Title: "The relevance of sociodemographic and health variables on MMSE normative data"

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Conflict of Interest

None declared.

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Abstract

The *Mini-Mental State Examination* (MMSE) is the most broadly used cognitive screening instrument in clinical and research contexts. The MMSE was administered to a community-based sample of cognitively healthy adults (*n*=850), stratified according to several sociodemographic variables, with a distribution similar to that observed in the Portuguese population. This study aimed to analyse the influence of sociodemographic (age, gender, educational level, marital and employment status, geographic region, geographic localisation, and residence area) and health variables (subjective memory complaints of the participant and evaluated by the informant, depressive symptoms and family history of dementia) on the subjects' performance on the MMSE and to establish normative data for the Portuguese population. Educational level and age significantly contributed to the prediction of the MMSE scores, explaining 26% of its variance. Regarding health variables, only the subjective memory complaints of the participant showed a small contribution (4%) to the variance of the MMSE scores. According to these results, age and education were considered in the development of the normative data of the MMSE for the Portuguese population.

Keywords: Neuropsychology tests; Aging; Clinical assessment/diagnosis.

Introduction

The *Mini-Mental State Examination* (MMSE; Folstein, Folstein, & McHugh, 1975) is the most broadly used brief cognitive screening instrument in clinical, epidemiological and research contexts. The MMSE has been widely validated for different populations and is extensively referred to in the literature (Nieuwenhuis-Mark, 2010; Tombaugh & McIntyre, 1992). When first presented in the 1970s, this instrument represented incontestable progress in the field of cognitive screening compared with the methods used thus far (Nieuwenhuis-Mark, 2010). Presently, MMSE is still widely used in national and international research and represents a common reference in the communication between health professionals, including psychologists, neurologists, and psychiatrists (Mitchell, 2009; Nieuwenhuis-Mark, 2010). Despite the limitations currently pointed out in the literature (Freitas, Simões, Alves, & Santana, 2013; Naugle & Kawczak, 1989; Wind et al., 1997) to the MMSE as a cognitive screening test for the mildest stages of cognitive decline, the value of this analysis for the evaluation of moderate to severe dementia cases has been demonstrated (Freitas et al., 2013; Harvan & Cotter, 2006; O'Bryant, et al., 2008).

Several studies have shown that sociodemographic variables have a significant effect on cognitive screening test performance, mainly age and educational level. Older age has been found to significantly increase the probability of obtaining lower scores, whereas the worst performance has been found among those with lower education levels, and ceiling effects have been observed among highly educated individuals (Anderson, Sachdev, Brodaty, Trollor, & Andrews, 2007; Bravo & Hébert, 1997; Gallacher et al., 1999; Matallana et al., 2011; Moraes, Pinto, Lopes, Litvoc, & Bottino, 2010). The magnitude of the effect of education level is so strong that the education is invariably considered a criterion for the establishment of normative-data for the MMSE

(Han et al., 2008; Mathuranath et al., 2007; Measso et al., 1993). Previous studies regarding gender have proved to be more controversial; only few found a significant association between this variable and cognitive screening tests performance (Mías, Sassi, Masih, Querejeta, & Krawchik, 2007; Ribeiro, Oliveira, Cupertino, Neri, & Yassuda, 2010; Scazufca, Almeida, Vallada, Tasse, & Menezes, 2009). The influence of marital status is more contentious between studies, as some have reported greater performances among married individuals (Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Nguyen et al., 2002; Ribeiro et al., 2010; Wu, Lan, Chen, Chiu, & Lan, 2011). Information regarding employment status is rather scarce (Freitas, Simões, Alves & Santana, 2012); individuals currently employed and individuals with occupations with high intellectual demands seem to achieve better scores on the MMSE (Anderson et al., 2007; Moraes et al., 2010). Finally, it is difficult to investigate the influence of geographical variables on cognitive tests and international inter-study comparison has revealed itself as meaningless due to the specificities of the populations and territories. Nevertheless, some studies found an IQ discrepancy in different geographical regions of a country (Lynn, 1979; Kaufman, McCLean, & Reynolds, 1988), which could be associated with average regional incomes (McDaniel, 2006; Almeida, Lemos, & Lynn, 2011). There are no Portuguese studies on the influence of geographic variables on the MMSE performance, however in a previous study from our group with the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), no association was found between geographic variables and the performance of the cognitively healthy adults (Freitas et al., 2012). Other variables were occasionally analyzed in previous studies. In this context the variable "epoch" studied by Morgado and collaborators (2010) in the Portuguese population stands out. They found that the epoch contributes to variations in three of the MMSE subtests: temporal orientation (five-item score), attention and

