



Development of the Brazilian version of the Mini-Addenbrooke Cognitive Examination (M-ACE BR) to screen for cognitive impairment in older adults

Desenvolvimento da versão brasileira do Mini-Addenbrooke Cognitive Examination (M-ACE BR) para rastreio de comprometimento cognitivo em idosos

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Abstract

Background Age is the most important risk factor for develop dementia, and the recommendation is that older adults are cognitively tested to detect impairment in the initial stage for adequate treatment. The demand for the care of these older adults is great, drawing attention to the need for rapid tests, with good accuracy and simple application to identify cognitive impairment.

Objective To develop and validate the Brazilian Mini-Addenbrooke Cognitive Examination (M-ACE BR) as a short screening test for cognitive impairment in older adults.

Methods The M-ACE BR was developed using the Mokken scaling analysis in 352 participants (cognitively unimpaired [CU] = 232, cognitive impairment no dementia [CIND] = 82; and dementia = 38) and validated in an independent sample of 117 participants (CU = 25; CIND = 88; and dementia = 4).

Results The Mokken scaling analysis derived 9 items (spatial orientation, anterograde memory, retrograde memory, delayed recall, recognition [name and address], letter verbal fluency, repetition of 4 words, naming of 10 items, and comprehension) with a maximum score of 51 points and an average duration time of 7 minutes. The cut-off score $\leq 43/51$ for CIND had a sensitivity of 59.09% and a specificity of 80%. For a screening test in which sensitivity is prioritized for further investigation, we suggest using a cutoff of ≤ 47 (sensitivity 85.23% and specificity 24%), maintaining a good positive predictive value (79.8%).

Keywords

- ▶ Dementia
- ▶ Diagnosis
- ▶ Mental Status and Dementia Tests
- ▶ Cognitive Dysfunction
- ▶ Neuropsychological Tests

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Resumo

Conclusion The M-ACE BR is a brief and adequate instrument to detect cognitive impairment in older Brazilian adults. However, screening for CIND and for different educational levels should be further explored.

Antecedentes A idade é o fator de risco mais importante para o desenvolvimento de demência, e a recomendação é que os idosos sejam testados cognitivamente para detectar comprometimento na fase inicial para o tratamento adequado. A demanda pelo atendimento desses idosos é grande, chamando atenção para a necessidade de testes rápidos, com boa acurácia e de simples aplicação para identificar o comprometimento cognitivo.

Objetivo Desenvolver e validar a versão brasileira do Mini-Addenbrooke's Cognitive Examination (M-ACE BR) como um teste rápido para rastreamento de comprometimento cognitivo em idosos.

Métodos A M-ACE BR foi desenvolvida usando análise da escala de Mokken em 352 participantes (cognitivamente saudáveis [CS] = 232, comprometimento cognitivo sem demência [CCSD] = 82; e demência = 38) e validado em uma amostra independente de 117 participantes (CS = 25; CCSD = 88; e demência = 4).

Resultados A análise de escala de Mokken derivou 9 itens (orientação espacial, memória anterógrada, memória retrógrada, evocação tardia, reconhecimento [nome e endereço], fluência verbal de letras, repetição de 4 palavras, nomeação de 10 itens e compreensão) com pontuação máxima de 51 pontos e tempo médio de duração de 7 minutos. O escore de corte $\leq 43/51$ para CCSD teve sensibilidade de 59,09% e especificidade de 80%. Para um teste de rastreamento, em que a sensibilidade é priorizada para investigação posterior, sugerimos utilizar um ponto de corte ≤ 47 (sensibilidade 85,23% e especificidade 24%), mantendo um bom valor preditivo positivo (79,8%).

Conclusão A M-ACE BR é um instrumento breve e adequado para detectar comprometimento cognitivo em idosos brasileiros. No entanto, o rastreamento para a identificação de CCSD e para diferentes níveis de escolaridade deve ser melhor explorado.

