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Cognition, Functional Status, Education, and the Diagnosis of Dementia and Mild Cognitive Impairment in Spanish-Speaking Elderly

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A group of 314 Spanish-speaking elders were classified in 55 participants with mild to moderate dementia, 74 participants with mild cognitive impairment (MCI), and 185 control participants, according to clinical evaluation derived. Sensitivity, specificity, and detection characteristics of frequently cognitive and functional tests were calculated in comparison with the clinical evaluation: Minimental State Examination, Brief Neuropsychological Test Battery, Short Blessed test, Pfeffer Functional Activities Questionnaire, and Blessed Dementia Scale. Influence of education on sensitivity and specificity values varied along the tests. For all the cognitive and functional measures, a great number of MCI participants who fulfilled Mayo's clinical criteria (Petersen et al., 1999) were misclassified as controls and a few were misclassified as demented. Level of education plays a very important role in both cognitive and functional assessment. The cognitive tests that are commonly used to screen demented patients may fail to detect MCI particularly in high-functioning individuals as well as those who are well educated.

Key words: dementia, mild cognitive impairment, sensitivity, specificity, Spanish-speaking, cognitive and functional assessment

Clinical and epidemiological studies on dementia and normal aging depend of the accurate assessment of cognitive functioning and functional capacity. Neuropsychological assessment is a crucial component for early detection, for accurate diagnosis, as well as for the monitoring of disease progression and for the evaluation of treatment. Currently, neuropsychological assessment of dementia includes administration of screening tests in at-risk participants or suspected cases. The administration of neuropsychological batteries is employed to confirm or reject the diagnosis of dementia. A fundamental requirement of any neuropsychological examination is that it should have high specificity (adequate discrimination of individuals without pathology) and high sensitivity (adequate detection of individuals with cognitive deterioration). Furthermore, a major challenge in the diagnosis of dementia is the detection of cognitive markers for early and preclinical stages that can differentiate participants with cognitive impairment due to neurodegenerative process from those with cognitive impairment due to other, nondegenerative etiologies, including depression and normal aging. Several classifications of participants who manifest no evidence of neurodegenerative disease but with memory impairment have been proposed. Some classifications include the diagnosis of mild cognitive impairment (MCI; (Petersen et al., 1999) and questionable dementia (Hughes, Berg, Danziger, Coben, & Martin, 1982). These entities could represent the earliest stages of neurodegenerative disease.

There are many clinical batteries and rating scales for dementia that have been developed in response to the growing need to assess cognitive function and functional skills in at-risk participants. However, there are several factors that can confound the interpretation of test scores, including age, education, gender, and cultural background. Therefore, to increase the sensitivity and specificity of cognitive tests, it is important to take into consideration the effect of these factors. In Latin America and generally in all Spanish-speaking countries, most

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of the clinical measures have only been translated and adapted from the original ones without having normative data, or sensitivity and specificity indexes, which could allow a better estimation of the diagnostic validity of the test in this type of population. Therefore, the adaptation and validation of cognitive and functional measures become a highly relevant issue.

The purpose of this study was to assess the validity in terms of sensitivity, specificity, and detection characteristics of frequently used cognitive and functional screening tests when they are compared with the consensus of an experienced geriatrist team assisted by clinical and laboratory data, in a group of Spanish-speaking elderly participants with dementia and mild cognitive impairment.

Material and Methods

Procedure

The sample was derived from the Prevalence Survey of Dementia in Elderly Population of Mexico City (Gutiérrez et al., in press). This survey was conducted in a representative sample of 3,934 adults older than 65 years of age. People who were detected as having suspected cases of dementia or cognitive impairment were referred to the Instituto Nacional de Ciencias Médicas y Nutrición *Salvador Zubirán* (a reference center of third-level medical care in Mexico City) to confirm the presumptive diagnosis. A total of 332 suspected cases of dementia and 240 control participants were referred for a more detailed clinical assessment. Four hundred participants constitute the base of this study.

