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ORIGINAL RESEARCH

Prediction equation for the mini-mental state examination: influence of education, age, and sex

Equação de predição para o miniexame do estado mental: influência da educação, idade e sexo

Ecuación de predicción para el mini-examen del estado mental: influencia de la educación, edad y sexo

Liliane Patrícia de Souza Mendes[1], Fernanda Ferreira Malta[2], Thaís de Oliveira Ennes[3], Giane Amorim Ribeiro-Samora[4], Rosângela Corrêa Dias[5], Bianca Louise Carmona Rocha[6], Marina Rodrigues[7], Larissa Faria Borges[8], Verônica Franco Parreira[9]

ABSTRACT | The mini-mental state examination (MMSE) is a screening test used worldwide for identifying changes in the scope of cognition. Studies have shown the influence of education, age and sex in the MMSE score. However, in Brazil, the studies consider only one factor to score it. The aim of this study was to establish a prediction equation for the MMSE. An exploratory cross-sectional study was developed and trained researchers examined participants at the community. The volunteers were evaluated by the MMSE and also by the Geriatric Depression Scale (GDS). The MMSE score was the dependent variable. Age, educational level, sex, and GDS score were the independent variables. Multivariate regression analysis was used to determine the model of best prediction value for MMSE scores. A total of 250 participants aged 20-99 years, without cognitive impairment, were assessed. The educational level, age, and sex explained 38% of the total variance of the MMSE score ($p<0.0001$) and resulted in the following equation: MMSE=23.350+0.265(years of schooling)-0.042(age)+1.323(sex), in which female=1 and male=2. The MMSE scores can be better explained and predicted when educational level, age, and sex are considered. These results enhance the knowledge regarding the variables that influence the MMSE score, as well as provide a way to consider all of them in the test score, providing a better screening of these patients.

Keywords | Cognition; Geriatric Assessment.

RESUMO | O mini-exame do estado mental (MEEM) é um teste de rastreio mundialmente utilizado para identificar alterações no âmbito da cognição. Estudos têm demonstrado a influência da educação, idade e gênero na pontuação do MEEM. No entanto, no Brasil, os estudos consideram apenas um fator para a pontuação no teste. O objetivo do estudo foi estabelecer uma equação preditiva para o MEEM. Um estudo transversal exploratório foi desenvolvido e examinadores treinados avaliaram participantes da comunidade. Os voluntários foram avaliados pelo MEEM e pela Escala de Depressão Geriátrica (EDG). A pontuação do MEEM foi a variável

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[1]Rehabilitation Sciences Program, Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: lilicev@yahoo.com.br. Orcid: 0000-0002-2602-3433.
[2]Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: fernandinha_0109@hotmail.com. Orcid: 0000-0002-9830-8913.
[3]Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: thaisennes120@gmail.com. Orcid: 0000-0003-0269-3456.
[4]Rehabilitation Sciences Program, Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: gribeirosamora@gmail.com. Orcid: 0000-0001-5102-369X
[5]Department of Physical Therapy, Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: rcorreadias8@gmail.com. Orcid: 0000-0002-1027-7746
[6]Rehabilitation Sciences Program, Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: bianca.carmona94@gmail.com. Orcid: 0000-0001-9047-7555
[7]Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: inarodrigues22@gmail.com. Orcid: 0000-0002-7658-8459
[8]Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: larifborges@hotmail.com. Orcid: 0000-0001-5763-6884
[9]Department of Physical Therapy, Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil. E-mail: veronicaparreira@yahoo.com.br. Orcid: 0000-0003-0374-9319

Corresponding address: Verônica Franco Parreira – Department of Physical Therapy, Universidade Federal de Minas Gerais (UFMG) – Av. Antônio Carlos, 6.627, Pampulha – Belo Horizonte (MG), Brazil – Zip Code: 31270-901 – Phone: +55 (31) 3409-4794 – E-mail: veronicaparreira@yahoo.com.br/veronica.parreira@pesquisador.cnpq.br – Financing source: CNPq, Fapemig and Capes (Finance code 001) – Conflict of interests: Nothing to declare – Presentation: Jan. 10st, 2018 – Accepted for publication: Dec. 11th, 2018 – This study was approved by the Ethics Committee of the UFMG (process number CAAE-48091215.8.0000.5149).