calculation and language (written and oral). Yet, this variable had no influence on the other tasks of the MMSE. This study shows the lifelong secular improvement in cognitive performance and stresses the need to update cognitive normative values.

The influence of health variables on the performance of the MMSE has also been investigated. However, the results are conflicting, considering the disparity of the methodologies used. While a few studies have shown a general tendency towards lower cognitive performance in the presence of depressive symptoms (Gallacher et al., 1999; Moraes et al., 2010), results regarding subjective memory complaints or a positive family history of dementia are more controversial. Some studies have found worse performances on cognitive tests among subjects with memory complaints, but other investigations have made evident that memory complaints are a poor indicator of cognitive function (Reid & MacLullich, 2006). Family history of dementia is a well-known risk factor for Alzheimer's disease; however, scarce studies have investigated the influence of this variable on the cognitive performance of healthy subjects. Mías and collaborators (2007) observed a lack of association between these variables. In a previous study, we explored the impact of these health variables on cognitive performance and observed that only the subjective memory complaints referred by the participant (not by the informants) showed a small contribution to the variance of the scores obtained from the MoCA (Freitas et al., 2012).

In Portugal, the first systematic study using the MMSE was conducted by Guerreiro and collaborators (Guerreiro et al., 1994; Guerreiro, 1998). In addition to transcultural adaptation and the analyses of psychometric properties, these authors gathered normative data based on a control group of 137 subjects and conducted validation studies on a clinical heterogeneous group comprising 151 patients. It was observed that the educational level had a strong influence on the performance of the

test. Thus, the normative data and proposed cut-off points were defined according to this criterion. The following cut-off points have been consensually and extensively used in Portugal: I) illiterate: 15/16 points (sensitivity = 63.6%; specificity = 91.4%); II) 1 to 11 years of schooling: 22/23 points (sensitivity = 77.4%; specificity = 96.8%); and III) more than 11 years of schooling: 27/28 points (sensitivity = 66.7%; specificity = 90%).

More recently, Morgado and collaborators (2009) have updated the MMSE normative data for the Portuguese population. This community-based study, comprising 411 subjects, was conducted in the urban and sub-urban regions of Lisbon. Although a minor yet significant effect of the age variable was observed, this study confirmed that the educational level showed a higher predictive capacity of the performance of the test. Hence, the normative data were re-established considering three literacy groups: I) 0 to 2 years (M = 25.16; SD = 2.16; cut-off points: 22); II) 3 to 6 years (M = 27.82; SD = 1.78; cut-off points: 24); and III) 7 or more years (M = 29.05; SD = 1.11; cut-off points: 27).

The referred national MMSE-normative studies did not include a stratified and representative sample of the Portuguese population, as both samples were restricted to subjects living in the Lisbon metropolitan area, whereas Portugal has a great diversity of regions and cultural contexts. Additionally, our sample includes not only elderly participants but also adults aged 25 and older. Due to the extensive use of the MMSE in several clinical populations [e.g., traumatic brain injury (de Guise, et al., 2011), cancer (Meyers & Wefel, 2003), substance abuse (Smith, Horton, Saitz, & Samet, 2006)], we decided to include participants aged 25 years and older in order to allow the use of this instrument with younger subjects with other diseases beyond the dementia spectrum. Therefore, our main objective was to conduct a normative study of the MMSE in the Portuguese population, based on a stratified and greater sample size that was determined

by a range of socio demographic variables representative of the target population, so as to ensure a more precise use of the instrument in this country. In addition, we also examined the impact of sociodemographic variables (age, gender, educational level, marital status, employment status, geographic region, geographic localization, and area of residence) and health variables (depressive symptoms, subjective memory complaints, and family history of dementia) on the cognitive performance of the individuals responding to the MMSE.