The clinical evaluation was conducted by a team of physicians, who elicited each participant's medical and neurological history and conducted a standardized physical and neurological examination. All participants had a computed axial tomography scan, and the presence of a history of depression, and signs or symptoms of stroke, diabetes, or hypertension, were noted. Prescribed medication was recorded. Estimation of level of function was based on a structured interview. Diagnostic criteria was derived from the participant's history taken form the participant and informant, the clinician's examination, and the neuropsychological profile (with out considering cutoff scores). Based on a study by Petersen and Morris (2003), a MCI diagnosis was made if the participant met all of the following criteria: (a) memory complaints, (b) normal activities of daily living, (c) normal general cognitive function, (d) memory impairment for age and education, and (e) no dementia. Controls were defined as individuals who (a) had normal functioning in the community, (b) did not have neurological or psychiatric conditions, (c) had no cognitive impairment or complaints, (d) had a normal neurological exam, and (e) were not taking any psychoactive medications in doses that could impact cognition. The diagnosis of dementia was based on the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (rev. 4th ed.; DSM–IV; American Psychiatric Association, 1994; see Figure 1). Information

1. The development of multiple cognitive deficits manifested by both
    a. memory impairment
    b. one or more of the following cognitive disturbances:
        (1) aphasia
        (2) apraxia
        (3) agnosia
        (4) disturbance in executive functioning
2. The cognitive deficits in Criteria 1a and 1b each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.

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Figure 1. General diagnostic criteria for dementia (American Psychiatric Association, 1994).

from all these evaluations was presented at a diagnostic conference of physicians and a consensus diagnosis was made for the presence or absence of dementia, and classification of MCI. This team did not have access to cognitive or functional test scores. The neuropsychological and formal functional evaluations were assessed with different tests and questionnaires (discussed later) and were applied by a trained neuropsychologist. Conventional criteria scores to classify participants with dementia were employed.

Participants

Initially, a total sample of 400 participants was studied: 297 women and 103 men, with a mean age of 75.7 years (*SD* = 5.5, range = 71–83) and an educational level average of 3.9 years (*SD* = 3.9, range = 0 to 20). Participants with mild to moderate depressive symptoms as well as those with low levels of performance limiting their self-sufficiency and independence on everyday activities, as well as those with physical disabilities that precluded the proper application of the test (i.e., severe reduction of visual acuity or blindness, hypoacusia or deafness), had to be excluded. Due to the importance of the educational level, the sample was stratified according to three educational levels: illiterates (0 years of school), low educational level (1–4 years of school), and middle educational level (5–9 years of school). Participants with a high educational level of 10 or more years were excluded due to the small number of group members. Thus, a total of 314 participants between the ages of 65 and 85 were studied and analyzed. From this sample, 55 participants were classified with a diagnosis of mild to moderate dementia regardless of its etiology, 74 participants received a diagnosis of MCI, and the rest (*n* = 185 participants) were considered as part of a comparison group. The dementia group included probable AXXXX DXXXX, vascular dementia, one case of posttraumatic XXXX and one case of Parkinson's associated dementia. Groups showed significant differences in age and education. Table 1 summarizes the demographic characteristics of the total sample.

Instruments

Cognitive functioning was assessed with the following tests:

1. A Spanish version of the Minimental State Examination (MMSE)—As Ostrosky, Lopez, and Ardila (2000) pointed out, currently in Mexico City; there are several translations of the MMSE. After interviewing 10 clinicians, the version used by 6 of them was selected. The score is from 0 to 30 points, with a cutoff point of 23 out of 24, under which some type of cognitive dysfunction is estimated. This is one of the instruments most frequently used for the detection of dementia (Crum, Anthony, Bassett, & Folstein, 1993).
2. The Brief Neuropsychological Evaluation for Spanish-Speaking Subjects (NEUROPSI; Ostrosky, Ardila, & Rosselli, 1999) is a brief neuropsychological battery evaluating a wide spectrum of cognitive functions including orientation, attention, memory, language, visuo-perceptual abilities, and executive functions. It contains items that are sensible and relevant for the Hispanic population and that can be used for illiterate people. Both the language stimuli and the drawings included were previously standardized according to high, medium, and low frequency of occurrence in the Spanish language (Aveleyra, Gómez, & Ostrosky–Solis, 1996). Drawings were adapted from the Snodgrass and Vanderwart (1980) drawing test. The NEUROPSI has standards obtained in the Mexican population, considering four levels of age, (16–30, 31–50, 51–65, and 66–85) and within each age range,