Palavras-chave

- ▶ Demência
- ▶ Diagnóstico
- ▶ Testes de Estado Mental e Demência
- ▶ Comprometimento Cognitivo
- ▶ Teste Cognitivo

INTRODUCTION

Recent data indicates that 14.6% of the Brazilian population is ≥ 60 years old, which corresponds to 30.3 million people, calling attention to diseases related to aging, such as dementia.¹ A Brazilian study showed a high prevalence of dementia among relatively younger older adults (< 70 years old).² Besides that, almost 80% of people with dementia do not receive an early diagnosis, which draws attention to the need to increase the efficiency of cognitive screening in different contexts.³

Adequate service provisions would be, among other exams, a comprehensive cognitive assessment for older adults when cognitive decline is suspected; however, there is a great demand of the population in public services, the duration of neuropsychological evaluation, and the need for trained professionals makes it difficult. Thus, researchers have long sought to develop instruments for rapid application with high sensitivity and specificity in diagnosing cognitive impairment.

Dementia is a syndrome characterized by the presence of a decline in at least two of the following domains: memory, executive functions, visuospatial skills, behavior, and language, and interfere with an individual's social or

professional activities.⁴ Cognitive impairment no dementia (CIND) is a broad diagnosis developed in epidemiological studies;⁵ it classifies all individuals with impaired memory and/or other cognitive impairments, irrespective of the presence of a cognitive complaint, including all underlying etiologies, who show below-average decline but do not meet the criteria for dementia.^{5,6}

The Addenbrooke Cognitive Examination-Revised (ACE-R) is a brief cognitive screening translated and adapted into several languages. It has good accuracy to detect cognitive decline and dementia subtypes, and it takes 12 to 20 minutes to complete, with a maximum of 100 points; additionally, its sensitivity for mild dementia is 84 to 94%, depending on the cut-off score.^{7,8}

The Brazilian version of the ACE-R was applied to a group of healthy older adult individuals with heterogeneous education and proved to be easy to administer and to understand,⁸ as well as in a sample of Parkinson disease (PD) patients with a good correlation with clinical criteria.⁹

In a Brazilian epidemiological study, the ACE-R revealed a sensitivity of 73% and a specificity of 65% for the diagnosis of CIND, and a sensitivity of 91% and a specificity of 76% for dementia in individuals with low education.¹⁰

In order to reduce the administration time, the Mini-Addenbrooke Cognitive Examination (M-ACE) was derived from the Addenbrooke Cognitive Examination-III (ACE-III) through Mokken scaling analysis¹¹ in 117 patients and validated in an independent sample of 164 patients, with the Mini-Mental State Examination (MMSE) as the gold standard.¹² The M-ACE has a maximum score of 30 and a cutoff point of 25 for detecting dementia with a sensitivity of 85% and specificity of 87%. Five items were generated: orientation (to time), learning and recall of the name and address, verbal fluency (animals), and drawing a clock face. The total and domain scores on the M-ACE distinguished frontotemporal dementia (FTD), Alzheimer disease (AD), and corticobasal syndrome (CBS) patients, which are useful for the differential diagnosis of dementia in a clinical setting with approximately five minutes of administration.¹²

A recent study compared the sensitivity and specificity of the 3 versions (ACE, ACE-III, and M-ACE) in 552 patients diagnosed with PD. The M-ACE was the best to discriminate cognitive impairment in patients with more than 12 years of education.¹³

Due to the high prevalence of dementia and the high cost it generates for the health system, the diagnosis of cognitive impairment is necessary in primary care through use of a reliable screening tool. Cognitive impairment can be caused by conditions that can be treated (i.e., depression, hypothyroidism), and its screening can, therefore, be an effective measure to prevent dementia.

In this study, we first aimed to develop the M-ACE BR derived from the ACE-R data using a Mokken scale analysis, with sub-items that could better predict the diagnosis of cognitive impairment. Secondly, we aimed to evaluate the diagnostic accuracy of the M-ACE BR, determine the cut-off score to differentiate cognitively unimpaired and cognitively impaired groups, obtain inter- and intra-examiner reliability and internal consistency values, and verify the validity of the criteria of the M-ACE BR (→ **Figure 1**).

