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Clinical characteristics and diagnostic accuracy of the revised Addenbrooke Cognitive Examination (ACE-R) in older adults with a low educational level

Características clínicas e acurácia do Exame Cognitivo Addenbrooke Versão revisada (ACE-R) em idosos com baixa escolaridade

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ABSTRACT

Objective: To determine the diagnostic accuracy of the Addenbrooke's Cognitive Examination Revised (ACE-R) as a cognitive screening tool for older adults with low levels of schooling and healthy aging, MCI and dementia in Brazil. **Methods:** All participants underwent neurological and psychiatric examinations and were administered a validated version of ACE-R. **Results:** A total of 85 participants were evaluated; most were females (84.7%, n = 72). The *post hoc* analysis showed statistical differences in ACE-R total scores between older adults with mild cognitive impairment (MCI) and controls (p < 0.001) and in subitem scores including verbal fluency, language, visuospatial skills and attention (p < 0.001). The visual-spatial skills subitem was the most strongly correlated with schooling level (r = 0.509, p < 0.001), whereas late, immediate recall and recognition memory were not influenced by schooling. The ACE-R had the best diagnostic accuracy in discriminating between MCI and controls = 0.69 (<57.5; 80/66), MD and controls = 0.98 (<50; 100/96), MCI and MD = 0.86 (<49.5; 100/74). **Conclusions:** ACE-R and Mini-Mental State Examination (MMSE) scores for older adults with MCI and controls were significantly lower than those reported in similar studies. These preliminary findings support the need for establishing reliable cut-off scores for cognitive assessment of older Brazilian adults with low schooling at risk for dementia taking into consideration ecological and local variables.

KEYWORDS

Dementia, cognitive screening, illiterate, Northeast, Addenbrooke, accuracy.

RESUMO

Objetivo: Determinar a precisão diagnóstica do Exame Cognitivo de Addenbrooke (ACE-R) como uma ferramenta de triagem cognitiva para adultos idosos com baixos níveis de educação e envelhecimento saudável, MCI e demência no Brasil. **Métodos:** Os indivíduos submeteram-se à avaliação clínica e psiquiátrica e foi administrada uma versão validada da versão revisada da bateria cognitiva ACE-R (ACE-R). **Resultados:** Oitenta e cinco indivíduos foram avaliados, predominando as mulheres (84,7%, n = 72). Na análise *post hoc*, controles e CCL exibiram diferenças estatísticas nos escores globais do ACE-R (p < 0,001) e seus subdomínios, incluindo fluência verbal, linguagem, habilidades visuoespaciais e atenção (p < 0,001). A habilidade visuoespacial foi o item mais correlacionado com a escolaridade (r = 0,509, p < 0,001), enquanto a memória tardia, de recordação e reconhecimento não foi influenciada pela educação. A precisão do ACE-R produziu melhores resultados para CCL *versus* controles = 0,69 (<57,5; 80/66), demência *versus* controles = 0,98 (<50; 100/96), CCL *versus* demência = 0,86 (<49,5; 100/74). **Conclusões:** Os escores de ACE-R e MMSE para controles e CCL foram consideravelmente inferiores aos encontrados em estudos semelhantes. Resultados preliminares confirmam a necessidade de estudos brasileiros estabelecerem pontos de corte confiáveis para baterias cognitivas em idosos com baixa escolaridade e em risco de demência, reconhecendo variáveis ecológicas e regionais.

PALAVRAS-CHAVE

Demência, triagem cognitiva, analfabetos, Addenbrooke, acurácia.

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INTRODUCTION

The increase in life expectancy in Brazil has been associated with a higher prevalence of age-related mental conditions such as Alzheimer's disease (AD)^{1,2}. Brazil is one of 10 countries with the largest population of older adults in the world (WHO-UN). According to the Brazilian Institute of Geography and Statistics (IBGE) data from the 2000 Population Census, 9.7% of Brazil's population is 60 years old or more³. By 2020, the Brazilian population of older adults aged 60 or more is projected to reach 29.8 million, and those over 80 are expected to reach 4.7 million⁴, and around 3 million people (11%) will have dementia. In the Northeast city of Fortaleza, it is estimated that at least 23,000 adults have dementia³.