Table 1. *Sample Characteristics (N = 314)*

	Controls ***N* = 185**	**MCI** ***N* = 74**	**Dementia** ***N* = 55**	
	***M* (*SD*) %**	***M* (*SD*) %**	***M* (*SD*) %**	***p***
Age	72.7 ± 6.4	75.2 ± 6.9	80.3 ± 8.2	< 0.01
Gender: Male/Female	53/132	15/59	17/38	*NS*
Years of education	3.4 ± 2.9	2.5 ± 2.5	2.8 ± 2.7	< 0.05
Educational levels				
Illiterates	43	26	17	*NS*
1 to 4 years	72	31	23	
5 to 9 years	70	17	15	

Note. MCI = mild cognitive impairment. *p* for analysis of variance and chi-square where appropriate; *NS* = nonsignificant.

four school levels (0 years, 1 to 4 years, 5 to 9 years, and more than 10 years of study).

3. The Short Blessed Test is a reduced version of the Information-Memory-Concentration Mental Status Test originally devised by Blessed, Tomlinson, and Roth in 1968 with 26 items. Katzman, Brown, Fuld, and Peck (1983) validated the six-item Orientation-Memory-Concentration test as a measure of cognitive impairment. Participants are classified in three groups: minimally impaired (score of 0–8), moderately impaired (score of 9–19), and severely impaired (score of 20–33). In our study, the cutoff point was 8 out of 9.

Activities of Daily Living were assessed with two tests:

1. The Blessed Dementia Scale is the modified version of the informant-derived Blessed Dementia Scale (Blessed et al., 1968). It determines changes in activities of daily living. Scores range from 0 to 17 points, where higher scores indicate higher deterioration. It is included in the Consortium to Establish a Registry for Alzheimer's Disease (CERAD; Morris, Heyman, & Mohs, 1989). The score for the mild dementia group in the CERAD study is 3.7 ± 1.9. In our study, the cutoff point was 1.5.

2. The Pfeffer Functional Activities Questionnaire (Pfeffer, Kurosaki, & Harrah, 1982) is a questionnaire of 11 questions for an informant to rate participant's functional activities on a scale from 0 to 3, where 0 is *normal* and 3 is *dependent.* Scores ranges from 0 to 33 points, where higher scores indicate higher functional impairment. It has been shown to be highly sensitive for differentiation between normal and demented individuals with a cutoff point of 7.

Statistical Analysis

Means and standard deviations are reported when comparing continuous variables. To establish differences between the scores of the cognitive and functional tests according to classification group (demented, MCI, and control), controlling by covariates (educational level, age, and gender), multivariate analyses of variance were conducted.

Sensitivity, specificity, and positive and negative predictive values were calculated as conventional and expressed in percentages. Due to the significant effect of the age and education, classification tables obtained by multivariate logistic regression analyses were used for calculation of sensitivity and specificity, adjusting for them as covariates. Sensitivity and specificity were calculated separately for the diagnosis of dementia and for the diagnosis of MCI.

For the diagnosis of dementia, sensitivity was calculated as the number of test-positive cases (i.e., participants with a MMSE score of dementia) divided by the number of true-positive cases (i.e., participants with dementia) and specificity, as the number of test-negative cases (i.e., participants with a MMSE score of control) divided by the number of true-negative cases (i.e., normal participants). Overall accuracy is the percentage of participants who were accurately categorized either as demented or as controls by the instrument. Analyses were conducted for each group considering different levels of education within each group and total scores.