Methods

Participants and Procedures

A community-based sample of subjects aged 25 years and older, living in all geographic regions of the Portuguese continental territory, and representative of the Portuguese population, was recruited from health care centers and nursing homes. Several demographic and clinical inclusion criteria were considered in the initial subject selection: cognitively healthy adults; age 25 years and older; Portuguese as their native language and schooling in Portugal; and the absence of significant motor, visual or auditory deficits that may influence the performance on tests. To ensure that subjects were cognitively healthy adults, the following exclusion criteria were defined: loss of autonomy in daily living activities; history of alcoholism or substance abuse; relevant neurological or psychiatric diseases or chronic unstable systemic disorders that impact cognition; significant depressive complaints; and medication with a possible impact on cognition (e.g., psychotropic or psycho-active drugs). To confirm these general criteria, the subjects were interviewed by a psychologist with a standard questionnaire including a complete sociodemographic questionnaire, an inventory of current clinical health status, and the collection of past habits and medical history. For older subjects, this

information was also confirmed by a general practitioner, community centre directors and/or an informant (usually an individual in co-habitation or a close relative). For further inclusion in the study, all the subjects were required to score zero on Clinical Dementia Rating scale (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982; Garret et al., 2008) and below 20 points on Geriatric Depression Scale (GDS-30; Yesavage et al., 1983; Barreto, Leuschner, Santos, & Sobral, 2008). The results of other instruments of the assessment battery used in this study (see "Materials") were not used as inclusion or exclusion criteria because there are no Portuguese-validated data at the time of sample collection. Each subject was assessed in a single session by one of two psychologists with expertise in neuropsychological assessment.

From the initial community-based sample of the 1187 subjects, 264 subjects (22.24 %) were excluded after the interview (most frequent reasons were history of neurological or psychiatric disorder, history of alcohol abuse and memory complaints with impact in day-to-day activities, reported by subjective self-evaluation). Moreover, 73 subjects (6.15 %) were excluded due to the presence of cognitive impairment on the assessment battery and significant depressive symptoms. The final sample comprised 850 cognitively healthy adults that met all the inclusion criteria. The stratification according to sociodemographic variables confirmed that this final sample was representative of the distribution observed in the Portuguese population (Table 1).

Informed consent was obtained from the subjects after the aims and the procedures of the investigation and confidentiality requirements were fully explained to the subjects by a member of the study group. The present research complied with the ethical guidelines for human experimentation stated in the Declaration of Helsinki and it was approved by the Fundação para a Ciência e Tecnologia [Portuguese Foundation for

Science and Technology] and by the Faculty of Psychology and Educational Sciences Scientific Committee.

Materials

The assessment battery for the global assessment of each participant was composed of the following instruments:

a) Complete sociodemographic questionnaire.
b) Inventory of current clinical health status.
c) Inventory of past habits and medical history.
d) Mini-Mental State Examination (MMSE; Folstein et al., 1975; Guerreiro et al., 1994).It is the most widely used brief screening instrument for detecting cognitive deficits and, therefore, it is not described in detail here.
e) Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005; Simões et al., 2008).It is a brief cognitive screening instrument that was developed for the screening of milder forms of cognitive impairment. The tool is a one-page test with paper-and-pencil format, and the application time is approximately 10 to 15 minutes. The maximum score is 30 points, with higher scores indicating better cognitive performance. It evaluates the following six cognitive domains: executive functions; visuospatial abilities; short-term memory; language; attention, concentration and working memory; and temporal and spatial orientation. The MoCA total score refers to the raw score without the correction point for educational effects proposed in the original study (Nasreddine et al., 2005), because this correction point is not used in the Portuguese population (Freitas et al., 2011).
f) Clinical Dementia Rating scale (CDR; Hughes et al., 1982; Garret et al., 2008). It is a global staging tool for dementia that is based on the assessment of cognitive function

and functional capacity (in six cognitive-behavioural categories: memory; orientation; sense and problem solving; community activities; home activities and hobbies; and personal care). A global score of zero was used as a criterion for inclusion.