AD is the most common type of dementia syndrome accounting for about 50% to 70% of dementia cases, alone or in combination⁵. Mild cognitive impairment (MCI) is considered an intermediate stage between healthy aging and dementia⁶⁻⁹. The prevalence of MCI in people over 65 years of age is 12-18%¹⁰, and the annual rate of progression from MCI to AD is 10-15%^{7,11}. In Brazil, the estimated incidence rate of MCI is 13.2%¹². Early detection of MCI in older adults using validated screening tests is of great importance since this population group could benefit from new drugs that are being investigated for the treatment of degenerative diseases such as AD. Also, evidence shows that, since MCI is a transitional stage between normal aging and AD, there is less brain involvement and those affected are theoretically more likely to benefit from drug therapies⁹.

Cognitive tests are commonly used for screening cognitive impairment, etiological diagnosis, establishing disease severity and monitoring disease progression¹³. A major challenge for the initial assessment of age-related cognitive disorders is to select a screening test that is both sensitive and specific for differential diagnosis. Ceiling and floor effects limit the ability of a test or some of its items to accurately assess cognitive impairment¹⁴. The ceiling effect occurs when score distribution is skewed and variance in a cognitive domain is no longer "achieved", thereby preventing to assessment test performance. This effect has been reported in several studies and is primarily related to educational background. Another important aspect is the need for cognitive assessment tests that are fast tools that do not require specialized training and have the ability to accurately discriminate adults with healthy aging, MCI and dementia.

In Brazil, several epidemiological studies have investigated age-related memory changes in older adults. In a study by Almeida¹⁵, Mini-Mental State Examination (MMSE) cutoff scores of 23-24 yielded 84% sensitivity, but low specificity (60%) to discriminate between MCI-normal aging and dementia. Brucki¹⁴ reported that schooling level was the most important factor influencing MMSE scores (ANOVA F[4,

425] 100.45, $p < 0.0001$), and cutoff scores for illiterate people (score = 20) were the lowest across all groups evaluated.

Few cognitive screening studies of dementia and neuropsychiatric disorders in older adults have been conducted outside major metropolitan areas in Brazil, including most northeastern cities.¹⁶ This is mainly because these studies involve expensive assessments in specialized services. We conducted an electronic search in the PUBMED database and found only two studies conducted in Northeast Brazil – one from 2005 by Brito-Marques and Cabral Filho¹⁷ and another one from 2012 by Caldas *et al.*¹⁸. Cognitive assessment of adults who are either illiterate or with low levels of schooling poses additional challenges. About 14 million people are estimated to be illiterate in Brazil and a large proportion of them are older adults. Together with aging, educational background is a known important variable associated with cognitive decline. Despite the large proportion of older adults who are either illiterate or with low levels of schooling in Brazil (20.4%), there is great controversy about reliable approaches for cognitive assessment of this population. Previous studies have sought to establish valid cutoff scores for illiterate adults^{1,2}, but there is no consensus on whether data can be replicable in populations from different regions nationwide. Sociocultural aspects, e.g., living in rural areas and having limited access to the internet, banking services and public transportation, may influence cognitive performance¹⁹.

The existing body of evidence supports the study of psychometric properties of cognitive instruments available to make their use practical and adapted to the local reality¹⁸, especially in Northeast Brazil, as well as to avoid educational bias usually seen in cognitive scales validated to the Brazilian population. Our study aimed to determine the diagnostic accuracy of the Addenbrooke's Cognitive Examination Revised (ACE-R) as a cognitive screening tool for older adults with low levels of schooling and healthy aging, MCI and dementia in Brazil. This study will be also supported by data from our research project – the Addencog project. Our main hypothesis is that specific cutoff scores can be used for cognitive assessment of older adults with low levels of literacy living in Northeast Brazil.

METHODS

The Addencog research project is a multicenter initiative conducted in two metropolitan areas in Northeast Brazil – the city of São Luís (state of Maranhão) and Fortaleza (state of Ceará). Participants were older adults consecutively recruited in 3 community centers from January 2018 to April 2019 as well as patients attending two geriatric neuropsychiatry outpatient services. The present study evaluated a total of 87 participants comprising 9 adults with mild dementia (MD) (4 from Fortaleza and 5 from São Luís), 49 with MCI (24 from