For the analysis of how participants with MCI were classified by each of the instruments, classification tables of logistic regression adjusting for age and education were also used. The number of participants with MCI classified as demented (false positives) and classified as controls (false negatives) was calculated.

Results

Analysis of total scores and multivariate analysis of cognitive and functional test by group, education, gender, and age, are presented in Table 2. Significant differences were observed between the three groups. The dementia group performed worse, followed by the mild

Table 2. *Means and Standard Deviations in Total Test Scores and Multivariate Analysis for Group, Education, Gender , and Age.*

	Controls	MCI	Dementia	Group Effect *P*	Educational Effect *P*	Gender Effect *P*	Age Effect *P*
MMSE	23.8 ± 4.2	21.2 ± 4.4	17.1 ± 5.3	< 0.01	< 0.01	*NS*	*NS*
Neuropsi	90 ± 16	70.6 ± 16.4	47.1 ± 18.6	< 0.01	< 0.01	*NS*	< 0.01
Short Blessed Test	3.5 ± 4.1	8 ± 5.2	17.7 ± 6.3	< 0.01	< 0.01	*NS*	< 0.05
Blessed Dementia Scale	1 ± 0.7	1.6 ± 1.2	4.8 ± 3.8	< 0.01	< 0.05	*NS*	*NS*
Pfeffer	2.9 ± 4	5.1 ± 5	13.6 ± 9.8	<0.01	*NS*	*NS*	< 0.05

Note. MCI = mild cognitive impairment; MMSE = Minimental State Examination. *P* for analysis of variance and chi-square where appropriate; *NS* = nonsignificant.

cognitive impairment group, which also performed below the control level on each of the cognitive tests. Although gender did not have a significant effect, age effect was observed on NEUROPSI, the Short Blessed Test, and on the Pfeffer questionnaire. Educational effect was observed on all of the cognitive measures and on one of the functional instruments: Blessed Dementia Scale. No educational effects were found for the Pfeffer Functional Activities Questionnaire.

When the sample was divided according to educational level, cognitive test scores on the three groups (dementia, MCI, and controls) and on the three educational levels (illiterates, l–4 years and 5–9 years) were significantly different. Tables 3 and 4 present the average test scores of the three groups (control, MCI, and demented) according to the three educational levels on each cognitive measure (Table 3), on the two functional measures (Table 4), and the results of a multivariate analysis by group and education.

Because all cognitive measures were developed to classify control versus dementia, we first calculated the sensitivity, specificity, and overall accuracy for all cognitive tests in each group (control and dementia) and each educational level (illiterates, 1–4 years and 5–9 years). These values are presented in Table 5.

With a cutoff point of 23 out of 24, the MMSE showed adequate sensitivity and specificity only in the middle educational group. However, in the illiterate and low educational level, this measure showed high sensitivity at the expenses of a low specificity. When sensitivity and specificity were analyzed for the NEUROPSI, it was observed that there is a high sensitivity, specificity, and overall accuracy in all three educational levels. The Short Blessed Test showed high sensitivity, specificity, and overall accuracy in the low and middle educational levels but low specificity in illiterate groups.

Both functional tests showed high specificity at the expenses of a low sensitivity in the low and middle educational group. However, the Blessed Dementia Scale had better classification values in the illiterate group.

Classification tables of logistic regression adjusting for age and education were used to determine the number of participants with MCI misclassified as demented (false positives) or as controls (false negatives). False negative and false positive rates in the cognitive and functional measures according to educational level are presented in Table 6. In the NEUROPSI, MMSE, and the two functional measures in the three educational levels, a high percentage of MCI participants were classified as controls and a low percentage were classified as de-

Table 3. *Means and Standard Deviations of Cognitive Measures By Group and Education (Multivariate Analysis).*

