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Spanish Consortium for Ageing Normative Data (SCAND): Screening Tests (MMSE, GDS-15 and MFE)

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Abstract

Background: Detecting cognitive impairment is a priority for health systems. The aim of this study is to create normative data on screening tests (MMSE, GDS and MFE) for middle-aged and older Spanish adults, considering the effects of sociodemographic factors. **Method:** A total of 2,030 cognitively intact subjects who lived in the community, aged from 50 to 88 years old, participated voluntarily in SCAND consortium studies. The statistical procedure included the conversion of percentile ranges into scalar scores. Secondly, the effects of age, educational level and gender were verified. Linear regressions were used to calculate the scalar adjusted scores. Cut-off values for each test were also calculated. **Results:** Scalar scores and percentiles corresponding to MMSE, GDS-15 and MFE are shown. An additional table is provided which shows the points that must be added or subtracted from MMSE score depending on the subject's educational level. **Conclusions:** The current norms should provide clinically useful data for evaluating Spanish people aged 50 to 88 years old and should contribute to improving the detection of initial symptoms of cognitive impairment in people living in the community, taking into account the influence of gender, age and educational level.

Keywords: Normative data; screening test; ageing; SCAND; descriptive survey study.

Resumen

Consorcio Español para la Obtención de Datos Normativos del Envejecimiento: Pruebas de Cribado (MMSE, GDS-15 y MFE). **Antecedentes:** detectar el deterioro cognitivo es una prioridad del sistema sanitario. El objetivo de este estudio es la presentación de datos normativos de pruebas de cribado (MMSE, GDS y MFE) para adultos españoles de mediana edad y adultos mayores, considerando los efectos de factores sociodemográficos. **Método:** en los estudios realizados por el consorcio SCAND participaron voluntariamente 2.030 personas cognitivamente sanas, de 50 a 88 años, residentes en su comunidad. El procedimiento estadístico supuso la conversión de rangos percentiles en puntuaciones escalares. Posteriormente, se comprobaron los efectos de la edad, el nivel educativo y el género. Se utilizaron regresiones lineales para calcular las puntuaciones escalares ajustadas. También se calcularon los puntos de corte para cada prueba. **Resultados:** se muestran las puntuaciones escalares y los percentiles correspondientes a MMSE, GDS-15 y MFE. Además, se presenta una tabla que muestra los puntos que deben sumarse o restarse a la puntuación del MMSE dependiendo del nivel educativo del individuo. **Conclusiones:** los datos normativos presentados tienen una utilidad clínica para evaluar a población española de 50 a 88 años, y contribuyen a mejorar la detección de los síntomas iniciales del deterioro cognitivo teniendo en cuenta la influencia del género, la edad y el nivel educativo.

Palabras clave: datos normativos; pruebas de cribado; envejecimiento; SCAND; estudio descriptivo.

The population of Spain continues its progressive aging process. Longevity and dependency are part of the same social reality: success and risk. As the population ages, the number of people with chronic non-communicable diseases, including dementia, increases. Dementia has become a global public health challenge (Alzheimer's Disease International, 2019), thus early, accurate diagnosis is essential in the initial stages.

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The clinical study of cognitive impairment of aging populations, including sufficiently large and representative samples and valid and reliable tools seems to confirm the existence of a continuum, a process of continued brain degeneration, which would range from subjective cognitive decline (SCD), mild cognitive impairment (MCI) and dementia (Ávila-Villanueva & Fernández-Blázquez, 2017; Petersen et al., 2018; Picón et al., 2019). The existence of affective factors like depression that interact and make detection more difficult (Lang et al., 2019), the discrete beginnings of this continuum, and the imprecise nature of the phases through which it runs (Facal et al., 2019), make it even more necessary to develop accurate screening methods which are easy to apply and score, with good sensitivity and specificity, and with little educational bias, allowing an actual early detection of cognitive impairment.