METHODS

Participants

Participants for scale reduction

Secondary data were obtained from an epidemiological study carried out in the city of Tremembé, SP, Brazil.² The Brazilian adapted version of the ACE-R⁸ was applied to the participants as an additional instrument, but it was not used for the final diagnosis of cognitive status.¹⁰ The individuals were classified into three diagnostic groups: cognitively unimpaired (CU), cognitive impairment no dementia (CIND), and dementia. These diagnoses were established in consensus based on the information and data obtained from the evaluation of the participants. The diagnosis of CIND was given to individuals who performed below expectations for their age and education, even without the complaint of cognitive decline.⁶ These individuals were classified using the MMSE,^{14,15} verbal fluency (VF),^{16,17} Brief Cognitive Screening Battery (BCSB),¹⁸ Informant Questionnaire on

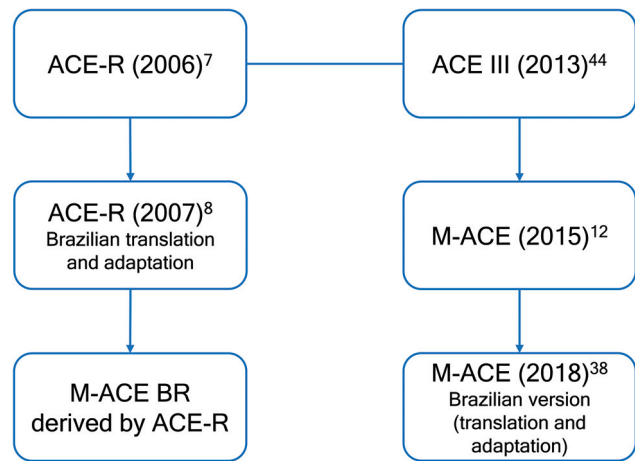


Figure 1 Different versions of the ACE: the ACE-R was published in 2006 by Mioshi et al.,⁷ and, in 2007, Carvalho and Caramelli⁸ translated and adapted the Brazilian version. This version was used to create the M-ACE BR. In 2013, Hsieh et al.⁴³ created the ACE-III, a similar version of the ACE-R, but without the MMSE items. In 2015, Hsieh et al.¹² extracted items from the ACE-III using the Mokken analysis and creating M-ACE, and, in 2018, Miranda et al.³⁷ translated and adapted the M-ACE for a Brazilian version.

Cognitive Decline in the Elderly (IQCODE),^{19–21} and Functional Activities Questionnaire (FAQ).²² The diagnosis of dementia was made according to clinical criteria recently updated by the National Institute on Aging-Alzheimer's Association (NIA-AA).⁴

Participants for testing the reduced scale

Participants were from the Brazilian Aging and Memory Study (BRAMS), the outpatient clinic of the Cognitive Neurology and Behavior Unit of the Teaching Hospital of the School of Medicine of Universidade de São Paulo. This was a longitudinal study with biannual clinical and annual neuropsychological assessments for a total period of 4 years (→ **Figure 2**).

Assessment protocol

Participants were interviewed by a neurologist who performed the anamnesis, socioeconomic questionnaire, and neurological physical examination, as well as cognitive screening assessments and functional evaluation. The volunteers performed laboratory, structural, and functional neuroimaging exams, in addition to a comprehensive neuropsychological evaluation (Estimated Intelligence Quotient Assessment;²³ Matrix Reasoning²⁴ and Vocabulary;²⁴ Attention and executive functions: Rey Complex Figure Test [copy],²⁵ Trail Making Test –A and B,²⁶ Stroop Test,²⁶ Digit Span [forward and backward],²⁷ VF [letters P, F, A, S,²⁸ and animals¹⁶]; Memory: Logical Memory [immediate and delayed recall];²⁹ Visual Reproduction [immediate and delay recall];²⁹ Rey Complex Figure [delayed recall];²⁵ Rey Auditory Verbal Learning Test [RAVLT] [learning; delayed recall and recognition];³⁰ and Language: Boston Naming Test).³¹ The exclusion criteria were any co-existing neurological conditions and substance dependence. All participants provided informed consent by signing an informed consent form, and