Fortaleza and 25 from São Luís) and 29 healthy aging controls (14 from Fortaleza and 15 from São Luís). Sociodemographic information was collected from medical history and clinical examination through an interview conducted by a geriatric psychiatrist and three senior neurologists (GSA, JISN, PB and WL). The ACE-R was used to assess different cognitive domains including memory, attention, language, verbal fluency and visuospatial skills²⁰. All participants underwent neurological and psychiatric examination and imaging studies (computerized tomography or magnetic resonance imaging). They were initially evaluated using the Clinical Dementia Rating (CDR) and the Functional Activities Questionnaire (FAQ)²¹ to assess functional ability and were categorized as cognitively healthy, MCI and MD if CDR = 0, CDR = 0.5 and CDR = 1, respectively. Healthy and MCI participants showed normal FAQ scores whereas those with MD had scores >5 in FAQ, which suggests impaired functional ability. The ACE-R and MMSE were then administered to all participants; these instruments were not used to establish a diagnosis. Only those with up to 5 years of formal schooling (verified by family members) were considered eligible for the study. MCI diagnosis was based on Petersen criteria⁶. We used weighted scores to interpret MMSE results for illiterate participants as described by Brucki et al.¹⁴ and confirm healthy aging status or MCI. The diagnosis of dementia was based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the International Statistical Classification of Diseases and Related Health Problems (ICD-10) criteria^{22,23}. The main exclusion criteria were neurological diseases such as a history of stroke, traumatic brain injury, epilepsy, multiple sclerosis, or previous psychiatric conditions (major depression, bipolar disorder, schizophrenia, or alcohol dependence). As the total ACE-R score and its subitems and MMSE scores exhibited normal curve distribution in the Kolmogorov Smirnov Test, parametric testing was performed, with Pearson correlation and ANOVA independent group test with Bonferroni correction for multiple comparisons being performed. A p-value < 0.05 was adopted as statistically significant. SPSS version 26.0 was carried out for calculation.

The study was approved by the National Research Ethics Committee (CAAE: 75982215.2.0000.5054) and followed the Declaration of Helsinki. All participants received information of the study protocol before signing the consent form.

RESULTS

Sociodemographic characteristics

Table 1 shows the main clinical characteristics of the study participants. A total of 87 participants were evaluated (mean age 73.16; SD 8.71). The mean age was lower among controls

compared to MCI and MD participants, but this difference was not statistically significant. There were no other significant differences in age and education.

The majority of the participants were married, homemakers, diagnosed with MCI, and had at least 2 medical comorbidities (most commonly hypertension, dyslipidemia, or thyroid disorders) (Table 1). Their mean income was 493.26 US dollars (SD 502.78), which is considered an average income level in Brazil²⁴.

Correlation between variables

Schooling was moderately correlated with MMSE (0.481, $p \leq 0.001$) and ACE-R scores (0.484, $p \leq 0.001$). In the ACE-R, the subitem most strongly correlated with the literacy level was visuospatial skills ($r = 0.509$, $p < 0.001$). Conversely, other subitems such as immediate memory, late anterograde memory, and recognition memory were less influenced by schooling level ($p > 0.05$).

Controls versus MCI

Controls showed mean MMSE scores of 25.66 (Table 2), which were significantly higher than those for MCI and MD participants (Table 2). Mean ACE-R scores and subitem scores for attention, memory, verbal fluency, language and visuospatial skills were higher in controls than MCI participants (Table 2).

Receiver operating characteristic (ROC) curve analysis

We assessed sensitivity and specificity for the MMSE and ACE-R using receiver operating characteristic (ROC) curves (Figures 1 and 2). Optimal sensitivity and specificity values were defined based on Youden's index²⁵: $J: \max\{sensitivity_i + specificity - 1\}$ where i represents the pair of coordinates on the graph.

When we compared MD versus MCI, the area under the ROC curve (AUC) for the MMSE was 0.84, which is considered very good using Meyers' scale²⁶; it showed 0.89 sensitivity and 0.85 specificity for a cutoff score of 19.5 (Figure 3). For the ACE-R, the AUC was 0.86, which is considered very good²⁶; it showed 1.00 sensitivity and 0.74 specificity for a cutoff score of 49.5 (Figure 3).

When we compared MD versus controls, the AUC for the MMSE was 0.96, which is considered excellent using Meyers' scale²⁶; the MMSE showed 0.89 sensitivity and 1.00 specificity for a cutoff score of 20 (Figure 1). For the ACE-R, the AUC was 0.98, which is considered excellent²⁶; it showed 1.00 sensitivity and 0.96 specificity for a cutoff score of 50 (Figure 1).