		Controls	MCI	Dementia	Group Effect *P*	Educational Effect *P*
MMSE	Illiterates	20.4 ± 5	18.7 ± 4.5	14.4 ± 5.1	< 0.01	< 0.01
	1 to 4 years	23.6 ± 3.4	22.2 ± 4	18.1 ± 4.6		
	5 to 9 years	26.2 ± 2.6	23.5 ± 2.5	19.3 ± 5.7		
NEUROPSI	Illiterates	75.3 ± 15	58.5 ± 13	38 ± 13	< 0.01	< 0.01
	1 to 4 years	85 ± 11.7	71.5 ± 12	49 ± 18		
	5 to 9 years	103 ± 10	88 ± 12.5	55 ± 21.3		
Short Blessed Test	Illiterates	5.3 ± 5	10.7 ± 5.2	20.7 ± 5	< 0.01	< 0.01
	1 to 4 years	3.7 ± 3.9	7.1 ± 5	16 ± 6.2		
	5 to 9 years	2 ± 2	4.9 ± 3.7	17 ± 6.7		

Note. MCI = mild cognitive impairment; MMSE = Minimal State Examination.
P = XXXX.

Table 4. *Means and Standard Deviations of Functional Measures By Group and Education (Multivariate Analysis).*

		Controls	MCI	Dementia	Group Effect *P*	Educational Effect *P*
Blessed Dementia Scale	Illiterates	0.9 ± 0.8	1.6 ± 1.1	3.4 ± 2.2	< 0.01	*NS*
	1 to 4 years	1 ± 0.7	1.7 ± 1.4	4.9 ± 4.2		
	5 to 9 years	0.9 ± 0.7	1.3 ± 0.9	6.5 ± 4		
Pfeffer	Illiterates	2.8 ± 3	1.6 ± 1	12.5 ± 8	< 0.01	*NS*
	1 to 4 years	3.2 ± 3.6	5.4 ± 4.8	13.3 ± 9		
	5 to 9 years	2.3 ± 3.9	4.1 ± 3.4	12 ± 10		

Note. mild cognitive impairment.
P = XXXXX.

Table 5. *Sensitivity, Specificity, and Overall Accuracy of Mental Status Test for Total Scores and Different Educational Levels*

Cognitive and Functional Measures	Educational levels		
	Illiterates	1–4	5–9
NEUROPSI			
Sensitivity (%)	82	87	93
Specificity (%)	95	98	98
Overall accuracy (%)	92	96	98
Minimental State			
Sensitivity (%)	95	90	83
Specificity (%)	23	28	85
Overall accuracy (%)	75	76	83
Short Blessed Test			
Sensitivity (%)	100	91	93
Specificity (%)	76	96	99
Overall accuracy (%)	83	95	98
Blessed Dementia Scale			
Sensitivity (%)	82	65	73
Specificity (%)	84	94	96
Overall accuracy (%)	87	87	92
Pfeffer Functional Questionnaire			
Sensitivity (%)	71	36	36
Specificity (%)	79	89	98
Overall accuracy (%)	76	76	87

Table 6. *False Negative and False Positive Rates for Classification of Participants With Mild Cognitive Impairment*

Cognitive and Functional Measures	Educational Levels		
	Illiterate	1–4	5–9
MMSE			
False negatives (%)	96	93	87
False positives (%)	17	23	46
NEUROPSI			
False negatives (%)	73	84	71
False positives (%)	23	13	29
Short Blessed Test			
False negatives (%)	42	54	76
False positives (%)	58	45	24
Blessed Dementia Scale			
False negatives (%)	62	58	94
False positives (%)	38	22	12
Pfeffer Questionnaire			
False negatives (%)	84	87	93
False positives (%)	27	23	27

Note. MMSE = Minimental State Examination.

mented. In the Short Blessed, illiterate, and low educational groups, the classification was at chance level.

Discussion

In this study, we compare the sensitivity, specificity, and detection characteristics of frequently used cognitive and functional screening tests in a group of Spanish-speaking elderly participants and we evaluate the overall ability of the instruments to predict true diagnostic status, as defined by the consensus of a team of experienced geriatrists assisted by clinical and laboratory data.