g) Irregular Word Reading Test (TeLPI: Teste de Leitura de Palavras Irregulares; Alves, Simões, & Martins, 2009). It is a tool for estimating premorbid intelligence that consists of a list of 46 irregular words that the subject reads.

h) Geriatric Depression Scale (GDS-30; Yesavage et al., 1983; Barreto et al., 2008). It is a brief scale to assess depressive symptoms in adults. It is composed of 30 dichotomous response questions that assesses emotional and behavioural symptoms of depression (score range = [0-30]).

i) Subjective Memory Complaints scale (SMC; Schmand, Jonker, Hooijer, & Lindeboom, 1996; Ginó et al., 2008). This scale consists of 10 multiple choice items that assesses the presence of subjective memory complaints (score range: = [0-21]). It was administered under two conditions: i) SMC-participants: answered by the subjects to evaluate their own subjective memory complaints, and ii) SMC-informants: answered by informants to assess their opinion about the memory capacity of the participant (when a close informant was available).

Variable Definitions and Sample Stratification

To enhance the representativeness of the observed distribution in the Portuguese population, the sample of 850 subjects was stratified according to the following sociodemographic variables:

I. age [3 age intervals: 25 – 49 (“adults”: mean age = 37.77 ± 8.10), 50 – 64 (“older adults”: mean age = 56.79 ± 4.57), and 65 and older (“elderly”: mean age = 70.61 ± 7.32)];

II. gender [female and male];

III. educational level [four educational levels were considered, according to the number of school years successfully completed in the Portuguese education system: 1-4 (primary education), 5-9 (middle school), 10-12 (high school) and over 12 years of education (university/college); these categories corresponds to the Portuguese educational system];

IV. geographic region [according to the NUTS-II classification (Instituto Nacional de Estatística, 2010) the Portuguese continental territory is divided into five geographic regions: North, Centre, Lisbon, Alentejo and Algarve];

V. geographic localisation [two geographic localisations were considered: coast and inland];

VI. residence area [according to the Types of Urban Areas (Instituto Nacional de Estatística, 2010), categorised into predominantly urban areas (PUA), moderately urban areas (MUA) and predominantly rural areas (PRA)].

In this study, we also included the following sociodemographic and health variables that were not criteria for sample stratification:

VII. marital status [classified into “single” (single, divorced or widowed subjects) or “married” (married or living in union subjects)];

VIII. employment status [classified into “active” (subjects with an active work situation) or "inactive" (subjects unemployed, retired, or domestic)];

IX. family history of dementia [only the information about first-degree relatives was considered relevant, and classification was dichotomised into "positive" or "negative"];

X. depressive symptoms [according to the GDS-30 score]. As the subjects with severe depressive symptoms were excluded, this study analysed the influence of depressive symptom levels among non-depressed to mildly-depressed individuals on MMSE performance;

XI. subjective memory complaints [according to SMC score, considering: i) SMC-participants and ii) SMC-informants].

Statistical Analysis

All data analyses were performed using the *Statistical Package for the Social Sciences*, version 19.0 (SPSS, v.19.0). Descriptive statistics were computed for all sociodemographic and health variables. Cronbach's alpha coefficients and the observed correlations (using the Pearson correlation coefficient; Cohen, 1988) were also calculated. The differences on the MMSE scores among subgroups were examined using analysis of covariance (ANCOVA), with control of the age and educational level covariates. Partial eta squared (η_p^2) was used as an estimate of the effect size (Cohen, 1988). The correlation between the MMSE scores, age and educational level was investigated with the Pearson correlation coefficient (r) (Cohen, 1988). Multiple Linear Regression (MLR) analysis, using the enter method, was performed to examine the significance of age (in years), and education (years of schooling completed successfully) as influencing factors for the MMSE. The multicollinearity was examined through Tolerance and Variance Inflation Factor (VIF) statistics (Meyers, Gamst & Guarino, 2006). The coefficient of determination (R^2) was considered in the analysis of