dependente. A idade, nível educacional, gênero e pontuação na EDG foram as variáveis independentes. A análise de regressão multivariada foi utilizada para determinar o modelo de melhor valor preditivo para os escores do MEEM. Foram avaliados 250 indivíduos entre 20 e 99 anos, sem comprometimento cognitivo. O nível educacional, a idade e o sexo explicaram 38% da variância total da pontuação do MEEM (p<0,0001) e resultaram na equação: MEEM=23,350+0,265(anos de escolaridade)-0,042(idade)+1,323(gênero), em que mulher=1 e homem=2. A pontuação do MEEM pode ser melhor explicada e predita quando o nível educacional, idade e gênero são considerados. Os resultados contribuem para o conhecimento sobre as variáveis que influenciam o escore do MEEM, bem como fornece uma maneira de considerá-las na pontuação do teste, proporcionando uma melhor triagem desses pacientes.
Descritores | Cognição; Avaliação Geriátrica.

RESUMEN | El mini-examen del estado mental (MEEM) es una prueba de rastreo mundialmente utilizada para identificar alteraciones en el ámbito de la cognición. Los estudios han demostrado la influencia de la educación, la edad y el sexo en la puntuación del MEEM. Sin embargo, en Brasil, los estudios consideran sólo un factor para la puntuación en la prueba. El objetivo del estudio fue establecer una ecuación predictiva para el MEEM. Un estudio transversal exploratorio fue desarrollado y examinadores entrenados evaluaron a participantes de la comunidad. Los participantes fueron evaluados por el MEEM y la Escala de Depresión Geriátrica (EDG). La puntuación del MEEM fue la variable dependiente. La edad, nivel educativo, sexo y puntuación en la EDG fueron las variables independientes. El análisis de regresión multivariada fue utilizado para determinar el modelo de mejor valor predictivo para los escores del MEEM. Se evaluaron 250 individuos entre 20 y 99 años, sin comprometimiento cognitivo. El nivel educativo, la edad y el sexo explicaron el 38% de la varianza total de la puntuación del MEEM (p <0,0001) y resultaron en la ecuación: MEEM=23,350+0,265(años de escolaridad)-0,042 (edad)+1,323 (sexo), en que mujer = 1 y hombre = 2. La puntuación del MEEM puede ser mejor explicada y predecible cuando se considera el nivel educativo, la edad y el sexo. Los resultados contribuyen para el conocimiento sobre las variables que influencian el score del MEEM, así como proporciona una manera de considerar las variables en la puntuación de la prueba, proporcionando una mejor forma de triar a estos pacientes.
Palabras clave | Cognición; Evaluación Geriátrica.

INTRODUCTION

Brazil has been going through a process of population aging that will result in the increase in the proportion of older people[1]. The increase in longevity has influenced the cognitive impairments, such as dementia, which stands out among the current prevalent chronic diseases, being considered a public health problem nowadays[2]. The large and accelerated demographic changes have a direct impact on public expenditure. Therefore, the early identification of individuals with cognition alterations is important to accelerate the referral for diagnosis confirmation by specific tests and to later guarantee their distribution between the health levels of services for prevention and/or treatment.

For the screening, simple and easy applicable tests able to detect these alterations may be used. In this context, the mini-mental state examination (MMSE) fits as a rating test of the current cognitive state of the individual, largely used worldwide for identifying alterations within the cognition[3]. The MMSE is an easy applicable test[4], which has a high test-retest reliability[5], does not require applicator's expertise and requires only a small collaboration from the person tested[4].

Several studies[6-10] indicate the influence of the educational level in the MMSE score, showing that individuals with a low educational level present lower scores on the test when compared to those of the same age, but higher educational level[6-10]. Furthermore, an impact of age is observed on the test scores, with a report of a lower performance in older people[7,9,11]. The influence of sex remains controversial, as some studies present the absence of influence of sex on MMSE scores[12] and others found a better performance in males[13,14]. In Brazil, some studies[7-9] set cutoff points for the MMSE. However, all of them only considered the impact of one of these factors on the test scores.

Considering the wide use of the test as a clinical and research tool for screening of cognitive deficits, it is recommended that the proposed scores consider all the factors which may influence the test. To our knowledge, in Brazil, no study has tried to establish a cutoff point based on all the factors that influence the score obtained in the test. Thus, this study aims to establish reference equations for the MMSE.