When we compared MCI versus controls, the AUC for the MMSE was 0.69, which is considered not good²⁶; it showed 0.96 sensitivity and 0.34 specificity for a cutoff score of 26.5 (Figure 2). For the ACE-R, the AUC was 0.69, which is considered not good²⁶; it showed 0.80 sensitivity and 0.66 specificity for a cutoff score of 57.5 (Figure 2).

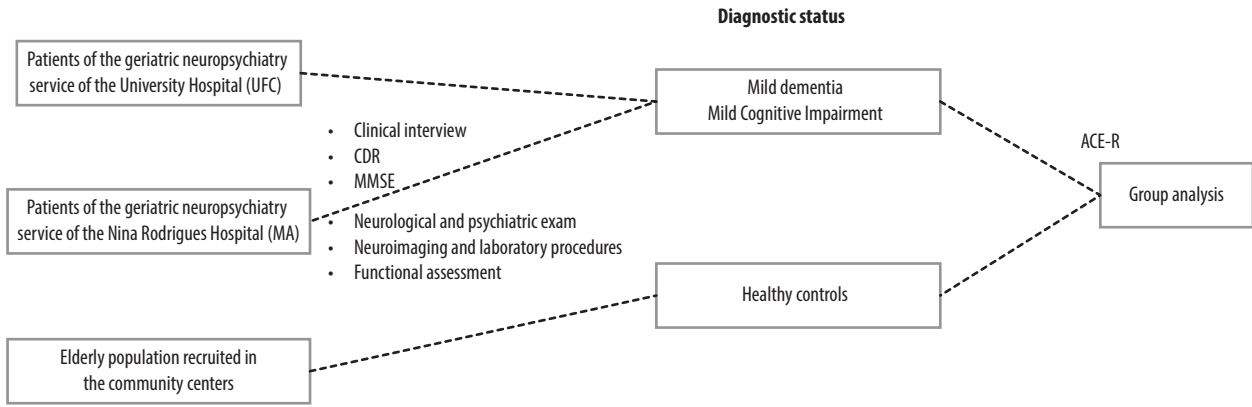
Table 1. Socio demographic characteristics

Variable	Group Frequency (%)			
	Controls 29 (33.33)	MCI 49 (56.32)	Dementia 9 (10.34)	Total 87 (100)
	25 (28.73)	41 (47.13)	8(9.19)	74 (85.05)
Gender (women)				
Ethnicity				
Black African	8 (9.19)	6 (6.90)	1 (1.15)	15 (17.24)
Brown	14 (16.09)	35 (40.23)	4 (4.60)	53 (60.92)
White and other	7 (8.05)	8 (9.19)	4 (4.60)	19 (21.84)
Marital status				
Married	13 (14.94)	11 (12.64)	7 (8.05)	31 (35.63)
Widowed	9 (10.34)	5 (5.75)	2 (2.30)	16 (18.39)
Divorced	3 (3.45)	13 (14.94)	0	16 (18.39)
Single	4 (4.60)	20 (22.99)	0	24 (27.59)
Previous occupation				
Employed	7 (8.05)	6 (6.90)	2 (2.30)	15 (17.25)
Domestic worker	13 (14.94)	26 (29.88)	6 (6.90)	45 (51.72)
Self employed	5 (5.75)	10 (11.49)	1 (1.15)	16 (18.39)
Employer	4 (4.60)	7 (8.05)	0	11 (12.65)
Comorbidities				
Less than one	5 (5.75)	4 (4.60)	0	9 (10.35)
1 comorbidity	9 (10.34)	16 (18.39)	5 (5.75)	30 (34.48)
≥ 2 comorbidities	15 (17.24)	29 (33.33)	4 (4.60)	48 (55.17)
Hypertension	20 (22.99)	30 (34.48)	5 (5.75)	55 (63.22)
Dyslipidemia	8 (9.19)	18 (20.69)	2 (2.30)	28 (32.18)
Diabetes	4 (4.60)	5 (5.75)	1 (1.15)	10 (11.50)
Thyroid and osteo metabolic diseases	1 (1.15)	14 (16.09)	0	15 (17.24)
Other medical comorbidities	0	10 (11.49)	0	10 (11.49)
Family report of dementia	7 (8.05)	12 (13.79)	1 (1.15)	20 (22.99)
Alcohol use (previous or current use)	7 (8.05)	16 (18.39)	1 (1.15)	24 (27.59)
Tobacco (previous or current use)	8 (9.19)	12 (13.79)	5 (5.75)	25 (28.73)