effect size in the regressions (Cohen, 1988). Further, the influence of health variables on the MMSE performance was investigated using MLR analysis, enter method, for variables with significant Pearson correlations. Finally, the norms of the MMSE were stratified and determined according to the sociodemographic variables most significantly associated with the MMSE scores. The normative data are expressed as the means ± standard deviations (S.D.s), and those of the distributions are given as means below 1S.D., 1.5S.D.s and 2S.D.s.

Results

The final study sample comprised 850 cognitively healthy subjects (mean age = 57.34 ± 15.20, age range = [25-91]; mean education = 7.89 ± 4.56, education range = [2-27]). The sociodemographic characteristics of the sample are shown in detail in Table 1, considering the stratification variables as well as the other sociodemographic variables included in this investigation. The distribution of the study sample in several strata was comparable to the distribution of the target Portuguese population.

(Table 1 about here)

The Cronbach's alpha coefficients and observed correlations among the different measures of this study are presented in Table 2. Table 3 summarizes the analyses of the relationships between the MMSE score and the sociodemographic variables using analysis of covariance to examine whether the differences in the MMSE scores were significant when controlling for the effects of the covariates (age and educational level) and to estimate the respective effect sizes.

(Table 2 about here)

(Table 3 about here)

The results demonstrated that only the educational level contributed significantly to the explanation of variance of the MMSE scores with a large effect size, explaining approximately 18% of the variance.

Considering the sociodemographic variables, statistically significant correlations were observed between the MMSE scores and educational level (r = .463, p <.01) or age (r = -.307, p <.01). Multiple linear regression, using the enter method, was conducted to compare the independent influence of age and educational level on the MMSE scores and to examine the additional contributions of these significant variables and their interactions. This analysis resulted in two significant regression models. The first model ($F_{(1,848)}$ = 260.926, p <.001) only included the educational level variable (ß = .485, t = 16.153, p <.001), which significantly explained 23% of total variance of the MMSE scores. In the second regression model, the two variables were combined, and no evidence of multicollinearity was detected. In this model ($F_{(2,847)}$ = 151.466, p <.001), both variables contributed significantly to the prediction of the MMSE scores (educational level: ß = .412, t = 12.819, p <.001; age: ß = -.183, t = -5.688, p <.001). The beta weights suggest that the educational level was a major contributor to the prediction of the MMSE scores, but that age also contributed to this prediction. The adjusted R squared value indicates that 26% of the variance in the MMSE scores was explained by this model.

The following health variables were considered in this study: (1) family history of dementia (16.3% of the subjects had a positive family history), (2) depressive symptoms (GDS mean = 7.06 ± 5.373, range = [0-20]), (3) and subjective memory complaints [two conditions: i) SMC-participants (mean = 5.56 ± 3.516, range = [0-17]) and ii) SMC-informants (mean = 4.14 ± 2.756, range = [0-11])]. No significant correlations were observed between the MMSE scores and the family history of

dementia (r = -.016, p =.638) and SMC-informants scores (r = -.051, p =.515). We observed that MMSE scores only showed statistically significant and negative correlations with depressive symptoms (GDS scores; r = -.139, p <.001) and the subjective memory complaints of the participants (SMC-participants scores; r = -.187, p <.001). The influence of these health variables on MMSE performance was investigated using MLR analysis with the enter method. The resulting model ($F_{(2,847)}$ = 15.262, p <.001) only included the subjective memory complaints of the subject, explaining 4% of the total variance on the MMSE scores. The depressive symptoms did not reveal a significant contribution to the model ($ß$ = -.059, t = -1.451, p = .147).