Current evidence indicates that subjective cognitive complaints would be the first stage of impairment in the continuum from healthy cognitive aging to dementia. Subjective memory complaints (SMC) represent the self-reported perception of decreases in cognitive capacity from a previous function level (Boggess et al., 2020). The association between SMC and changes in objective memory remain unclear (Snitz et al., 2015). In this line, the researchers have argued that different factors such as personality traits (Luchetti et al., 2015), or depressive symptoms (Bhang et al., 2019), among others, are directly involved in the subjective perception that persons have about their cognitive performance. Jessen et al. (2006) introduced a new term, subjective cognitive decline (SCD), to characterize persons with subjective cognitive concerns in the absence of objectively measured cognitive impairments (Jessen et al., 2020).

Subjective assessment of memory complaints is usually carried out with two methodologies, general questions or specific questionnaires. Although they are not equivalent, both correlate positively (Abdulrab & Heun, 2008). Questionnaires analyze the frequency and intensity of memory failures in daily life and reflect the subjective assessment that the person does about the functioning of their memory through the responses to different questions. The Memory Failures of Everyday (MFE, Sunderland et al., 1984) is one of the most widely used questionnaires in different pathologies and contexts. A study has provided normative data for Spanish people older than 64 years old (Montejo et al., 2011). There is some evidence supporting associations with sociodemographic variables (age and a low educational level; Hülür et al., 2014; with age, poor performance and cognitive impairment: Trouton et al., 2006). Calero-García et al. (2008) only found an association between age and memory complaints in the extreme age ranges of the elderly. However, other authors have not found any relationship between memory complaints and factors such as age, sex or studies (Mendes et al., 2008; Montejo et al., 2012a).

There are several validated cognitive impairment screening tests in Spanish, including the Mini-Mental State Examination (MMSE, Lobo et al., 1979), which is the most used internationally. In Spain, Contador et al. (2016) have published a study using MMSE-37 stratified by age (from 65 to 97 years old), gender, and education in a large population-based cohort of older Spanish adults without dementia. Results showed that age, gender, and education affect test score. Nagaratnam et al. (2020) have reported the results of a systematic search of longitudinal studies from 2007 to 2017, and a mixed-effect meta-regression analysis. Their results demonstrated a significant decrease in MMSE scores with higher age, and also that the average annual decline in MMSE scores identified at the age of 41 and 84 years old were –0.04 and –0.53, respectively. They concluded that between the age of 29 and 105 years MMSE scores decline, with the highest decline between age 84 and 105 years.

Mood status is involved in the early detection of cognitive impairment, not only because of the relation with the subjective perception of cognitive complaints, but also because persons with cognitive impairment presenting depressive symptoms have worse quality of life and more chronic conditions (Lucas-Carrasco, 2012). Nevertheless, there are few questionnaires of depression screening for middle aged and older adults appropriately validated to Spain. It includes the Spanish version of the abbreviated Geriatric Depression Scale of Yesavage (GDS). The GDS-15 was developed as a self-report instrument to detect clinical depression in older adults, focusing on the psychological symptoms of depression excluding disease-related somatic symptoms (Sheikh & Yesavage, 1986). A review of literature reveals there is a majority of studies that have found negative evidence about age, education, or gender influence on GDS-15 scores (Apostolo et al., 2018; Zang et al., 2020; Zhao et al., 2018), and only a few showing some influence of these factors (see Asokan et al., 2019, for example).

The availability of accurate normative data, adjusted by age, educational level, or gender, is a requirement for the early detection of cognitive declines and the measurement of clinically significant changes, allowing a reliable diagnosis (Miller et al., 2015; Stein et al., 2012) of SCD, MCI and dementia. The effect of age has been repeatedly investigated in neuropsychological testing and in topological neuroimaging measures (Mancho-Fora et al., 2020). Previous initiatives have provided norms for some of the most commonly used neuropsychological tests (Mayo's Older Americans Normative Studies [MOANS] for Latino American adults, Guàrdia-Olmos et al., 2015; Spanish Multicenter Normative Studies [NEURONORMA Project], Peña-Casanova et al., 2009). The aim of this study is to complement these initiatives by creating specific standards for Spanish older adults (over 50 years old) that enable early detection of cognitive decline, depression or SMC in community settings, taking into account the effects of age, gender and education.