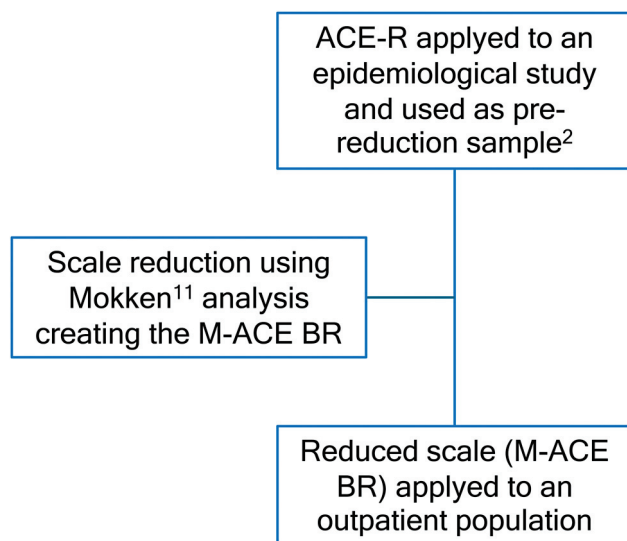


Figure 2 Representing the creation of the M-ACE BR: the Brazilian version of the ACE-R was applied in the epidemiological study (pre-reduction sample).² The M-ACE BR was reduced using a Mokken analysis, which provided the test item's difficulty and the discriminatory capacity. The items identified after the Mokken analysis were applied to the sample of an outpatient population (post-reduction sample).

the protocol was approved by the local and national ethics committees (local protocol 1.633.08; national protocol CAAE: 55781316.9.0000.0068).

Derivation of the M-ACE

Based on the study by Hsieh et al. (2015)¹², the ACE-R scale was reduced using a Mokken analysis, which provided the test items' difficulty and discriminatory capacity. The Mokken scale is a one-dimensional scale consisting of hierarchically ordered items that measure the same underlying latent concept. This technique indicates the difficulty and discriminatory ability of test items. A Mokken scale analysis first searches for one-dimensional sets of items based on various scalability coefficients. For the entire set of items, there is a test scalability coefficient (H); for each item within a test, there is an item scalability coefficient (Hi); and for each item pair, there is an item scalability coefficient (Hij). H is a measure of how far the test item pairs completed by the participant appear in the same relative order, ranging from 0 (no scalability) to 1 (perfect ordering), and 0.3 is generally considered the minimum value for a Mokken scale.^{12,32} A set of items forms a Mokken scale if all the scalability coefficients of the main item are 0.3, and the scalability coefficient of the item pair is a positive value for all item pairs.³³ Subsequently, a Mokken scale analysis identifies items that conform to the monotonous homogeneity (MHM) model. Scores on items conforming to this model increased as the level of the latent trait increased, and items that did not fit the MHM could be removed. When items are within the MHM, Hi can be interpreted as a measure of the discrimination of items, with higher values indicating greater discrimination.^{12,34} One-dimensional sets of items that meet the MHM criteria can be examined for invariable item ordering

(IIO), which is necessary in developing hierarchies that are replicable across the sample. Invariably, ordered items were answered in the same order by all respondents, regardless of the participant's level of cognitive ability. The IIO identifies items that the "item response" function does not replace. H-trans (HT) refers to the distance between item response functions, and the highest values indicate greater IIO accuracy.³⁵

Data analyses

Data were analyzed using the IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA) and the R program (open source). Statistical significance was set at p -value < 0.05 . The Shapiro-Wilk test was used to test the normality of the sample, and according to the data distribution, non-parametric tests were used for descriptive and comparative analyses. The three diagnostic groups (CU, CIND, and dementia) were compared in terms of age, education, and performance on the ACE-R using the analysis of variance (ANOVA) test, followed by a multiple-comparisons test (post-hoc Bonferroni). Categorical variables (sex, socioeconomic status, and color) were compared using a Pearson Chi-squared test. The sensitivity and specificity of the M-ACE BR and MMSE were calculated using a receiver operating characteristic (ROC) curve that plotted sensitivity and specificity across the range of possible cut-off scores. The area under the curve (AUC) was used to measure the ability of each test to distinguish between participant groups. The cut-off score was based on the Youden index. The criterion validity between the M-ACE and neuropsychological tests, considered the gold standard, was analyzed using the Spearman correlation coefficient. The following criteria were adopted: very weak (0.00–0.3), weak (0.3–0.5), moderate (0.5–0.7), strong (0.7–0.9), and very strong (> 0.9).³⁶ The Reliability of stability (test-retest) and equivalence (interobserver) were assessed using the intraclass correlation coefficient (ICC), and the reliability of internal consistency (homogeneity) was assessed using the Cronbach alpha test.