Based on these results, age and education were considered in the development of the normative data of the MMSE for the Portuguese population. The normative data were determined and stratified according to the distributional properties of each variable. The MMSE scores 1.5 standard deviations below the means can be considered as cutoff points for possible cognitive impairment (Table 4). From the initial community-based sample, 73 subjects (mean age = 65.32 ± 10.91, age range = [36-91]; mean education = 4.18 ± 1.87, education range = [1-11]) were excluded due to the presence of cognitive impairment on the assessment battery and significant depressive symptoms. Considering these cutoff points, it was possible to observe that 43.8% of these excluded participants obtained a score below the respective cutoff point.

(Table 4 about here)

Discussion

In this study, we conducted a systematic analysis of the influence of sociodemographic and health variables on MMSE performance and were able to determine the normative data of the Portuguese population in the MMSE. The results

reflect a community-based sample of cognitively healthy adults that were stratified according to several sociodemographic variables with a distribution similar to that observed in the Portuguese population. Although the MMSE is the most commonly used cognitive test worldwide, few international studies have analyzed the wide variety of sociodemographic and health variables that might influence MMSE performance; thus, the relevance of this study becomes more evident. In addition, this robust normative data contributes to a more precise and reliable cognitive evaluation in this country, as stratified community-based samples representative of the Portuguese population are still lacking.

Along with most of the previous studies conducted with the MMSE (Anderson et al., 2007; Bravo & Hébert, 1997; Matallana et al., 2011), our results show that educational level is the variable that most significantly contributed to the prediction of the MMSE scores, followed by age. Together, these variables explained 26% of the results variance; therefore, as in previous Portuguese studies (Guerreiro et al., 1994; Guerreiro, 1998; Morgado et al., 2009) and in most of the international normative studies, these variables were the optimal criteria for the establishment of MMSE normative data for the Portuguese population. We determined the means and S.D. for each sub-group result from the crossing of the various educational and age levels, and in addition, the cutoff values were 1.5 S.D. lower than the means.

As expected, and as demonstrated in previous studies (Gallacher et al., 1999; Han et al., 2008; Moraes et al., 2010), these results confirm that the MMSE score increases as the educational level increases and decreases as age progresses. There are fewer studies that have focused on other sociodemographic variables and the respective results are rather controversial. Like most of the studies, which report no association between these variables and the cognitive performance, in this study, gender, marital

status, and employment status did not show significant effects on the MMSE results. Considering the geographical variables, consistent with the results obtained in a previous study using the MoCA (Freitas et al., 2012), our results indicate that there were no statistically significant differences between subjects living in different geographic regions, the coast *vs.* inland areas, or in predominantly urban *vs.* rural areas.

Regarding the influence of health variables on the MMSE scores, our results showed that the subjective memory complaints of the participants slightly contributed (4%) to the explanation of the MMSE scores variance; this is a convergent result with the association observed between subjective memory complaints of the participants and MoCA performance (Freitas et al., 2012). Depressive symptoms, assessed through the GDS-30, presented significant and negative correlations with the MMSE scores; however, the contribution for prediction performance was not significant. Similar to other studies (Freitas et al., 2012; Mías et al., 2007), no associations were observed between the cognitive screening scores and family history of dementia or memory complaints evaluated by the informant.

A linear comparison between the present study and previous studies conducted in the Portuguese population can not be established. The major point of convergence – not only with the previous studies in the Portuguese population, but also with most international studies – pertains to the influence of the education variable on MMSE performance, as the most significant contribution to the explanation of the MMSE scores variance. Drawing comparisons regarding normative values for a younger age group is not possible as the results of the present study are original in this respect; the other Portuguese studies carried out only included older adults. Although it is not possible to establish a precise comparison of the normative data for the elderly subjects, because the age and education groups of the three Portuguese studies are not a match,

there seems to be a trend of increasing normative values. This tendency is consistent with the findings of Morgado and collaborators (2010) concerning the lifelong secular improvement in the MMSE cognitive performance. Hence, this study also responds to the need to update normative values.