Therefore, the Spanish Consortium for Ageing Normative Data (SCAND) initiative takes the data from three Spanish cohort studies, Aging Brain Projects of the Complutense University of Madrid, the Vallecas Project, and the Compostela Aging Study. The SCAND initiative is developed with the aim of sharing normative data on the Spanish middle-aged and older adult population. The objectives of the consortium are to establish normative data from a group of neuropsychological tests commonly used in the community setting, and to study longitudinally the predictive value of these test with respect to SCD, MCI or dementia conversion of individuals in the cohort.

This paper describes the normative data of the MMSE, MFE and GDS, as instruments of first choice in the screening for cognitive impairment, subjective memory complaints and depression, taking into account sociodemographic factors (age, gender and education), using data from the SCAND studies. The paper also explains the methodology used to recruit the sample in the different studies, and document the statistical procedures used to obtain normative data within the SCAND initiative.

Method

Participants

A total of 2,030 cognitively unimpaired subjects, aged between 50 and 88 years (1,362 women and 668 men), participated in the study. All were selected given that they have been involved in different studies about the aging process, as mentioned before. All subjects were recruited between 2008 and 2019.

Participants were selected following the inclusion criteria: (1) community-dwelling individuals; (2) over 50 years of age; (3) normal cognitive development, not meeting diagnostic criteria for MCI (Petersen, 2004) in at least two consecutive assessment within the corresponding research project; (4) able to manage and independent life without any severe mental disorder (cognitive or psychiatric) impeding daily functioning; (5) normal or corrected hearing and vision; (6) basic reading, understanding spoken and writing abilities Spanish language; and (7) who signed a written informed consent.

The exclusion criteria were as follows: (1) dementia or severe cognitive deterioration, operationalized through an MMSE below the cut-off point according to age and educational level; (2) significant impact on activities of daily living; any pathology of the central nervous system that could affect cognition (tumors, history of cerebral infarction, brain trauma with loss of consciousness during the last 5 years); (4) severe psychiatric disorder; (5) presence of a severe systemic disease (e.g., cancer under treatment, malignant hypertension, etc.); (6) history of alcohol and other drug use; and (7) chronic use of neuroleptics, antiepileptics, hypnotics, anxiolytics, sedatives, or high doses of benzodiazepines.

All studies complied with the ethical standards of the Declaration of Helsinki and was approved by the local Ethics Committees of the Participant Institutions.

Instruments

For the present study, MMSE, GDS and MFE were considered, all of which are part of the comprehensive neuropsychological evaluation protocol used by each of the SCAND consortium research groups.

The MMSE (Folstein et al., 1975) is a screening test for the detection of cognitive impairment. Its psychometric properties have been studied by many researchers (Bravo & Hébert, 1997) demonstrating that the MMSE has acceptable reliability and validity, and emphasizing the influence of age and educational level (Crum, Anthony, Bassett, & Folstein, 1993). Lobo et al. (1999) carried out the adaptation and validation in Spain, and reported a sensitivity of 85% and a specificity of 90%, and later, in the study by Blesa et al. (2001) estimated a sensitivity of 87.32% and a specificity of 89.19%.

The GDS (Yesavage et al., 1983) is a scale that assesses mood. The version used in SCAND consists of 15 dichotomous questions in which the person must answer how she/he have felt in the last week. The instrument is adapted and validated for the Spanish geriatric population with 81,1% sensitivity and 76,7% specificity indices (Martínez-de la Iglesia et al., 2002). The instrument is adapted and validated for the Spanish geriatric population with good psychometric properties, reliability equal to .994, convergent validity equal to .618 (with Mongomery-Asberg Depression Rating Scale), discriminant validity equal to .235, and sensitivity indices of 81.1% and specificity of 76.7% (Martínez-de la Iglesia et al., 2002).