RESULTS

The pre-reduction sample was divided into three groups, CU, CIND, and dementia, totaling 352 participants. The cognitively unimpaired and CIND groups were more educated and younger than the dementia group. Regarding the ACE-R, a statistical difference was observed in all domains, demonstrating greater cognitive impairment in the dementia group than in the CIND and CU groups (► **Table 1**).

The sample for the M-ACE BR (postreduction; $n = 117$) was also divided into 3 groups: CU ($n = 25$), CIND ($n = 88$), and dementia ($n = 4$). There was a difference between the educational levels of the groups, in which the control group had a greater number of years achieved than the CIND and dementia groups, being homogeneous as compared to the other variables. The total ACE-R score differed between the groups (► **Table 1**).

Exploratory (using varimax rotation) and confirmatory factor analysis were used to construct the factors in the

Table 1 Pre- and post-reduction sample's demographic characteristics and ACE-R performance (mean and standard deviation) by group

Prereduction		CU n = 232	CIND n = 82	Dementia n = 38	p-value
Demographics	Age (years)	70.04 (7.19) [†]	71.94 (6.81) [‡]	76.95 (7.86)	< 0.001*
	Education (years)	5.96 (5.17)	5.38 (4.55)	3.11 (3.52)	< 0.001*
	Sex (male:female)	95:137	38:44	18:20	0.587**
ACE-R	Attention/orientation	15.75 (2.23) [§]	14.44 (6.11)	10.79 (3.91)	< 0.001*
	Memory	17.42 (5.39) [§]	13.21 (5.25)	8.05 (4.57)	< 0.001*
	Fluency	7.78 (2.68) [§]	5.45 (2.69)	3.87 (2.60)	< 0.001*
	Language	20.97 (4.91) [§]	18.56 (5.11)	14.42 (5.97)	< 0.001*
	Visuospatial	12.09 (2.96) [§]	11.02 (2.91)	8.66 (3)	< 0.001*
	Total	74.08 (15.50) [§]	62.67 (15.01)	46.11 (17.46)	< 0.001*
Postreduction		CU n = 25	CIND n = 88	Dementia n = 4	p-value
Demographics	Age (years)	73.68 (6)	71.97 (6.14)	75 (5.72)	0.325*
	Education (years)	13.84 (4.09) [†]	10.81 (5.2)	7.75 (5.19)	0.011*
	Sex (male:female)	6: 19	16: 72	2: 2	0.271**
ACE-R	Attention/orientation	16.96 (1.10)	16.75 (1.59)	16.50 (1.30)	0.763*
	Memory	22.08 (3.25) [¶]	19.60 (4.66)	13.25 (3.87)	< 0.001*
	Fluency	10.92 (1.85) ^{†,‡}	9.65 (2.42)	8.00 (0)	0.014*
	Language	24.44 (1.92)	23.22 (2.67)	21.50 (5.75)	0.047*
	Visuospatial	15.12 (1.33) [†]	14.19 (2.04)	12.50 (3)	0.027*
Total		89.52 (5.94)[¶]	83.41 (9.28)	71.75 (9.18)	< 0.001*

Abbreviations: ACE-R, Addenbrooke Cognitive Examination-Revised; CU, cognitively unimpaired; CIND, cognitive impairment no dementia; D, dementia.

Notes: *Kruskal-Wallis Test; **Chi-squared test; [†]CU > D; [‡]CU > CIND; [§]CIND > D; [¶]CU > CIND > D; p < 0.05.

M-ACE BR: factor 1: Retrograde and Recall Memory, Letter fluency (P), and Repetition of 4 words; factor 2: Naming 10 figures and Comprehension; and factor 3: Spatial Orientation, Anterograde Memory, and Recognition (see **►Supplementary Material Table S1**; <https://www.arquivosdeneuropsiquiatria.org/wp-content/uploads/2024/05/ANP-2022.0184-Supplementary-Material.docx>).

Factor 2 was the only factor that was not different between the groups, possibly because it did not contain memory items (see **►Supplementary Material Table S2**).