METHODOLOGY

Study population and design

This is an exploratory cross-sectional study. Participants were recruited from the community or from long-term care facilities located in the city of Belo Horizonte, Brazil. For part of the sample of participants aged 60 or more, previously collected data by the Frailty in Older Brazilians study (FIBRA – *Fragilidade em Idosos Brasileiros*) were used. The inclusion criteria were age between 20 and 99 years, to present Portuguese as their first language, and given written consent. Exclusion criteria included the presentation of serious uncorrected visual or hearing impairments[5,7,8], any motor abnormalities (rheumatological/orthopedic/neurological) of the hand movements that were harmful to the performance of the test sub-items[5,7,8] and known cognitive impairment and/or mental illness based on previous clinical diagnosis[8]. This study was approved by the Ethics Committee and all participants gave a written informed consent.

Measuring tools

The MMSE was used to evaluate the cognitive state of the participants. The test is divided into two sections: the first section requires vocal responses and covers orientation, memory, and attention. The second part tests ability to name, follow verbal and written commands, write a sentence spontaneously, and copy a complex polygon similar to a Bender-Gestalt Figure[4]. The score ranges from 0 (minimum score) to 30 (maximum score) and it is calculated by the sum of the sub-items scored 0 (incorrect answer) or 1 (correct answer)[4,9]. The higher the score attained by the individual, the better his or her cognitive state[9].

The Geriatric Depression Scale (GDS)[15] was another tool used. It is composed by 15 questions related to feelings and behaviors, considering for evaluations the seven days previous to the test. The volunteer can answer the questions with "yes" or "no" and these are scored as 0 or 1, depending on the question – answers scored 1 indicate emotional alteration. A score from 0 to 5 is considered normal, from 6 to 10 indicates mild depression, and 11 to 15, severe depression[15]. The GDS was used in this study to evaluate depressive symptoms and tested as an independent variable.

Procedures

Data collection was performed on a single day. Firstly, participants received information about the research. After signing the consent form, they responded to an open interview to collect sociodemographic and clinical information. The volunteers who met the inclusion criteria were evaluated by trained researchers for the MMSE to investigate the current cognitive state and also for the GDS, for screening of the emotional state.

Study variables

The MMSE score was the dependent variable. Age, educational level, sex, and GDS score were the independent variables. The educational level was assessed based on the number of years of study completed and categorized according to the statement of Bertolucci et al.[7] as illiterate; low educational level (1 to 4 incomplete years of study); mild educational level (4 to 8 incomplete years of study) and high educational level (8 or more years).

Statistical analysis

The sample size was calculated considering the data related to the MMSE score obtained by the overall Brazilian population, described by Brucki et al.[8]. A significance level of 5% and a power of 80%[16] were considered. The estimated sample size was 168 (at least 24 participants for each decade of age (from 20 to above 80 years).

Data were presented as measures of central tendency and dispersion, and data normality was verified by Shapiro-Wilk test. Comparisons between male and female sex, sociodemographic and clinical variables were performed by c square or Mann Whitney tests, according to the characteristics of the variable. In order to investigate the association between the MMSE, the sociodemographic variables and the GDS bivariate analyses were used: Spearman's test and biserial correlation analysis. Multivariate regression analysis was used to determine the model of best prediction value for MMSE. The final model was determined from the adjusted determination coefficient (R^2) and the statistical significance. For determination of the statistical quality of the model, the following aspects were checked: 1) absence of multicollinearity, by the variance inflation factor and 2) presence of homogeneity and normal distribution of the residuals, by analysis of the Q-Q plot. The lower limit of normality (LLN) corresponds

to percentile 5 of the predicted values and was obtained by the equation LLN=predicted value–(1.645×standard error of the estimate)[17].

The significance level was 5% and data were analysed using the statistical software Statistical Package for the Social Sciences – SPSS (version 19.0).

RESULTS

The flowchart of study participants is presented in Figure 1. A total of 163 participants from the community and long-term care facilities were initially recruited. From those, 25 refused to participate and 23 participants were excluded; therefore, 115 participants were assessed. In addition, data from 135 participants were randomly selected from the FIBRA base (≥60 years). Thus, the sample was composed from 250 participants.

