RESEARCH ARTICLE

ACTA Vol. 13, No. 2, 2015, 127-136
NEUROPSYCHOLOGICA

Received: 11.04.2015
Accepted: 28.06.2015

A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

DOI:10.5604/17307503.1168287

PSYCHOMETRIC AND NORMATIVE INDICATORS OF THE PORTUGUESE VERSION OF THE ADDENBROOKE'S COGNITIVE EXAMINATION- III. PRELIMINARY STUDY ON A SAMPLE OF HEALTHY SUBJECTS

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SUMMARY

Background: Recently a third version of the Addenbrooke's Cognitive Examination (ACE-III) was developed in order to improve previous versions. The present work aims to determine some psychometric properties ofACE-III, such as: internal reliability of ACE-III validity evidence pertaining to the instrument's internal structure, convergent and divergent validity evidence. Additionally, the influence of sociodemographic variables on the test's performance was studied and normative tables for the Portuguese version of ACE-III were produced.

Material/ Methods: The study enrolled a convenience sample made up of healthy volunteers (n=100) without any subjective complain of memory loss and completely independent in daily life activities. Internal reliability of ACE-III was determined trough Cronbach's alpha, validity evidence pertaining to the instrument's internal structure was established by using inter domain correlations, convergent and divergent validity were determined by correlations between. Multiple linear regressions were performed to determine the predictive variables and to generate normative equations.

Results: Results point to a good construct validity, with acceptable reliability (α=.732) and significant inter-domains correlations. The Portuguese version of ACE-III also revealed convergent and divergent validity. Multiple linear regression determined age and education as the sole predictors of the ACE-III results. Normative tables were created based on those variables.

Conclusions: The availability of ACE-III normative equations based on a healthy sample according to age and education enables the use of a brief screening tool for cognitive functioning.

Key words: neuropsychological assessment, cognitive impairment, dementia, screening test

INTRODUCTION

Dementia and cognitive impairment makes up a serious worldwide problem. Dementia is at the top 10 of the leading causes of burden of disease in high-income countries (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006). In Western Europe the prevalence of dementia for peoples' aged over 60 it is estimated in7.3% and the number of cases will increase up to 40% until 2030 (WHO, 2012) .International guidelines recommends keeping a surveillance attitude by using general cognitive screening tests in individuals with suspected cognitive impairments(Petersen et al., 2001; Sorbi et al., 2012). This is especially relevant in primary care settings, where dementia and cognitive impairment are often under diagnosed because of the high number of patients by physician and the limits of the available instruments(Boustani, Peterson, Hanson, Harris, & Lohr, 2003; Pastor et al., 2003). Therefore, cognitive assessment is central to diagnosis and management of dementias(Sorbi et al., 2012). Eventually, the use of screening tests with high diagnostic utility, simplicity, celerity and with normative data for the target population is important in a time-constrained practice (Boustani et al., 2003; Sánchez, 2007).

Recently a third version of the Addenbrooke's Cognitive Examination (ACE-III) was developed in order to improve previous versions in response to weakness of certain domains such as repetition, comprehension and visuospatial items(Hsieh et al., 2015; Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013; Matias-Guiu et al., 2014; Velayudhan et al., 2014). With a mean time of administration of 15 minutes, ACE-III meets the requirements of a screening test, evaluating different cognitive dimensions and enabling an overall picture of subject's neurocognitive functioning.

ACE-III is scored out of 100 and assesses five cognitive domains: Attention (maximum score 18 points), assessed through orientation, immediate verbal evocation of words and serial subtraction tasks; Memory (maximum score 26 points), evaluated by verbal delayed recall (free and recognition), verbal learning and semantic memory tasks; Verbal fluency (maximum score 14 points), including phonetic and semantic fluency tasks; Language (maximum score 26 points), assessed through comprehension, repetition, naming, reading and writing tasks; Visuospatial (maximum score 16 points), contemplating visuoconstructive (eg., Cube copy and clock drawing) and spatial perceptive (Counting dots and indentifying incomplete letters) tasks (Hsieh et al., 2013). Scoring criteria follow the norms of the English version of the test (http://www.neura.edu.au/).

Since the clinical value of a test is limited without the determination of its psychometric characteristics and the possibility to compare the individual performance with a reference group, this work aims to: determine the internal reliability of ACE-III(Cronbach's alpha), validity evidence pertaining to the instrument's internal structure, convergent and divergent validity evidence. Additionally, we aim to determine the influence of sociodemographic variables on the test's performance and to produce the normative tables for the Portuguese version of ACE-III.