Our results show that the level of education plays a very important role in both cognitive and functional assessment. The performance on all the cognitive measures was modified by the educational level, the agreement between diagnosis based on clinical criteria, and cognitive-functional measure increases with years of education. For example, on the MMSE, which is frequently used as a gold standard instrument for the classification of dementia, the performance of normal individuals without education was equal to 20, which is below the cutoff point of 23. However, from all the measures used, the NEUROPSI is the only one that takes into account the level of education.

Crum and colleagues (1993) reported the distribution of MMSE scores by age and education in a population of 18,056 individuals in the United States. The mean score was 29 for individuals with more than 9 years of schooling, 26 for 5 to 8 years, and 22 for those with 0 to 4 years of schooling. Their MMSE scores differ from our study because the two MMSE versions are different. In the Crum et al. study, two modifications were made to the original examination on orientation and attention items. Alterations of this kind mean that the results are not comparable with other studies, although the same pattern in the effect of education is seen in our study.

Our findings coincide with other studies (Bertolucci, Brucki, Campacci, & Juliano, 1994; Bird, Canino, Rubio, & Shrout, 1987; Escobar et al., 1986, Ostrosky et. al, 2000), which have also reported that the MMSE score is sensitive to the participant's educational level and cultural background. This has significant implications for both research and clinical practice. Epidemiological studies that only include the MMSE as a rating instrument will classify normal participants with low education as demented. Like other screening scales, the MMSE may be useful in monitoring changes associated with pharmacological treatment or other types of intervention, but not for diagnosis.

Although the Blessed Dementia Scale shows adequate sensitivity and specificity with the illiterate people, the specificity and sensitivity in low and middle educational ranges was markedly reduced. This is probably due to a ceiling effect that allows participants with low and middle educational levels to compensate and perform the tasks. Diagnosis of dementia requires evi-

dence of impaired social or occupational functioning, therefore, the assessment of functional capacity is regarded as an important part of a comprehensive diagnostic work-up for dementia. Furthermore, evaluation of functional capacity has also become increasingly important to reduce the likelihood of spurious education and cultural effects. However, even functional capacities are prone to cultural biases. Loewenstein, Ardila, Rosselli, Hayden, and Duara (1992) compared Spanish- and English-speaking dementia patients and normal controls on a comprehensive functional assessment battery and found that despite equivalent levels of cognitive impairment, Spanish-speaking dementia patients evidenced more difficulties on certain functional tasks relative to their English-speaking counterparts. They suggested that the extent of deterioration in specific functional subskills may be related to the degree to which they have been overlearned and practiced. Therefore, they pointed out, that not only for neuropsychological measures but also for functional scales, there is a need for normative data for older adults who belong to different ethnic and cultural groups.

For all cognitive and functional measures, a great number of MCI participants (approximately 70%) who fulfill clinical criteria were misclassified as controls and a few were misclassified as demented. This was due to the fact that cutoff points classify participants as demented or controls and not as MCI. This is expected because clinical criteria for MCI requires normal general cognitive function and intact activities of daily living. However, currently a large proportion of studies are looking for preclinical indexes of dementia. Thus, when screening for dementia with these measures, a large proportion of the participants who are currently classified as controls will be included in the MCI group. This implies that the MCI population will not be considered a risk group and will not receive treatment at a stage when treatment should be implemented. Cognitive tests that are commonly used to screen demented patients (e.g., MMSE) may fail to detect MCI, particularly in high-functioning individuals and those who are well educated. Modifications to current diagnostic criteria for MCI to increase their capacity to detect incipient dementia have been suggested (Zaudig, 2002). Therefore, accurate clinical diagnosis of MCI can be enhanced by the use of objective and structured cognitive status examinations such as the test currently used in this study. Cutoff points proposed should consider age and educational level. Furthermore, cognitive testing of memory, attention, language, problem solving, and visual spatial abilities, will help to corroborate these findings and also to identify subgroups of MCI (Petersen, 2003).

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