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Validation of Addenbrooke's Cognitive Examination (ACE) in a Persian-Speaking Population

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Key Words

Cognitive assessment · Persian-speaking · Mini mental state examination · Addenbrooke's cognitive examination · Dementia

Abstract

Use of reliable screening and diagnostic tests for assessment of cognitive abilities in neurological patients is rapidly increasing in clinical practice. This is due to the increase in the prevalence of dementias and the raised awareness of cognitive impairment in neurological disorders. Two well-known bedside screening tests for dementias among the English-speaking population are the Mini Mental State Examination (MMSE) and Addenbrooke's Cognitive Examination (ACE). However, such tests have not been developed for the Persian-speaking population, which is estimated at 120 million worldwide. In this study we developed the Persian ACE and MMSE, adopted from the English version. We also assessed the sensitivity and specificity of these tests in the identification of Alzheimer's disease (AD) and mild cognitive impairment (MCI). We found that the Persian ACE at a cutoff point of 84, has a sensitivity of 93% and a specificity of 91% in discriminating MCI from a normal population; at 78, the test has a sensitivity of 73% and a specificity of 93% in differentiating MCI from AD, and at a similar cutoff point has a sensitivity of 100% and specificity of 96% in discriminating AD from a normal population. We conclude that the Persian ACE is a valuable tool in clinical practice in the Persian-speaking population.

Introduction

The application of bedside cognitive assessment has rapidly spread in clinical practice. This is mainly due to the increase in incident rate of dementias in the elderly [1–4], as well as increasing awareness of the cognitive symptoms in neurodegenerative disorders (e.g. multiple sclerosis, Parkinson's disease), not traditionally seen as causes of cognitive impairment in the early stages of these disorders. Formal cognitive assessment often takes 2–4 h and requires highly trained staff, which may not be available in district hospitals. Although bedside screening does not replace thorough neuropsychological assessment, it reduces inappropriate referrals to neuropsychologists.

The most popular bedside screening test is the Mini Mental State Examination (MMSE) [5]. Evidence suggests that this test has relatively low sensitivity in the ear-

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Table 1. Demographic characteristics of participants and mean scores in ACE and MMSE tests

Group	Normal (n = 71)	MCI (n = 35)	AD (n = 30)	F	p
Female	23 (32.4%)	10 (28.6%)	15 (50%)	–	–
Age, mean ± SD					
Years	58.34 ± 10.61	62.17 ± 10.61	63.10 ± 12.53	1.388	0.241
Range	41–83	42–81	46–85		
Education, mean ± SD					
Years	10.30 ± 3.75	10.86 ± 3.91	9.20 ± 2.53	1.569	0.185
Range	4–18	4–18	4–18		
Mean ACE score (SD) calculated from 100	90.59 ± 4.80	76.71 ± 7.60	73.00 ± 3.22	146.02	<0.001
Mean MMSE score (SD) calculated from 30	27.84 ± 1.03	27.54 ± 0.74	21.90 ± 2.1	239.22	<0.001

ly stages of dementia [6], particularly in frontotemporal dementia (FTD) [7, 8]. The Addenbrooke's Cognitive Examination (ACE) greatly increased the sensitivity of MMSE [8]. The ACE was developed by extending the memory, language, and visuospatial abilities components of the MMSE and adding a verbal fluency component [2, 8]. The ACE has been translated into many languages including French [9], Malayalam [1] and Spanish [10, 11]. Recent findings in mild cognitive impairment (MCI), FTD and Alzheimer's disease (AD) showed that while the diagnostic ability of this test is not influenced by scholastic experience, different cutoff points should be established for various educational levels [2, 10]. The present research is aimed at validating the ACE among a native Persian-speaking population. The results should be beneficial for examining Persian-speaking populations in Iran, Afghanistan and Tajikistan as well as these countries' expatriates.

Subjects and Methods

Subjects

This study was approved by the local ethics committee. All subjects provided written and informed consent to participate in this study. The study's cohort consisted of 139 subjects (106 males and 33 females), of whom 71 were normal subjects, 30 were diagnosed with AD, and 35 had MCI. Demographic information of the cohort is provided in table 1. Normal subjects were randomly recruited from cultural centers, parks, and elderly clubs.