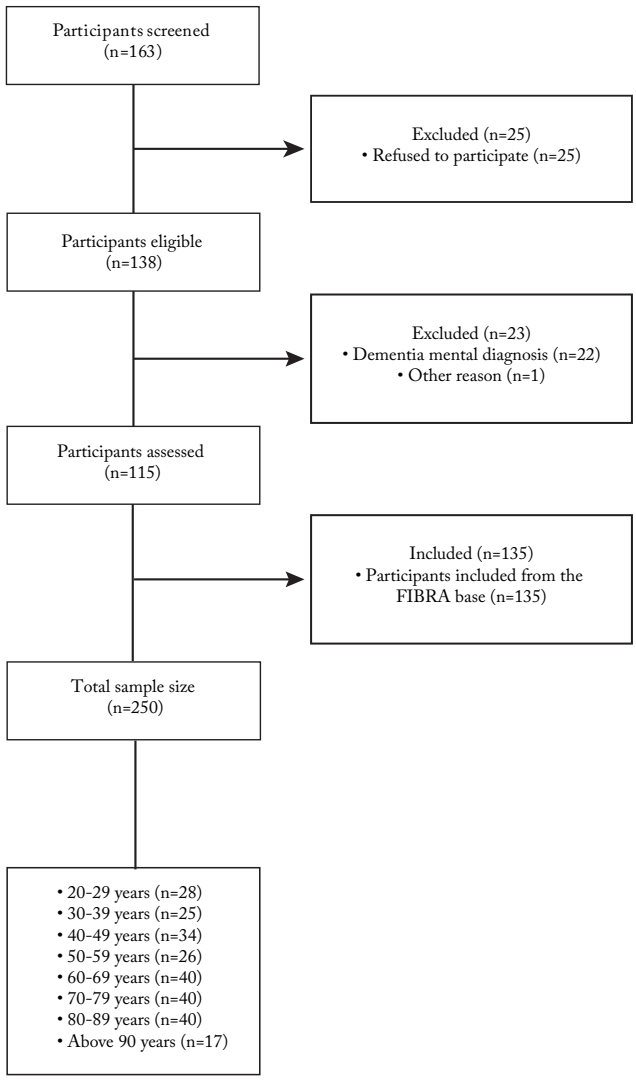

Figure 1. Flowchart of participants through the study

Table 1 shows the sociodemographic and clinical data of the participants. The sample consisted mainly of women and the groups were homogeneous for all the analysed variables.

Table 1. Sociodemographic and clinical data of the evaluated participants

Variables	Total	Male	Female	p value
Sex, %	250 (100)	118 (47.2)	132 (52.8)	0.411
Age, years	60.26±20.76 [20-99]	59.51±20.86 [22-98]	60.94±20.72 [20-99]	0.610
Years of schooling	7.90±5.76	8.29±5.98	7.56±5.55	0.413
Educational level				
Illiterate, %	16 (6.4)	5 (4.2)	11 (8.3)	0.210
Low educational level, %	49 (19.6)	25 (21.2)	24 (18.2)	0.999
Mild educational level, %	63 (25.2)	29 (24.6)	34 (25.8)	0.615
High educational level, %	122 (48.8)	59 (50.0)	63 (47.7)	0.786
GDS	**5.79 (3.03)**	**5.64 (2.92)**	**5.92 (3.13)**	**0.398**
Normal, %	106 (42.7)	52 (44.4)	54 (41.2)	0.923
Mild depression, %	129 (52.0)	59 (50.4)	70 (53.4)	0.379
Severe depression, %	13 (5.2)	6 (5.1)	7 (5.3)	0.999

Data presented as mean±standard deviation, except sex, classification of educational level and classification of GDS (%). Minimum and maximum for age in brackets. GDS: Geriatric Depression Scale; p: significance level.

Determinants and prediction equation of the MMSE

Significant correlations were observed between MMSE scores and the educational level (r=0.615, p<0.001), age (r=-0.531, p<0.001), sex (r=0.220, p=0.005), income (r=0.483, p<0.001), and GDS (r=-0.381, p<0.001).

The multiple linear regression model showed that only the variables of educational level, age, and sex were statistically significant in the final model and explained 38% of the total variance of the MMSE (R^2=0.38; p<0.001). Despite the GDS and income have shown association with the MMSE, in the multivariate model they were not significant for its prediction (p>0.05). Table 2 presents the coefficients and the prediction equation for the MMSE score. The lower limit of normality can be calculated by: Predicted value–(1.645×SEE).

Table 2. Multiple linear regression model with MMSE scores as the dependent variable

	Coefficients (B)	95%CI for B	p value
Constant	23.350	21.23 to 25.47	<0.001
Years of schooling	0.265	0.18 to 0.35	<0.001
Age, years	-0.042	-0.07 to -0.02	<0.001
Sex	1.323	0.56 to 2.09	=0.001
PREDICTION EQUATION			
MMSE=23.350+0.265(Years of schooling)–0.042(Age)+1.323(Sex) R^2=0.382; SEE=2.76 Sex:1=female; 2=male LLN=predicted value–(1.645×SEE)			

Data presented as coefficients (B) and their respective confidence intervals [CI 95%]; SEE: standard error of estimate; 95% CI for B: confidence interval of 95% of the coefficients; MMSE: mini-mental state examination; LLN: lower limit of normality; p: significance level.

