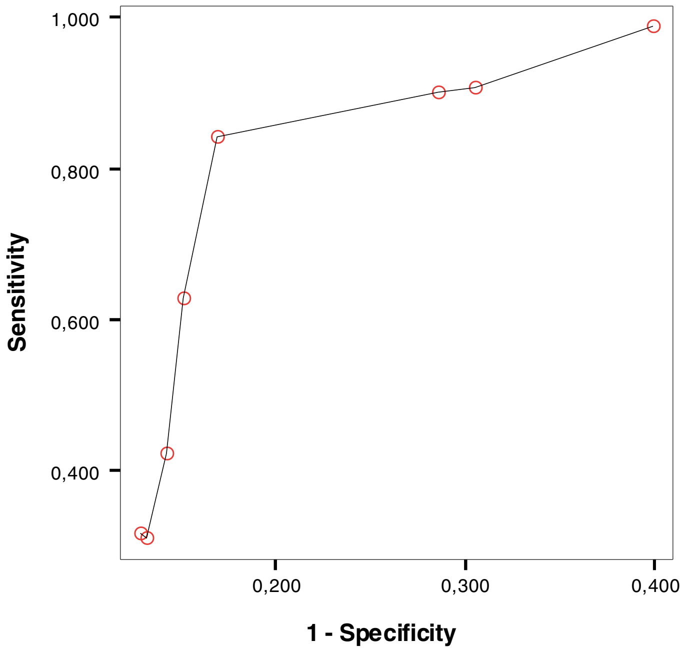

Fig. 1 COR curve for the estimation of the cut-off point located at 0.843 sensitivity and 0.831 specificity for AMMSE

compared it to the AMMSE values using the ROC curve, a classical technique to determine sensitivity and specificity in diagnosis (Table 5).

The general ROC curve graph drawn from the AMMSE values showed a higher diagnostic cut-off point in this population of around 24/25, compared with the figure of 23/24 for the MMSE.

4 Discussion

According to the bibliography (Ostrosky et al. 2000), diagnosis using MMSE raw scores is liable to a measurement error generated by the effect of age and years of formal education. In this paper, we present an adjusted version (termed the AMMSE) of the original examination in order to eliminate the effects of these variables. The effects differed from those found in the Spanish population, a finding that highlights the need to use the correction coefficients obtained here when studying Mexican populations. Compared with the normalization for the Spanish population (Blesa et al. 2001) our normalization process for the Mexican sample presents more than acceptable psychometric characteristics. We took Blesa et al.'s study as a starting point because of the similarities between the two populations. Our results reflected this point and, also, the similarities with other South American populations (Ostrosky et al. 2000; Lourenço and Veras 2006). The acceptable reliability and validity of the adapted version (similar to those found in other versions) suggest that the MMSE continues to be a high-efficacy clinical tool for this Mexican sample.

Similar normalization procedures have previously shown the effect of age and years of education on final scores. Our results provide a slight correction of final MMSE scores to consider the direct effect of age and years of education. The fact that the psychometric properties of the AMMSE version remained significant suggests that the original MMSE's reliability and validity were maintained.

Likewise, the sensitivity and specificity estimations obtained from the two samples showed that the optimal cut-off point was found, as expected, between AMMSE values 24 and 25. The discrimination ability of this test is sufficient to indicate a substantial reduction in false positives and negatives in illness and healthy conditions (Schultz-Larsen et al. 2006).

Clinically, the AMMSE is very easy to obtain. By adding the corrected value from Table 3 to the MMSE raw score, the new value will be free of measurement error due to age and years of formal education.

In conclusion, we obtained corrective values for MMSE scores to establish a corrected MMSE, or AMMSE, which will not be liable to the effects of age and years of education, but will retain the original scale's psychometric and clinical properties (Rosselli et al. 2006).

Comparison of our corrective table with the one that established for the Spanish normalization highlights the different effects of the variables analysed in each population. Whereas in the Spanish case the corrections are minimal, in the Mexican population the corrections seem abrupt and relevant. This finding demonstrates clearly that, when dealing with neuropsychological and psychological measurements, transcultural and multi-ethnic studies are necessary in order to establish evaluation and diagnosis criteria based on the realities of a specific population (Jones et al. 2002; Serra and Peña 2006), and not only on statistical criteria.

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