Subjects with MCI or AD were recruited through the Iranian Alzheimer's Society. All patients underwent physical and psychological examination as well as MRI scans. Patients were classified according to the Clinical Dementia Rating (CDR), in which scores <1 were classified as MCI and scores >1 were classified as AD. Diagnosis of AD and MCI were made by a cognitive neurologist in accordance with the internationally agreed NINCDS-ADRDA diagnostic criteria [12].

Exclusion criteria for normal controls were: (1) a history of major neurological or psychiatric disorders, (2) a history of stroke, heart attack, or head injury, and (3) hospitalization for any reason within the last year. In both AD and MCI groups, those with a diagnosis exceeding 9 months were also excluded. A subgroup of AD and normal group (15 in each group) were retested 1 month later to examine the reliability of the ACE.

Adoption of ACE from English to Persian

The ACE was translated to Persian and then back to English by separate teams of psychologists and professional translators. The following changes were made due to different linguistic properties of the 2 languages: the word 'divar' (means 'wall') in 'Attention and Concentration subtest' was replaced by 'world'. Both 'world' and 'divar' are similar in number of letters and phoneme-grapheme transparence. In the assessment of 'Anterograde Memory,' the address was given in the reverse order (i.e., name of the town, area, street, house number), as it is customary in Iran. In the 'Retrograde Memory' portion, the name of the current prime minister of England was replaced with the name of the current president of Iran. In the second question, the name of the prime minister who nationalized the Iranian oil industry (Dr. Mohammad Mosaddegh) and the name of Iran's Chief Justice who was assassinated by terrorists (Dr. Mohammad Beheshti) were used.

In order to identify a suitable letter for the 'Verbal Fluency' subtest, 3 letters (i.e., /b/, /p/, and /d/) were examined as a part of a pilot study. Eventually, letter /b/ was found to be the best equivalent to the letter of 'P', which is used in the English version. To choose suitable synonymous for 'above, beyond, and below' and "No 'ifs', 'ands', or 'buts'" in the 'Language' subtest, a list of possible surrogates were tested through a pilot study and the most appropriate ones were chosen.

Five out of 10 items were changed in the 'Naming subtest'. 'Kangaroo' and 'penguin' were replaced by 'giraffe' and 'owl', respectively. 'Harp' and 'accordion' were replaced with 'santoor' and 'setar' (both stringed musical instruments), which are more familiar to people in the targeted geographic region. Furthermore, 'barrel' was substituted for 'box'. In the 'Comprehension' section, the questions were changed in accordance to the changes made in the previous part. In the 'Reading Part of Language' portion, the 3 regular and 2 irregular words in the English version were replaced with an equal number of regular and irregular

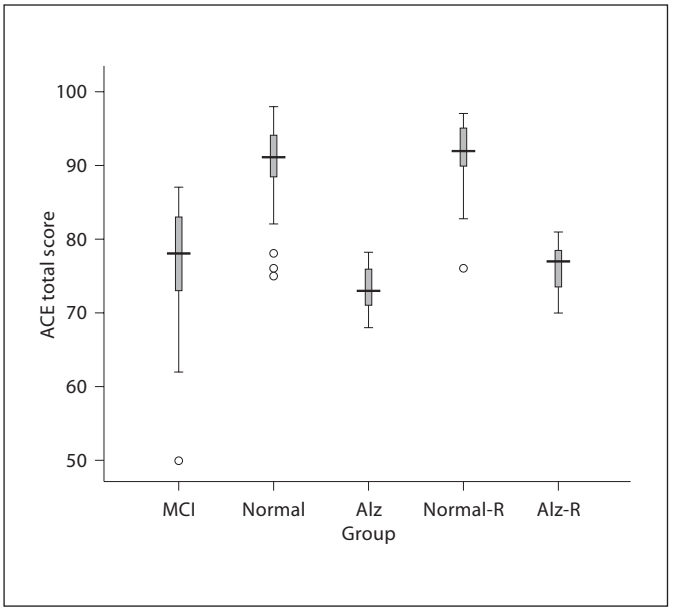

Fig. 1. Spatial distribution of subjects' ACE scores in each study group. The two right bars show retest results.