METHODS

Participants

ACE-III was administered to and healthy sample composed by 100 subjects, from both genders, with ages raging between 60 and 90 years (M=70.41; SD= 7.962) and with schooling raging between 1 and 17 years (M=6.24; SD= 4.07), without any subjective complain of memory loss and completely independent in daily life activities. Individuals with prior history of neuropsychiatric or other medical diagnosis liable to interfere directly on neurocognitive functioning were excluded. Individuals with results equal or lower than one standard deviation on the Montreal Cognitive Assessment were excluded from the sample. Participants were recruited in health units, day care centers and religious and civic associations, from several districts of Portugal. Table 1 shows the characteristics of the sample.

Assessment

Besides the ACE-III the following instruments were used: a sociodemographic questionnaire specially made for this study; an health status inventory; the Montreal Cognitive Assessment (MoCA)(Freitas, Simões, Martins, Vilar, & Santana, 2010; Nasreddine et al., 2005); the Geriatric Depression Scale (GDS) (Yesavage et al., 1983). The Montreal Cognitive Assessment was selected to include and exclude subjects and to obtain the convergent validity due to its high specificity (87%) and sensitivity (90%) in detecting mild cognitive impairment(Dong et al., 2010; Freitas, Simões, Alves, & Santana, 2011). The GDS was included in order to establish ACE-III's divergent validity.

Table 1. Characteristics of the sample

	n	%
Gender		
Male	44	44
Female	56	56
Type of Profession		
Blue Collar	80	80
White Collar	20	20
Professional Status		
Retired	95	95
Working	3	3
Unemployed	2	2

Procedure

The original version of the ACE-III was translated to Portuguese by two psychologists. Subsequently, our team discussed and assessed the two translations and a final version was achieved. Later, other psychologist made the retroversion of the instrument. The two forms were then again discussed in order to increment the semantic and idiomatic similitude between the two versions.

The instruments were administered to all subjects in a closed room. In the institutions with ethical committee, the approvals for the study were obtained. All the participants gave their informed consent.

Statistical Analysis

Statistical analysis was carried out using the program IBM *Statistics* version 22 for Windows.

Kolmogorov-Smirnov (KS) test was used to test the normal distribution of the ACE-III scores. Internal reliability was determined trough Cronbach's alpha, and the internal structure was analyzed by the correlations between the domains and the total scale and inter-domain correlations (Pearson´s correlations). Convergent validity was established by correlating ACE-III total score with results on MoCA and divergent validity by correlating the measure with GDS (Pearson´s correlations).

In order to determine the predictive model of ACE-III scores, multiple linear regressions (enter method) were performed. Normative equations were extracted from the multiple linear regressions in order to enable the determination of the expected results of a given individual according to the predictive variables of ACE-III and its domains.

Significance was determined with $p \leq .05$.

RESULTS

The results obtained by the subjects on the neuropsychological tests and on GDS are presented in table 2. In table 3 are the results obtained in each of the ACE-III domains. In accordance to Kolmogorov-Smirnov test, the results on ACE-III do not have a normal distribution (KS=0,101; p= .014). The Cronbach's alpha value is .732.

The correlations inter-domains (Table 4) and between the domains and ACE-III total score (Table 5) were significant.

Table 2. Results obtained by the sample on the tests

	M	SD	[Min.- Max.]
ACE-III	89.4	6.48	[63- 99]
MoCA	26.11	2.61	[18- 30]
GDS	7.85	4.26	[0- 19]

ACE-III total score showed a positive correlation with MoCA (ρ=.795; p=.001) and a negative correlation with GDS (ρ=-.33; p=.001).

The performance on ACE-III was related to gender (U=927; p=. 034), type of professional occupation (U=307; p=.002), age (ρ=-.439; p<.001) and education (ρ=.543; p<.001). The domain of Attention was related to was related to gender (U=969; p=. 033), type of professional occupation (U=520; p=.005) and education (ρ=0,345; p<.001). Memory domain was influenced by age (ρ=-.403; p<.001) and education (ρ=.289; p=.004). The results on Fluency were influenced by the type of professional occupation (U=355; p<.001) and age (ρ=-.267; p=.007). The Language domain was influenced by the type of professional occupation (U=495,5; p=.003), gender (U=941; p=.024) and education (ρ=-.287; p=.004).