The main limitation of the present study was the exclusion of illiterate subjects. It is our conviction that an adequate assessment of illiterate subjects requires a significant adaptation of the items or tools that would need to be specifically designed for this objective. Another weakness present in the study was the inability to completely match all age-subgroups in terms of education mean. The younger group showed higher education levels than the older group. This discrepancy reflects the demographic profile of Portugal, where, in the last decades, the educational system has rapidly changed, imposing higher obligatory educational plateaus. These changes are reflected in the younger strata of the population studied; while, the older group continues to be characterized by a very low education level. Another issue is the classification of subjects as cognitively healthy adults. To ensure this classification strict inclusion criteria were established, as previously explained, which were confirmed through a clinical interview and neuropsychological evaluation. In addition, for older subjects, the obtained information was verified through general practitioners, community center directors and/or informants. Given the sample size and geographical distribution of the participants, it was not possible to perform a neurological consultation or additional diagnostic exams. Furthermore, the data regarding the influence of the depressive symptoms should be strictly interpreted with caution in the context of cognitively healthy, non-depressed-to-mildly-depressed subjects. Moreover, in future studies, it would be important to consider a better operationalization of the variables, particularly subjective memory complaints and depressive symptoms.

This investigation presents a systematic analysis of the influence of sociodemographic and health variables on MMSE performance and provides MMSE norms for the Portuguese population. The use of a sample stratified based on different levels of sociodemographic variables, with a distribution similar to that observed in the Portuguese population ensures better equivalence with the target population and increases confidence in the conclusions drawn. These reference values are useful for a reliable evaluation in both clinical and research contexts where the MMSE is largely used to quickly assess cognitive performance and decline.

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Table 1. Sociodemographic characterization and stratification of the sample

	Levels	Sample		Portugal	
		n	%	*n*	%
Sociodemographic stratification of sample					
Age	25 - 49	226	26.6	-	
	50 - 64	310	36.5	-	
	≥ 65	314	36.9	-	
Gender	Female	491	57.8	3 946	52.6
	Male	359	42.2	3 559	47.4
Educational Level	Primary	345	40.6	2 426	36.6
	Middle	251	29.5	2 280	34.4
	High	122	14.4	960	14.5
	University	132	15.5	956	14.5
Geographic Region	North	338	39.8	2 722	36.0
	Center	235	27.6	1 794	24.0
	Lisbon	201	23.6	2 091	28.0
	Alentejo	53	6.2	577	8.0
	Algarve	23	2.7	321	4.0
Geographic Localization	Coast	724	85.2	6 379	85.0
	Inland	126	14.8	1 126	15.0
Residence Area	PUA	582	68.5	5 103	68.0
	MUA	140	16.5	1 200	16.0
	PRA	128	15.1	1 200	16.0
Others Sociodemographic Variables					
Marital Status	Married	633	74.5	-	
	Single	217	25.5	-	
Employment Status	Active	414	48.7	-	
	Inactive	436	51.3	-	

Abbreviations: PUA = predominantly urban areas; MUA = moderately urban areas; PRA = predominantly rural areas.

Note: The values (*n*) of the Portuguese population are expressed in thousands and represent the data of the resident population in continental Portugal aged over 24 years (Instituto Nacional de Estatística, 2010).

Table 2. Cronbach's alpha coefficients and observed correlations among measures

Variables	MMSE	MoCA	GDS	SMC-participants	SMC-informants
MMSE	(.46)				
MoCA	.61**	(.77)			
GDS	-.14**	-.19**	(.86)		
SMC-participants	-.19**	-.27**	.52**	(.79)	
SMC-informants	-.05	-.07	.29**	.31**	(.73)

Abbreviations: MMSE = Mini Mental State Examination; MoCA = Montreal Cognitive Assessment; TeLPI = Irregular Word Reading Test; GDS = Geriatric Depression Scale; SMC = Subjective Memory Complaints scale.