The MFE consists of 28 items that address the frequency with which situations and activities related to memory problems in everyday life are recalled. In different studies it has been verified that the complaints evaluated with simple questions that include frequency are advisable, although the sensitivity values (90.9%) are higher than the specificity values (45.7%) (Ramlall et al., 2013). García-Martínez & Sánchez-Cánovas (1993) made the adaptation to Spanish of the MFE, and researchers from the Center for the Prevention of Cognitive Impairment of Madrid have conducted several studies obtaining good values of reliability and validity, .85 and .94 respectively (Montejo et al., 2012b).

All the tests were administered and scored according to the standardized procedures published in each test's manual.

Procedure

All participants, from each research teams of the SCAND consortium's, completed a structured interview to collect socio-demographic data and a neuropsychological assessment administered by expert neuropsychologists specifically trained to evaluate middle-age and older adults. In each study, participants were informed about the main research aspects and they signed written informed consent that had been approved by the Local Ethics Committee.

Data analysis

The statistical procedure followed is that described in Peña-Casanova et al. (2012). First, a table of scalar scores (*SS*) was prepared. A cumulative frequency distribution of the raw scores was generated throughout the group. Percentile ranges were assigned to the raw scores depending on their place into distribution. Then the percentile ranges were converted to *SS* (range 2 to 18). This transformation of raw scores produced a normal distribution, with mean equal to 10 and standard deviation (*SD*) equal to 3, which allows the application of linear regressions to calculate the scalar adjusted scores (*SS*adjusted). Secondly, the effects of age, educational level and gender were verified. Correlation (r) and determination coefficients (R^2) of univariate regressions were calculated of SSs with age, educational level and gender for each of the tests considered. Corrections were only applied for those sociodemographic variables that explained more than 5% of the variance and that also had a significant regression coefficient (p <.05). Finally, the regression coefficient (β) was used as the basis for the corrections. Adjustments are made according to age, educational level and gender on the *SS*, for this the following formula was used (as is stated in Peña-Casanova et al., 2012):

$$SS\text{adjusted} = SS - [\beta 1 * (\text{Age} - 70) + \beta 2 * (\text{Education} - 2) + \beta 3 * \text{Gender}]$$

In the previous equation, Age is subtracted by participants' mean age (70) and Education by participants' median in education (2: secondary studies), given that Education is an ordinal level measured in our study. The inclusion of the statistic of central tendency corresponding to each variable, allows to obtain adjusted scores that provide a better standardized reference. All analyses were performed with SPSS version 25.

Results

Table 1 shows the characteristics of participants for the total sample and the mean and standard deviation for all test. Table 2 includes the age, gender and education of participants for each screening test.

As mentioned before, only corrections were applied for those sociodemographic variables that explained more than 5% of the total variance and that also presented a significant regression coefficient.

As can be seen in the previous table, it is not necessary to calculate the *SS*adjusted for MFE or GDS, since none of the sociodemographic variables reached the level of explanation of 5% of criterion's total variance. The highest percentage is reached by the variable Education in the case of the MFE (but it explains only 2.9% of the total variance), and Gender in the case of the

Table 1
Characteristics of Participants for the Total Sample, Mean (and Standard Deviation) for All Test

	Total sample n (%)	MMSE M (SD)	MFE M (SD)	GDS M (SD)
Gender				
Male	668 (32.9)	28.75 (1.36)	12.53 (7.64)	1.57 (2.04)
Female	1362 (67.1)	28.59 (1.51)	13.05 (7.58)	2.23 (2.45)
Education				
Without formal education	225 (11.1)	27.74 (1.68)	15.83 (8.55)	2.05 (2.49)
Primary	520 (25.6)	28.22 (1.58)	13.86 (8.20)	2.49 (2.69)
Secondary	582 (28.7)	28.80 (1.33)	12.55 (7.12)	2.02 (2.28)
Higher	702 (34.6)	29.10 (1.17)	11.61 (6.94)	1.64 (1.98)