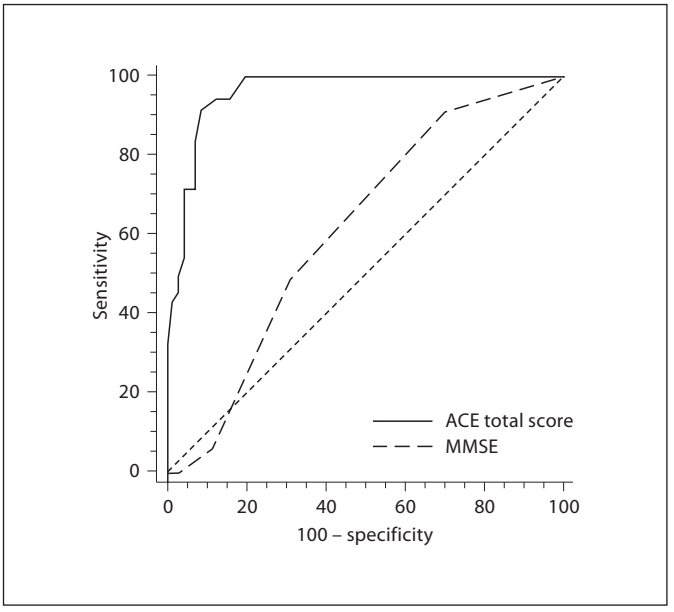

Fig. 2. ROC curve for ACE and MMSE scores (MCI versus controls).

words in the Persian language. In the 'Perceptual Abilities' section, 4 Persian letters replaced English letters with similar geometric complexity. In the 'Recall and Recognition' portions, relevant changes were made regarding the new address in 'Anterograde Memory'.

Results

There was no significant difference between the male and the female population in any group [$\chi^2 = 3.79$; $p = 0.15$]. Separate one-way analysis of variance (ANOVA) tests showed that there were no significant differences due to the effects of age [$F(2,135) = 1.38$; $p = 0.08$] or education [$F(2,135) = 1.56$; $p = 0.16$]. A similar set of analysis confirmed significant group effects on the mean scores of the MMSE [$F(2,135) = 239.22$; $p < 0.001$] as well as the ACE [$F(2,135) = 146.02$; $p < 0.001$] (fig. 1). Post-hoc analyses, however, revealed that the MMSE scores are sensitive enough to discriminate AD patients from those with MCI and normal subjects but not sensitive enough to discriminate between patients with MCI and normal participants. This lack of sensitivity was not the case in the ACE, as post-hoc analyses revealed significant differences between the 3 groups. We retested this including age, gender, and educational level as covariates but found no differences in the result of ANOVA.

Pearson's bivariate correlation analysis revealed a negative significant correlation between the total MMSE scores and age ($r = -0.28$; $p = 0.03$), but no significant correlation between total ACE scores and age ($r = -0.16$; $p = 0.06$). This would imply that age might have an effect on MMSE but not on ACE scores.

Cutoff Scores

Sensitivity and specificity indices were calculated for all possible ACE cutoff points. The receiver operating characteristics (ROC) curve was calculated to estimate discrimination power. The optimal ACE cutoff point to differentiate patients with MCI from normal subjects was 84, with a sensitivity of 93% and a specificity of 91%. The area under ROC curve for both ACE and MMSE scores were 0.96 and 0.63, respectively (fig. 2). Furthermore, the optimal ACE cutoff point to differentiate patients with MCI from patients with AD was 78, with a sensitivity of 73% and a specificity of 93% (fig. 3). Similar cutoff points were found for differentiating AD patients from normal subjects with sensitivity of 100% and specificity of 96% (fig. 4).