The final analysis results in spatial orientation (specific location) (5 points); anterograde memory (repeating a name and address 3 times) (7 points); retrograde memory (answer the name of the president: of the Republic, who built Brasília, from the United States of America, from the USA who was assassinated in the 60s) (4 points); recall (remember name and address) (7 points); recognition (if do not recall the name and address, recognize between three tips) (5 points); letter verbal fluency (say as many words starting with the letter P in 1 minute) (7 points); repetition – 4 words (repeat “hippopotamus”; “eccentricity”; “unintelligible”; and “statistical”) (2 points); naming 10 items (kangaroo, penguin, anchor, camel, harp, rhinoceros, barrel, crown, alligator, accordion) (10 points); comprehension (point pictures: what is associated with the monarchy, what is found in the Pantanal, what

is found in the Antarctica, and what has a nautical relationship) (4 points); total score 51 points. Memory items were the best for differentiating between the groups (**►Table 2**).

►Table 3 shows the diagnostic parameter values for the CIND cut-off scores with an area under the ROC curve of 0.692 and a CI of 0.60–0.78. Based on the Youden index, the most appropriate cut-off score was ≤ 43, with sensitivity and specificity of 59.09% and 80.0%, respectively. The cut-off score for dementia was not calculated because of the low prevalence (3.42%) in this sample. For a screening test in which sensitivity is prioritized for further investigation, we suggest using a cutoff of ≤ 47 to maintain a good positive predictive value (PPV).

The M-ACE BR had a better AUC compared with the MMSE, using the optimal cutoff and showed greater sensitivity but lower specificity (**►Table 4**).

Internal consistency, analyzed using the Cronbach alpha coefficient, presented an acceptable value (Cronbach $\alpha = 0.77$). Regarding the stability reliability (test-retest), the M-ACE BR total score obtained an intraclass correlation coefficient (ICC) of 0.99, suggesting excellent stability between the 2 evaluation moments. The inter-rater reliability analysis showed consistency in the degree of agreement between the responses of 2 evaluators in their total score (ICC = 0.993).

Table 2 Performance on the M-ACE BR items by group

Items	CU (n = 25)		CIND (n = 88)		D (n = 4)		p-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Spatial orientation	5 (0)	(5-5)	4.95 (0.21)	5 (5-5)	5 (0)	5 (5-5)	0.512
Anterograde memory	6.80 (0.5) [†]	7 (7-7)	6.42 (0.93)	7 (6-7)	5.5 (1)	6 (5-6)	0.013
Retrograde memory	3.76 (0.52) [†]	4 (4-4)	3.25 (1.17)	4 (3-4)	2.5 (1.3)	3 (2-4)	0.034
Recall	4.68 (2.12) [†]	5 (3-6)	3.64 (2.45)	4 (2-6)	1 (1.41)	1 (0-2)	0.010
Recognition	4.48 (0.77) [†]	5 (4-5)	4.20 (1.1)	5 (4-5)	3 (0.82)	3 (3-4)	0.030
Letter verbal fluency	5.40 (1.3)	5 (5-6)	4.75 (1.30)	5 (4-6)	4.5 (1)	4 (4-5)	0.068
Repetition- 4 words	1.76 (0.52)	2 (2-2)	1.56 (0.68)	2 (1-2)	1.6 (0.66)	2 (1-2)	0.230
Naming	9.12 (1.17)	9 (9-10)	8.64 (1.6)	9 (8-10)	8 (2.71)	9 (7-10)	0.252
Comprehension	3.76 (0.6) [†]	4 (4-4)	3.51 (0.71)	4 (3-4)	2.75 (1.9)	4 (2-4)	0.037

Abbreviations: CU, cognitively unimpaired; CIND, cognitive impairment no dementia; D, dementia; IQR, interquartile range; M-ACE BR, Brazilian Mini-Addenbrooke's Cognitive Examination; SD, standard deviation.

Notes: *Kruskal-Wallis test; [†]CU > D; p < 0.05. Significant data in bold.