Table 2. Socio demographic and cognitive profile and group comparisons

Variable	Controls (n = 29)	MCI (n=49)	Dementia (n = 9)	F	Significance – p level*		
	Mean (SD)	Mean (SD)	Mean (SD)		Con vs. MCI	MCI vs. Dem	Dem vs. Con
Age	70.48 (6.69)	74.76 (9.30)	73.11 (9.95)	2.253	0.110	1.000	1.000
Education (years)	2.90 (2.16)	2.55 (1.72)	2.33 (2.23)	0.422	1.000	1.000	1.000
MMSE	25.66 (2.47)	22.02 (3.48)	17.22 (3.42)	27.127	<0.001	<0.001	<0.001
ACE-R	70.14 (13.02)	52.49 (11.00)	39.89 (6.86)	33.181	<0.001	0.009	<0.001
Attention-orientation	14.86 (1.86)	12.57 (2.11)	9.22 (1.71)	29.837	<0.001	<0.001	<0.001
Memory component I	11.45 (3.59)	8.39 (3.01)	6.44 (1.67)	12.679	<0.001	0.269	<0.001
Memory component II	6.85 (2.51)	4.40 (2.17)	4.56 (1.88)	9.698	<0.001	1.000	0.033
Memory (total)	17.58 (6.10)	11.97 (4.51)	11.00 (2.64)	13.118	<0.001	1.000	0.002
Verbal Fluency	7.89 (2.79)	4.98 (3.05)	2.78 (1.92)	14.435	<0.001	0.112	<0.001
Language	19.14 (4.86)	14.98 (4.21)	9.78 (2.33)	18.421	<0.001	0.004	<0.001
Visuo-spatial skills	10.90 (2.66)	8.65 (2.59)	7.11 (1.62)	10.622	0.001	0.294	0.001

*p values according to group comparisons after post hoc Bonferroni correction; ACER: Addenbrooke cognitive battery – revised; MMSE: Mini Mental State Exam; MCI: Mild Cognitive Impairment; Attention-orientation: composite score; Memory component I: immediate recall, retrograde and anterograde; Memory component II: late recall e recognition; Memory total: composite score.



CDR: Clinical Dementia Rating scale; UFC: *Universidade Federal do Ceará*; MMSE: Mini-Mental State Exam; ACE-R: Addenbrooke's Cognitive Examination Revised.