Table 2
Characteristics of Participants for Each Test

	MMSE	MFE	GDS
N	2030	1554	1973
UCM	814	580	757
CIEN	873	873	873
USC	343	101	343
Age (years)			
M	70.19	71.11	70.17
SD	7.31	6.79	7.30
Range	50-88	50-86	50-88
Age (years)			
Male	668 (32.9)	540 (34.7)	649 (32.9)
Female	1362 (67.1)	1014 (65.3)	1324 (67.1)
Education *n (%)*			
Without formal education	225 (11.1)	173 (11.1)	223 (11.3)
Primary	520 (25.6)	356 (22.9)	504 (25.6)
Secondary	582 (28.7)	452 (29.1)	559 (28.3)
Higher	702 (34.6)	573 (36.9)	686 (34.8)

Table 3
Correlation and Determination Coefficients for Socio-demographic Variables Across the Screening Test

	Age		Education		Gender	
	r	R^2	r	R^2	r	R^2
MMSE	.093**	.009	.309**	.095	.033	.001
MFE	.097**	.009	.172**	.029	.038	.001
GDS	.061*	.004	.104**	.011	.137**	.019

**$p < .001$; *$p < .01$

GDS (which only explains 1.9% of the variance). To calculate the MMSE *SS*adjusted, only education was considered as a significant socio-demographic variable.

To use each of the tables presented below, first look at the patient's raw score and identify the associated *SS*. The range of percentiles that corresponds to each *SS* allows an assessment of a specific subject with its reference population.

Table 4 shows results in terms of scalar and percentiles corresponding to MMSE. To facilitate the calculation of MMSE *SS*adjusted, an additional table is provided which shows the points that must be added or subtracted from this score depending on the subject's educational level (Table 5).

Table 4
Scalar Scores and Percentile Ranges Corresponding to MMSE

MMSE		
Scalar score	Percentile ranges	Raw scores
2	≤1	≤ 23
3	1	24
5	4	25
6	5 - 9	26
7	10 - 18	27
9	19 - 36	28
11	37 - 65	29
18	66 - 99	30
N		2029

Table 5
Adjustments by Educational Level Corresponding to MMSE

	Without formal education	Primary	Secondary	Higher
MMSE	0	0	-1	-2

Tables 6 and 7 present the frequency distributions of raw scores, *SS*, and percentile ranges for all subjects who responded to the MFE and the GDS-15, respectively.

Discussion

This paper provides normative data for individuals aged 50–88 years according to age, gender, and level of education in the three tests (MMSE, GDS-15 and MFE) most commonly used to detect cognitive impairment, depression and SMC in community contexts. Performance in cognitive tests has been demonstrated that depends normally on age (Legdeur et al., 2018), gender (Jäncke, 2018) and educational level (Lezak et al., 2012). Our results confirm

Table 6
Scalar Scores and Percentile Ranges Corresponding to MFE Raw Scores

MFE		
Scalar scores	**Percentile ranges**	**Raw scores**
4	≤3	0 - 1
5	4	2
6	5 - 11	3 -4
7	12 - 18	5 - 6
8	19 - 30	7 -8
9	31 - 42	9-10
10	43 - 55	11 -12
11	56 - 68	13 - 15
12	69 - 76	16 - 17
13	77 - 87	18 - 21
14	88 - 93	22 - 25
15	94 - 96	26 - 28
16	97 - 98	29 - 34
17	99	35 - 38
18	>99	≥ 40
N		1554

Table 7
Scalar Scores and Percentile Ranges Corresponding to GDS-15 Raw Scores

GDS-15		
Scalar scores	**Percentile ranges**	**Raw scores**
9	≤31	0
10	32 - 55	1
12	56 - 69	2
13	70 - 85	3 - 4
14	86 - 91	5
15	92 - 96	6 -7
16	97 - 98	8 -9
17	98	10
18	≥99	≥11
N		1973

the existence of significant relationships between these socio-demographic variables (age, gender and education) and participants' performance in the MMSE, the GDS-15 and the MFE. However, the percentage of variance that explains each variable with respect to each test is small (between 0.1 and 2%), and it only approaches 10% in the case of educational level in MMSE. Thus, only the MMSE needs adjustment according with individual's educative level, as we stated previously in the statistical analysis subsection.