DISCUSSION

To our knowledge, this was the first Brazilian study to establish reference values for the MMSE through prediction equations. It was observed that 38% of the test score variance was explained by the educational level, age, and sex. Despite many studies reporting correlations between MMSE scores and educational level[6-9,18,19], age[5,7,9,11], and sex[12,14], none of them actually take into account these different factors to determine predict equations. Our results showed that might be important and necessary to consider these additional aspects, and not only the educational level.

Our results indicate that educational level was the most important factor in test performance, as previously observed in other studies[7-9,18]. The influence of education on MMSE score has been consistently shown in the literature[6-9,18,19]. The results show that the higher the educational level, the higher the score on the MMSE, suggesting that the test items involve knowledge acquired at the school environment. Different studies conducted in several countries suggest that a low level of education or no schooling increases the prevalence of dementia[20,21]. Previous studies indicate that education does not prevent the appearance of the brain lesions that cause dementia, but is able to delay the onset of cognitive symptoms[20,21].

Our results show that the higher the age, the worse the test performance. This association was also reported by different authors worldwide[5,7,9,11]. Almeida[9] and Bravo and Hebert[19] (r=-0.23, p=0.001) also showed negative associations between age and the MMSE score. Brucki et al.[8] have chosen to analyse the influence of age through the comparison of groups and found an influence of age on MMSE scores in the extreme groups of the sample (50≤age≥65). The relation between cognitive impairment and age can be explained by morphophysiological changes associated with aging[21].

Besides age and educational level, our results point to an influence of the sex on the test scores. Women had a worse performance when compared to men. Our findings are consistent with those reported by Argimon et al.[13] and Dealberto et al.[14], who observed a higher score in older men when compared to women of the same age. Some studies report a higher prevalence of dementia among women[13,14,22]. There is evidence that estrogen deprivation may result in climacteric women being more vulnerable to develop memory complaints and a slight decline in the performance on tests of episodic memory[13].

Some studies suggest a possible relation between depression and cognitive deficits[23,24], indicating that depression may precede or be considered as a risk factor for dementia[23,24]. According to Stella et al.[24], the relationship between depression and dementia may manifest itself in the different ways: depression symptoms integrating the dementing process, dementia preceding depression, and depression progressing to cognitive impairment[24]. However, this relationship is not yet well established and new studies are necessary to prove and provide a better understanding of this connection. Given the likely influence of emotional changes in cognition, this study aimed to verify the association of the MMSE score with clinical depression through the screening of emotional changes using the GDS. It was observed that the score in the GDS was negatively correlated to the MMSE score, but it was not significant in the multivariate model.

The choice of a single variable to establish the cutoffs may underestimate or overestimate the score achieved in the test, leading to screening failures that may result in consequences. False positive results can lead to an unnecessary spending on more specific tests as well as false negative tests may lead to failure on patients' screening, including no referral for specific tests and no later allocation within the health levels, either for treatment and/or follow-up. In order to establish the prediction equation for MMSE score, only the variables educational level, age, and sex, proposed by this study were used in the model. That leads to a higher individuality of the score, minimizing failures during the screening.

Some limitations of this study consist on the fact that most of the sample of participants over 60 years have been recruited from the FIBRA network database, whose MMSE were applied in their residence. Therefore, the

evaluation of spatial orientation may have been facilitated as the participants were used to the environment of their homes. Furthermore, although it is suggested that the test should be performed in calm and quiet places, this was not always possible, which might have affected the performance on the test, since it requires the participant's attention and concentration.

CONCLUSION

This study showed that MMSE scores can be better explained and predicted when educational level, age, and sex are considered. Thus, it was proposed an equation, which appears to be adequate to more accurately predict the scores considered as normal in the test to screen the cognitive state.

The cutoffs currently used in the literature considered only the educational level to scoring, despite the observed influence of other variables in the score. Therefore, the results of this study enhance the knowledge regarding the variables that influence the MMSE score, as well as provide a way to consider all of them in the score of the test.

Thus, this equation aims to reduce mistakes in the cognitive screening, by underestimation or overestimation of the MMSE, providing a better screening of these patients. The equation proposed by this study may be used in clinical practice and research to calculate the predicted value for adults and elderly people.

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