Figure 1. Flowchart depicting the study design

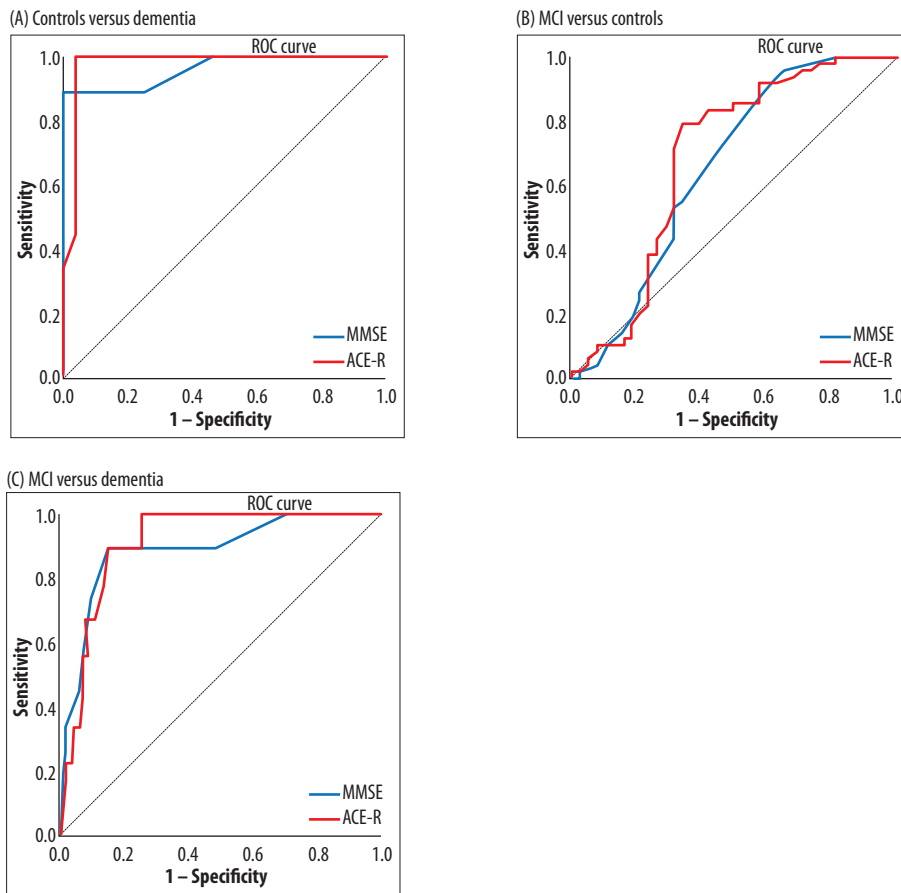


Figure 2. ROC curve of MMSE and ACE-R (for statistical details, see results).

ASSESSMENT OF EDUCATIONAL LEVEL

In a linear regression model, ACE-R and MMSE total scores were considered dependent variables and CDR,

years of schooling, income, and gender were considered independent variables. We found that 60% of the sample variance could be attributed to two main individual variables, CDR and years of schooling (Table 3).

Table 3. Logistic regression models of the factors related to the ACER and MMSE global scores

Hierarchical models	ACE-R			MMSE		
	B (β)	R2 (adj R2)	F change	B (β)	R2 (adj R2)	F change
1. Cognitive status (CDR)	-33.08 (-0.72)	0.52 (0.51) ^Δ	70.67	-8.24 (-0.67)	0.45 (0.44) ^Δ	51.78
2. CDR	-31.65 (-0.69)	0.60 (0.59) [§]	12.19	-7.71 (-0.62)	0.59 (0.58) ^Δ	22.84
Education*	2.15 (0.27)			0.80 (0.39)		

CDR: Clinical dementia Rating; ACER: Addenbrooke cognitive battery – revised; MMSE – Mini Mental State Exam.

Significant differences expressed in α levels: [§] $p \leq 0.01$; ^Δ $p \leq 0.001$. *Education in years.