Table 3 Diagnostic parameter values for CIND cut-off score

Cut-off/51	Sensitivity (%)	Specificity (%)	+LR (%)	-LR (%)	+PV (%)	-PV (%)
< 26	0.00	100		1.00		22.1
≤ 30	9.09	100		0.91	100	23.8
≤ 31	9.09	96.00	2.27	0.95	88.9	23.1
≤ 32	11.36	96.00	2.84	0.92	90.9	23.5
≤ 34	15.91	92.00	1.99	0.91	87.5	23.7
≤ 38	31.82	92.00	3.98	0.74	93.3	27.7
≤ 39	38.64	88.00	3.22	0.70	91.9	28.9
≤ 40	45.45	88.00	3.79	0.62	93.0	31.4
≤ 41	48.86	84.00	3.05	0.61	91.5	31.8
≤ 42	54.55	84.00	3.41	0.54	92.3	34.4
≤ 43	59.09	80.00	2.95	0.51	91.2	35.7
≤ 44	63.64	68.00	1.99	0.53	87.5	34.7
≤ 45	70.45	60.00	1.76	0.49	86.1	36.6
≤ 46	77.27	44.00	1.38	0.52	82.9	35.5
≤ 47	85.23	24.00	1.12	0.62	79.8	31.6
≤ 48	94.32	4.00	0.98	1.42	77.6	16.7
≤ 49	97.73	4.00	1.02	0.57	78.2	33.3
≤ 50	100	0.00	1.00		77.9	

Abbreviations: +LR, positive likelihood ratio; -LR, Negative Likelihood Ratio; +PV, positive predictive value; -PV, negative predictive value.

Notes: Cut-off based on the Youden index. Significant data in bold.

Table 4 Comparison of the M-ACE BR with the MMSE

Test	Optimal cutoff	AUC	Sensitivity (%)	95% CI	Specificity (%)	95% CI	+LR (%)	-LR (%)	+PV (%)	-PV (%)
M-ACE BR	≤ 43/51	0.692	59.10	48.1-69.5	80	59.3-93.2	2.95	0.51	91.2	35.7
MMSE	≤ 26/30	0.601	27.27	18.33-37.8	88	68.8-97.5	2.27	0.83	0.83	88.9

Abbreviations: CI, confidence interval; +LR, positive likelihood ratio; -LR, negative likelihood ratio; M-ACE BR, Brazilian Mini-Addenbrooke's Cognitive Examination; MMSE Mini-Mental State Examination; +PV, positive predictive value; -PV, negative predictive value.

Notes: Cut-off based on the Youden index. Significant data in bold.

DISCUSSION

The M-ACE BR (**–Supplementary Material – Table S3**) is a useful brief and sensitive cognitive tool for the detection of CIND in the Brazilian population, with a good PPV using a cutoff $\leq 43 / \leq 47$ points. It was developed through a Mokken scale analysis with 9 items (spatial orientation, memory anterograde and retrograde, delayed recall, recognition, letter verbal fluency, 4-word repetition, naming of 10 pictures, and comprehension).

In a study by Hsieh et al. (2015),¹² the Mokken analysis indicated that the 4 best domains to differentiate patients with behavioral variant frontotemporal dementia (bvFTD), primary progressive aphasia (PPA), AD, and control groups were orientation in time, memory anterograde, and delayed recall (remembering the name and address), language (verbal fluency animals), and visuospatial skills (clock drawing test). This seminal study observed good accuracy with an AUC. A screening test should not be based on the type of disease but on the suspicion of cognitive deficit; therefore, it should be applied to several conditions. As we apply this test to dementia and CIND, it is better suited as a screening test. The present study did not include patients with different dementia subtypes and did not investigate separate domains. Therefore, we suggest that the M-ACE BR is appropriate and accurate for detecting cognitive impairment in several settings. For the diagnosis of dementia syndrome, other assessments should be performed after cognitive screening (imaging examinations, laboratory tests, and when possible, a complete neuropsychological assessment).