Note: Alpha coefficients are presented on the diagonal and observed correlations below the diagonal (**$p < .01$).

Table 3. Analysis of group differences on the MMSE scores while controlling for the effect of covariates and estimation of the effect sizes

Variables	MMSE $M \pm SD$	F (ANCOVA)	*Effect Size*
Age			
25 - 49	29.47 ± 0.895	$F_{(2,844)} = 5.329$, $p = .005$	Small $\eta_p^2 = .012$
50 - 64	28.76 ± 1.344		
≥ 65	28.58 ± 1.439		
Gender			
Female	28.81 ± 1.366	$F_{(1,844)} = 4.515$, $p = .034$	Small $\eta_p^2 = .005$
Male	28.97 ± 1.273		
Educational Level			
Primary	28.12 ± 1.482	$F_{(3,843)} = 62.119$, $p < .001$	Large $\eta_p^2 = .181$
Middle	29.18 ± 1.010		
High	29.52 ± 0.784		
University	29.73 ± 0.594		
Geographic Region			
A. North	28.91 ± 1.376	$F_{(4,841)} = 9.230$, $p < .001$	Small $\eta_p^2 = .042$
B. Center	28.81 ± 1.274		
C. Lisbon	29.04 ± 1.146		
D. Alentejo	29.24 ± 0.992		
E. Algarve	27.31 ± 1.955		
Geographic Localization			
Coast	28.90 ± 1.314	$F_{(1,844)} = 2.133$, $p = .145$	Small $\eta_p^2 = .003$
Inland	28.79 ± 1.423		
Residence Area			
PUA	28.99 ± 1.240	$F_{(2,843)} = 3.892$, $p = .021$	Small $\eta_p^2 = .009$
MUA	28.86 ± 1.326		
PRA	28.41 ± 1.589		
Marital Status			
Married	28.82 ± 1.332	$F_{(1,844)} = 0.009$, $p = .926$	Null $\eta_p^2 = .000$
Single	29.06 ± 1.308		
Employment Status			
Active	29.16 ± 1.193	$F_{(1,844)} = 0.145$, $p = .704$	Null $\eta_p^2 = .000$
Inactive	28.62 ± 1.398		

Abbreviations: PUA = predominantly urban areas; MUA = moderately urban areas; PRA = predominantly rural areas; *M*: mean; *SD*: standard deviation; *F*: analysis of covariance (ANCOVA) values; η_p^2: partial eta squared values.

Note: According to Cohen (1988), η_p^2 values of .01, .06 and .14 are considered small, medium and large effect sizes, respectively.

Table 4. Normative data of the MMSE scores according to age and educational level

	Educational Level (years)				
Age	Primary (1-4)	Middle (5-9)	High (10-12)	University (>12)	All education
(*n*)	(39)	(89)	(68)	(62)	(258)
25 – 49	28.67 ± 1.33	29.26 ± 0.97	29.71 ± 0.62	29.89 ± 0.37	29.44 ± 0.94
M - 1.5 *SD*	**27**	**28**	**29**	**29**	**28**
(*n*)	(108)	(82)	(42)	(41)	(273)
50 – 64	28.00 ± 1.37	29.09 ± 0.92	29.24 ± 1.10	29.54 ± 0.71	28.75 ± 1.28
M - 1.5 *SD*	**26**	**28**	**28**	**28**	**27**
(*n*)	(190)	(76)	(28)	(25)	(319)
≥ 65	27.95 ± 1.51	29.13 ± 1.00	29.46 ± 0.79	29.48 ± 0.77	28.48 ± 1.45
M - 1.5 *SD*	**26**	**28**	**28**	**28**	**26**
	(337)	(247)	(138)	(128)	(850)
All age	28.05 ± 1.46	29.16 ± 0.96	29.51 ± 0.85	29.70 ± 0.61	28.86 ± 1.32
	26	**28**	**28**	**29**	**27**