As indicated in figure 2, ACE scores cover a larger area under the curve than MMSE scores. This pattern was reversed in AD patients as shown in figure 3 and 4. Areas under the ROC curve for MCI versus AD (fig. 3) and for

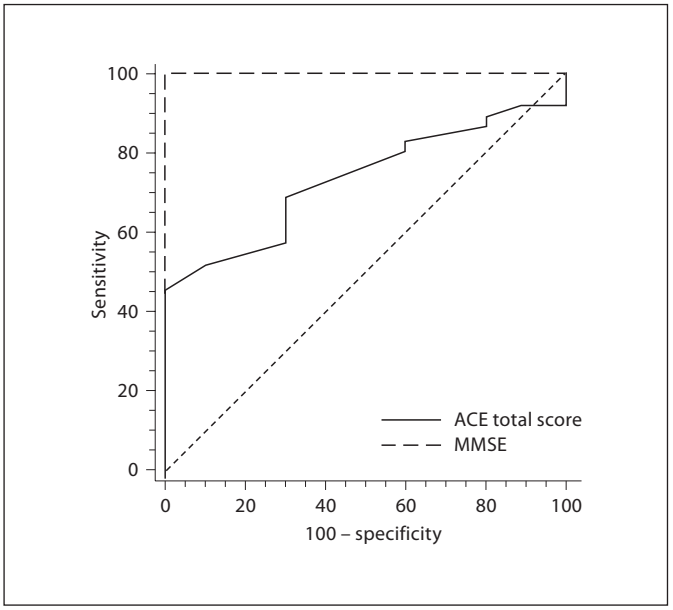

Fig. 3. ROC curve for ACE and MMSE scores (MCI versus AD).

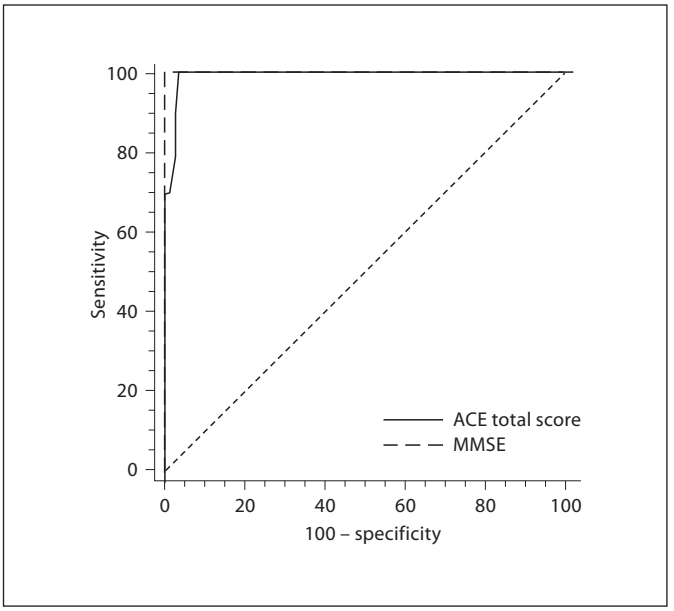

Fig. 4. ROC curve for ACE and MMSE scores (controls versus AD).

AD versus normal subjects were larger for MMSE scores than for ACE scores. The mean (ACE scores and subscores) VLOM ratio [derived using component scores: (verbal fluency + language)/(orientation + memory)] calculated for the patient group was 3.70.

Results of correlational analysis between test-retest scores of ACE in normal and AD groups revealed a high correlation between the 2 scores in both groups ($r = 0.95$ with $p < 0.001$, and $r = 0.88$ with $p < 0.001$). In addition, Cronbach's alpha coefficient (an index of test reliability) calculated in this study overall was 0.84 (0.93 for AD patients, 0.97 for normal patients and 0.88 for MCI patients).

Discussion

The present study is an attempt to adapt and validate the ACE for native Persian-speaking populations. We paid special attention to cultural and linguistic differences between English and Persian culture whilst maintaining the main concepts of the original version. We calculated new cutoff points for the translated version to define abnormality as suggested in previous work [13]. The original ACE was designed using an adult population with a high educational level and validated in a non-patient sample referred by the Memory Clinic of Cambridge, England [2]. The current study conducted the translation process over 4 phases including: initial translation, reverse translation, substitution of culturally dependent elements, and correction of these elements. At each stage a pilot study was carried out to assess the validity of any changes that were implemented in that stage. This ensured a dynamic and flexible method of translation, which was reliably informed by local knowledge and cultural differences.