Regarding MMSE normative data, Li et al. (2016) administered the test to Chinese community residents aged 65 years or over selected by cluster random sampling (cognitively normal, with MCI, and with dementia). They found that years of education, rural residence, age, and being female had significant effects on MMSE scores. As in our study, educational level was the sociodemographic variable which has the highest weight in relation with MMSE scores. In Japan, Sakuma et al. (2017) carried out a study with a random sample of older Japanese adults living in an urban district in Tokyo (n = 1319; mean age, 74.4 ± 6.4 years; mean years of formal education, 12.6 ± 2.9). Younger age and higher education were associated with better performance. Greater variation was seen among the oldest and least educated residents, especially among women. Using an Arabic version of the MMSE, El-Hayeck et al. (2019) have found similar results with a population of 1,010 literate community-dwelling Lebanese residents aged 55 and above, since their results showed that MMSE scores increased with education and decreased with age, and also that women had significantly lower scores than men.

In relation to GDS-15, Nyunt et al. (2009) did not found differences in GDS-15 among different age, gender, ethnicity and comorbidities at cutoff of 4/5. Zhao et al. (2018) have reported a repeated cross-sectional study with a sample of 945 elderly individuals in rural China. Among the participants, the majority was female (61.4%) and illiterate (81.5%) and had a general economic status (63.0%) and more than two kinds of chronic diseases (62.9%). They found that poor economic status, the presence of more than two chronic diseases, cognitive impairment and anxiety, were the main risk factors for geriatric depression in rural China. Apóstolo et al. (2018) made a multicentric study with 139 older adults (23 with depression diagnostic) recruited in a context of primary care attention. The results obtained demonstrated that the screening capacity of the Portuguese version of GDS-15 was not affected by having or not having formal education, however as the authors pointed out, the participants without any formal education represented 12% of the study sample. In a recent study, Zhang et al. (2020) compared GDS-15 and the Patient Health Questionnaire-9 (PHQ-9) for evaluating depression in older adults. A total of 1546 participants aged ≥60 years were investigated. Their results showed that GDS-15 was affected by urban–rural distribution, but no other influence was found. However, Knight et al. (2004), in a study with a sample of 272 healthy older adults in New Zealand, found that participants in the age range 65-74 had lower scores than the older group, for both the GDS and GDS-15. Thus, negative evidence about age, education, or gender influence on GDS-15 scores seems to predominate in the reviewed literature.

In relation to MFE, Montejo et al. (2012a) carried out a study with 647 spanish employees at a large company ranging in age from 19-64 years old. Results did not show a constant increase in MFE across age groups, but differences were revealed between the 19-29 and 40-49 age groups; no differences were observed between the remaining age groups. Only slight differences between men and women occurred, the women's mean being slightly higher than the men's, but the confidence intervals overlapped. The authors concluded that these results indicate that age, years of education, and sex had no significant effects. In other study of this group (Montejo, Montenegro, Fernández-Blázquez et al., 2014), in which they studied the association of SMC with perceived state of health, mood and episodic memory in a sample of 269 older adults (aged 65–87) with age-related memory changes, but without cognitive impairment, results pointed out that age was not associated with subjective memory and, with regard to level of education, only the illiterate level was associated with SMC. When they studied the factorial structure of MFE (Montejo, Montenegro, Sueiro & Huertas, 2014) only appeared a positive correlation between age with a factor that have to do with recognizing in different situations, faces and places or routes. Thus, in general, evidence is compatible with the results derived from our study regarding MFE.

Our study has some limitations, for example, the medical conditions and the psychological variables that interfere with cognition, mood and self-perception of memory functioning were self-reported by the participants themselves, thus we cannot rule out the possibility that some may have associated comorbidities.

Among the future lines of work of the SCAND consortium is to monitor the cohort of volunteers in order to explore the predictive power of these screening instruments in relation to the subsequent expression of cognitive decline.

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