In the study by Miranda et al.,³⁷ the M-ACE translated and adapted for Brazil, using the original version by Hsieh et al.¹² was applied to a sample of CU, MCI, and mild AD, with an accuracy of 91.67% in differentiating AD from CU and MCI, using a cut-off score of 20 points, with a maximum score of 30 points. The accuracy of the MMSE in the study was 83.33% for differentiating AD from the other groups, suggesting the superiority of the M-ACE in relation to the MMSE in this sample. The accuracy of identifying MCI was 68.85% for the M-ACE and 63.93% for the MMSE. The M-ACE was superior to the MMSE; however, both had low accuracies. Similar results were found in a Japanese study that compared the utility of five instruments (ACE-III, M-ACE, MMSE, Montreal Cognitive Assessment [MoCA], and Hasegawa Dementia Scale-Revised [HDS-R]) in detecting MCI and dementia. They compared, CU, MCI, and dementia and observed that ACE-III was the best instrument to detect MCI, and ACE-III and M-ACE were the best in detecting dementia.³⁸ A similar finding was depicted in comparing the accuracy of the M-ACE and the MoCA test in a sample of subjective memory complaints, MCI, and dementia, and both presented accuracy greater than 90% for the diagnosis of dementia (M-ACE = 90.5%, and MoCA = 91.4%), while for MCI, the accuracy of the M-ACE was 78.6%, and the MoCA was 82.3%.³⁹ Another study also observed a greater accuracy of the M-ACE in relation to the MMSE to detect MCI, with a sensitivity of 88% and specificity of 72%; although in the dementia group, the accuracy of both instruments was very similar.⁴⁰ The findings of the present study with the

M-ACE BR corroborate these studies, in which M-ACE BR identifies people with cognitive impairment better than the MMSE, being suitable for cognitive screening.

In the sample for the M-ACE BR, the MMSE did not differ between the diagnostic groups, whereas the M-ACE BR showed a significant difference in the memory subitem, suggesting a limitation of the MMSE in this domain. Unlike the MMSE, which makes the delayed recall of three words, the M-ACE BR makes the learning memory (three repetitions of the name and address), with a probable great difficulty to be encoding a systematic review that analyzed the ACE III and M-ACE for detecting dementia and MCI concluded that the sensitivity of the M-ACE for detecting dementia and MCI across patient populations and thresholds was generally high (64% to 99%), while the specificity varied more (32–100%).⁴¹ These data are compatible with those of the present study regarding the sensitivity of the M-ACE BR, with a cut-off score ≤ 43 for CIND had a sensitivity of 59.09% and a specificity of 80%.

The PPV for the M-ACE in the systematic review ranged from 20 to 100%, and the negative predictive value (NPV) ranged from 80 to 100%.⁴¹

The M-ACE BR also showed high internal consistency and adequate intra- and intra-rater reliabilities. As it is simple to apply and correct, there is no divergence between the examiners. The study that developed the M-ACE¹² obtained a Cronbach alpha of 0.8, which was also valid for the translated version for the Brazilian population.⁴²

The median of 11 years of education of the participants in the sample for the reduced scale was relatively high for our country.

A relative limitation of this study was the small sample size of patients diagnosed with dementia in the sample evaluating the behavior of the M-ACE BR. A scale that identifies mild cognitive impairment is also suitable for screening for dementia (where scores will be further impaired); therefore, we consider it unnecessary to include patients with dementia to prove its usefulness. Our sample of CIND had a higher frequency of amnesic and dysexecutive patients, probably influencing the remaining items in the M-ACE-BR without visuospatial tasks. This could influence the accuracy of detection of the prodromal phase of Lewy body disease or the prodementia phase in Parkinson disease.⁴² In the meantime, subcortical deficits could be evaluated with this reduced version by letter fluency; undoubtedly, memory tasks were the most predominant domain in this new version of the M-ACE.

The diversity in schooling across Brazil has long posed a challenge, as no single instrument demonstrates sufficient sensitivity and specificity across all educational levels. We recognize that certain instruments may be well-suited for a specific level of education but not for others. Given the considerable heterogeneity of the population in our study, which aims to accurately represent the Brazilian population, it appears that the instrument may not be universally suitable for all school groups. Nevertheless, we plan to further investigate our sample using a more tailored approach to educational divisions.

The present study is the first Brazilian study to create a version of the M-ACE using items from the ACE-R, which is better suited to the characteristics of our population. The M-ACE BR is an instrument that is easy and quick to apply, with adequate psychometric properties and accuracy in detecting cognitive impairment; however, the screening for CIND and for different educational levels should be further explored.

Author's Contributions

MOO, SMDB: conceptualization and design of the work; MOO, MTCG, KGC, RN, SMDB: data acquisition; MOO, MTCG, KGC, SMDB: analysis and interpretation; MOO, MTCG, KGC, SMDB: writing; MOO, MTCG, KGC, RN, SMDB: review of the manuscript. All authors approved the final version of the manuscript and agree to be responsible for all aspects of the work.

Conflict of Interest

The authors have no conflict of interest to declare.

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