Results revealed that individuals in different age groups obtained nearly equal ACE scores (table 2) supporting the notion that ACE scores are independent from the subject's age. Moreover, one-way ANOVA demonstrated the high diagnostic ability of the ACE in differentiating subjects with AD and MCI as the mean scores of patients and the normal group showed a significant difference. This indicates that ACE could be used as a reliable screening tool for early diagnosis of dementia and MCI in Persian speaking populations. The strong correlation between test-retest scores and Cronbach's alpha coefficients in clinical and normal groups suggests the Persian version of the ACE has high reliability.

The Persian ACE appeared with greater diagnostic value than the MMSE, because of the larger area under the ROC curve for the ACE. In addition, the VLOM ratio of MCI patients (3.7) indicates the high test sensitivity in differentiating subjects with and without dementia [14].

These results further confirm that additional subtests in the ACE provide greater diagnostic power in assessing dementia [10].

The cutoff level (84) in the Persian ACE is similar to the English version (83), but well above the Spanish version (68) [2, 10]. Although, the area under the ROC curve and VLOM ratio indicated that this score is sensitive and specific enough for differentiating MCI from normal individuals.

Conversely, the sensitivity and specificity of the Persian ACE for differentiating patients with MCI from AD (78) was lower than the English and Spanish versions [2, 10]. The reason for this is not entirely clear but cultural factors and general knowledge differences might play a role.

Finally, we conclude that this Persian version of the ACE is a useful and reliable clinical tool for differentiating patients with dementia from the normal population.

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References

1 Mathuranath PS, Hodges JR, Mathew R, Cherian PJ, George A, Bak TH: Adaptation of the ace for a Malayalam speaking population in southern India. Int J Geriatr Psychiatry 2004;19:1188–1194.

2 Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR: A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. Neurology 2000;55:1613–1620.

3 Mendez MF, Doss RC, Cherrier MM: Use of the cognitive estimations test to discriminate frontotemporal dementia from Alzheimer's disease. J Geriatr Psychiatry Neurol 1998;11:2–6.

4 Vandehey N, Garell P, Hampel J, Murali D, Smith E, Davidson R, Converse A, Nickles R, Christian B: PET measurement of changes in D2/D3 dopamine receptor binding in a non-human primate during chronic deep brain stimulation of the bed nucleus of the stria terminalis. J Neurosci Methods 2008;176:129–135.

5 Folstein MF, Folstein SE, McHugh PR: 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.

6 Tombaugh TN, McIntyre NJ: The mini-mental state examination: a comprehensive review. J Am Geriatr Soc 1992;40:922–935.

7 Gregory CA, Orrell M, Sahakian B, Hodges JR: Can frontotemporal dementia and Alzheimer's disease be differentiated using a brief battery of tests? Int J Geriatr Psychiatry 1997;12:375–383.

8 Hodges JR, Patterson K, Ward R, Garrard P, Bak T, Perry R, Gregory C: The differentiation of semantic dementia and frontal lobe dementia (temporal and frontal variants of frontotemporal dementia) from early Alzheimer's disease: a comparative neuropsychological study. Neuropsychology 1999;13:31–40.

9 Bier JC, Donckels V, Van Eyll E, Claes T, Slama H, Fery P, Vokaer M: The French Addenbrooke's cognitive examination is effective in detecting dementia in a French-speaking population. Dement Geriatr Cogn Disord 2005;19:15–17.

10 Garcia-Caballero A, Garcia-Lado I, Gonzalez-Hermida J, Recimil M, Area R, Manes F, Lamas S, Berrios G: Validation of the Spanish version of the Addenbrooke's cognitive examination in a rural community in Spain. Int J Geriatr Psychiatry 2006;21:239–245.

11 Sarasola D, de Luján-Calcagno M, Sabe L, Crivelli L, Torralva T, Roca M, García-Caballero A, Manes F: Validity of the Spanish version of the Addenbrooke's Cognitive Examination for the diagnosis of dementia and to differentiate Alzheimer's disease and frontotemporal dementia (in Spanish). Rev Neurol 2005;41:717–721.

12 McKhann G, Drachman D, Folstein M: Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 1984;34:939–944.

13 Hooman HA: Educational and psychological measurements. Tehran 2005.

14 Larner AJ: Addenbrooke's cognitive examination (ACE) for the diagnosis and differential diagnosis of dementia. Clin Neurol Neurosurg 2007;109:491–494.