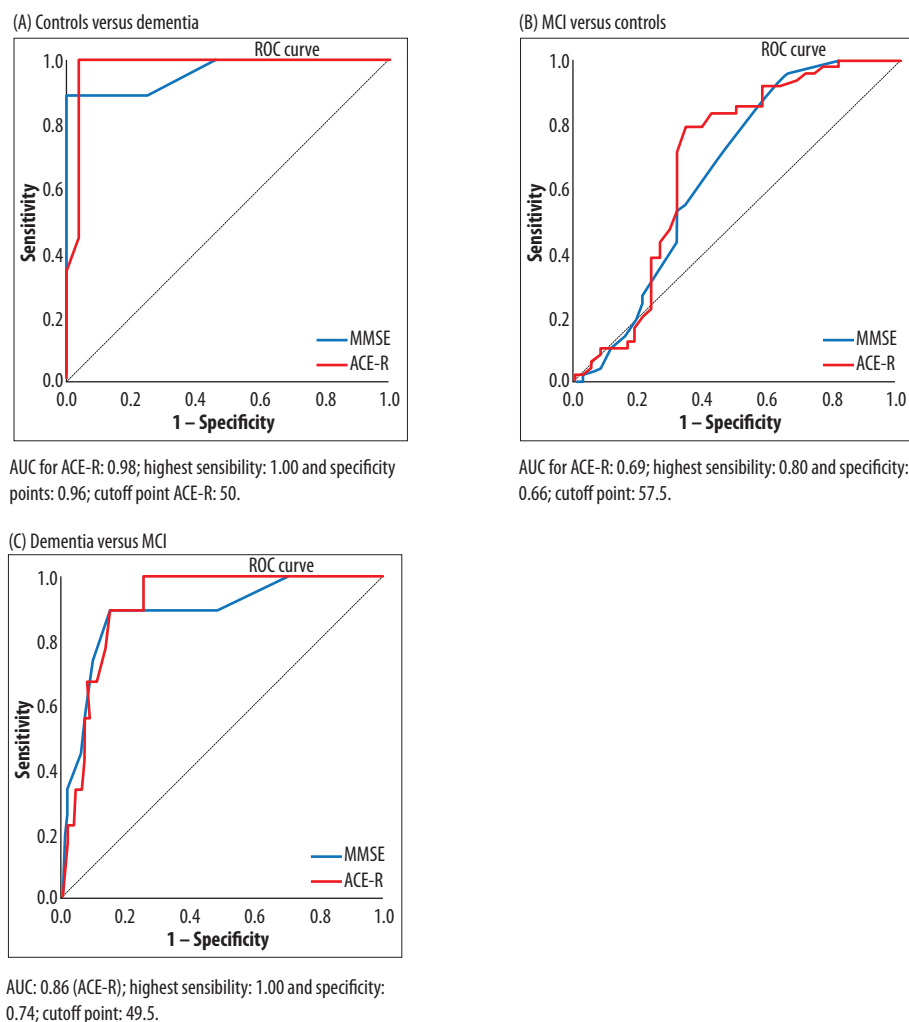


Figure 3. (A), (B) and (C) - accuracy of ACE-R between clinical groups and the area under the curve (AUC) are depicted (for detailed description, please refer to the results section).

DISCUSSION

Our study assessed the cognitive performance of a sample comprising cognitively healthy, MCI and MD participants using a short cognitive tool (ACE-R). The subitem with the strongest correlation with the educational level was visuospatial skills. The diagnostic accuracy of the MMSE and ACE-R was substantially lower than that reported in previous Brazilian studies with ACE-R. Overall, our preliminary findings

underline the importance of establishing different cutoff scores for the interpretation of test results using standard cognitive instruments taking into consideration factors related to the local context. Such adaptations can provide more robustness for the diagnosis of MCI and dementia and facilitate early therapeutic interventions.

Overall, mean scores among adults with MCI from both cities in our study (São Luís and Fortaleza) are considerably lower than those described in the literature. International

studies, such as Alexopoulos *et al.* study, have reported higher mean ACE-R scores for cognitive performance²⁷ (controls 90.37 ± 4.99 ; MCI 81.34 ± 9.09 ; dementia 64.80 ± 11.32). In Brazil, three studies by Caramelli *et al.* investigated ACE-R performance among Brazilian patients^{20,28,29}. In their first study, an adapted ACE-R version was used and they found a mean total score of 83.3 ± 10.0 for a total of 114 patients (age 75.4 ± 7.1 ; years of schooling 8.5 ± 4.3)²⁹. In a second study with 144 healthy older adults²⁸, they found higher ACE-R scores among adults 60 to 69 (80.25 ± 9.27) and 70 to 79 (78.75 ± 7.55) when compared to our study (70.14 ± 13.02). Furthermore, Carvalho conducted a study with more educated participants (mean years of schooling 8.5 vs. 2.5)²⁹, and found higher MMSE scores (26.9 vs. 22.0); a comparison of their results with our sample subset of health controls showed slightly lower scores for memory (20.0 vs. 17.58), verbal fluency (10.1 vs. 7.9), language (22.9 vs. 19.1) and attention/orientation (16.5 vs. 14.86). In our sample, the participants with AD also showed a performance below the described in the study with lower total scores in the MMSE (21.8 vs. 17.2)²⁹, and lower scores for verbal fluency (6.4 vs. 2.7), language (19.9 vs. 9.7) and visuospatial skills (12.8 vs. 7.1)³⁰. A recent study assessing the diagnostic accuracy of the ACE-R in patients with MCI who later transitioned to AD (MCI-AD) and 90 adults with mild probable AD²⁰ reported the following scores: MCI-AD vs. controls = 0.755 (<87; 100.0/45.9); AD vs. controls = 0.864 (<80; 77.7/79.6); MCI-AD vs. AD = 0.738 (<76; 60.0/84.2)²⁰. Another study conducted in Southeastern Brazil evaluated older adults with different levels of schooling and included patients with cognitive impairment, no dementia (CIND), AD and healthy controls. The scores for those with less than 5 years of schooling³¹ were: CIND vs. controls = 0.720 (<65; 76/60); and dementia vs. controls = 0.869 (<55; 85/76). Concerning ACE-R subitems, we cannot compare our data findings with data from this study because they used a different categorization of levels of schooling in the analysis. Declining scores for illiterate adults or adults with low levels of education are associated with greater risk of conversion to dementia^{32,33}. Faster cognitive decline has been associated with higher risk of AD (rate of risk 4.526, 95% confidence interval [95% CI] 2.993, 6.843, $p < 0.001$) and MCI (rate of risk 2.971, 95% CI 1.509, 5.849, $p = 0.002$)³². Each added year of education represents a delay in the rate of accelerated decline of around 0.21 years³⁴; an individual with 4 years of education may have a rate of accelerated decline before conversion to dementia of around 6.4 years³⁴.

To the best of our knowledge, this is the first multicenter study to assess the performance characteristics of a global cognitive screening tool in adults from Northeast Brazil. However, our study has some limitations that deserve consideration. First, we cannot establish cause-effect relationships from cross-sectional data. Second, the statistical power of our sample did not allow us to assess performance in subgroups of adults with cognitive

impairment (amnesic or non-amnesic MCI). Third, our sample included a few adults with dementia, which does not allow for generalization of our data findings for these individuals. Fourth, the participants' level of schooling was self-reported. Most studies do not consider the quality of literacy while studying adults with low levels of schooling, which may lead to an underestimation of the effect of this variable. Also, more recent research has investigated other variables including language skills³³, vocabulary³⁵, cognitive reserve³⁴, abstraction ability and formal-logical operational capacity deemed to be more sensitive to establish educational status.

CONCLUSIONS

In conclusion, our study assessed ACE-R performance in dementia, MCI and cognitively healthy adults. Average scores for healthy aging were considerably lower than those reported in prior Brazilian studies conducted with similar methodology. The analysis of ACE-R diagnostic accuracy between groups also evidenced lower cutoff scores compared to benchmark Brazilian studies. Our preliminary findings underline the need for more studies about cognitive changes in older adults with low levels of schooling and risk for dementia. The ecological value of these studies as well as potential variables associated with performance, such as cultural characteristics and heterogeneity of illiterate groups, should be considered. These studies can provide additional evidence to support screening approaches and facilitate early diagnosis and therapeutic intervention.

INDIVIDUAL CONTRIBUTIONS

José Wagner Leonel Tavares-Júnior – Sample selection, manuscript writing.

Pedro Braga-Neto – Study design, manuscript writing and revision.

Janine de Carvalho Bonfadini – Cognitive assessment.

Lays Bittencourt – Cognitive assessment.

Candida Helena Lopes – Study supervision.

Larissa Mendes – Cognitive assessment.

José Ibiapina Siqueira-Neto – Study design, manuscript writing and revision.

Valéria Sousa – Statistical analysis.

Anina Amaral – Statistical analysis.

Carolina Gomes Carrilho – Data revision, manuscript writing.

Jonatan Oliveira Espindola – Data discussion.

Maria Eduarda Avancini Casali – Manuscript revision.

André Barciela Veras – Study design, manuscript revision.

Gilberto Sousa Alves – Study design, manuscript writing and final revision.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

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SUPPLEMENTARY MATERIAL

Table 1. Accuracy, sensitivity, and specificity of ACE-R

Group Comparison	AUC	Optimal Cutoff	Sensitivity	Specificity	significance	IC	LR+	LR-
Controls versus MCI	0.69	<57.5	0.80	0.66	<0.001	0.61-0.83	2.35	0.30
MCI versus Mild Dementia	0.86	<49.5	1.00	0.74	<0.001	0.72-1.0	3.85	0.00
Control versus Mild Dementia	0.98	≤50	1.00	0.96	<0.001	0.93-1.00	25	0.00

Table 2. Accuracy, sensitivity, and specificity of MMSE

Group Comparison	AUC	Optimal Cutoff	Sensitivity	Specificity	significance	IC	LR+	LR-
Controls versus MCI	0.69	<26.5	0.96	0.34	<0.001	0.60-0.84	1.45	0.12
MCI versus Mild Dementia	0.84	<19.5	0.89	0.85	<0.001	0.65-1.00	5.93	0.13
Controls versus Mild Dementia	0.96	≤20	0.89	1.00	<0.001	0.88-1.00	89	0.11

Table 3. Accuracy, sensitivity, and specificity of the ACE-R in the Brazilian literature

Author	Group comparison	AUC	Sensitivity	Specificity	LR+	LR-
Caramelli et al. 2017	Controls versus MCI	0.75	1.00	0.46	1.85	0.00
	MCI versus AD	0.74	0.60	0.84	3.80	0.47
	Controls versus AD	0.86	0.78	0.79	3.81	0.28

AD: Alzheimer's Dementia; MCI: Mild Cognitive Impairment.