Table 3. Results obtained by the sample on ACE-III domains

	M	SD	[Min.- Max.]
Attention	17.16	1.42	[13- 18]
Memory	23.95	2.42	[18- 26]
Fluency	9.69	1.82	[5- 14]
Language	25.13	1.43	[17- 26]
Visuospatial	13.47	2.27	[8- 16]

Table 4. Correlations between ACE-III domains

	Attention	Memory	Fluency	Language	Visuospatial
Attention	-	0.42*	0.289*	0.344*	0.293*
Memory		-	0.285*	0.297*	0.37*
Fluency			-	0.35*	0.296*
Language				-	0.48*
Visuospatial					-

* p=.001

Table 5. Correlations between ACE-III and its domains

	ACE-III
Attention	0.635*
Memory	0.74*
Fluency	0.631*
Language	0.672*
Visuospatial	0.741*

* p=.001

Table 6. Multiple linear regression models for ACE-III and its domains

Domain	Variable	B	SE B	β	t	*p*	Model	
							R^2	*p*
Total							.47	<.001
	Age	-0,257	0,065	-0,315	-3,954	<.001		
	Education	0,708	0,212	0,445	3,342	.001		
Attention							.37	.002
	Education	0,127	0,055	0,365	2,332	.022		
Memory							.45	<.001
	Age	-0,107	0,029	-0,353	-3,704	<.001		
Fluency							.455	<.001
	Age	-0,054	0,021	-0,237	-2,609	.011		
Language							.366	.008
	Education	0,078	0,056	0,224	1,404	.004		
Visuospatial							.6	<.001
	Age	-0,068	0,025	-0,238	-2,764	.007		
	Education	0,305	0,079	0,547	3,864	<.001		

The Visuospatial was related to gender (U=783,5; p=. 002), type of professional occupation (U=469,5; p=.004), age (ρ=-.372; p<.001) and education (ρ=.461; p<.001).

The multiple linear regression points to age and schooling as the main predictors of the performance on ACE-III (Table 6). This model accounts for 47% of the results variance.

The domains of Memory and Fluency were predicted by age and the domains of Attention and Language were predicted by education. The Visuospatial domain was predicted by age and education.

From the multiple linear regression models, predictive equations were extracted (Table7) to calculate the expected results of an individual with given age and education, on ACE-III and its domains.

Table 7. Equations of the multiple linear regression models to the calculus of the expected results on ACE-III and its domains

	Formula
ACE-III (total)	103,762 + 0,791 * **EDUCATION (years)** - 0,255 * **AGE (years)**
Attention	16,705 + 0,127 * **EDUCATION (years)**
Memory	30,476 - 0,107 * **AGE (years)**
Fluency	16,522 - 0,054 * **AGE (years)**
Language	24,503 + 0,078 * **EDUCATION (years)**
Visuospatial	15,873 + 0,305 * **EDUCATION (years)** - 0,068 * **AGE (years)**

DISCUSSION

The mean score of ACE-III in our sample (89.4) is similar to the ones in the Australian (95.4) and Spanish studies (81.8) (Hsieh et al., 2013; Matias-Guiu et al., 2014). Despite age and schooling differences between samples, there is also a similitude concerning the results obtained on ACE-III domains.

Despite the reliability (α=.732) of ACE-III Portuguese version it is lower than those reported by the two studies, it is acceptable for a cognitive screening test (Mitrushina, 2009). In fact, most of the screening tests like the Mini-mental State Examination (Freitas et al., 2010; Morgado, Rocha, Maruta, Guerreiro, & Martins, 2009), the Phototest (Dias et al., 2014) or the Montreal Cognitive Assessment (Freitas et al., 2010), presents levels of internal consistency ranging from moderate to acceptable due to the inclusion of different cognitive tasks in their composition. Furthermore, ACE-III's reliability is reinforced by significant correlations between its domains and between them and the total score, pointing to a satisfactory internal structure.

Regarding the concurrent validity, ACE-III correlated with a well-known neurocognitive screening test (MoCA). This psychometric aspect it has been studied in other versions. The Spanish version showed a positive correlation with the Mini Mental State Examination (Matias-Guiu et al., 2014) and the original version was found to correlate significantly with standardized neuropsychological tests used in the assessment of attention, language, verbal memory and visuospatial attention (Hsieh et al., 2013; Velayudhan et al., 2014).

The negative correlation between ACE-III and the measure of depression it was expected, since the inverse relation between depressive mood and cognitive functioning it is well established (Austin, Mitchell, & Goodwin, 2001).

The performance on ACE-III was influenced by gender, type of professional occupation, age and education of the subjects, however, the multiple linear regression determined that age and education were the sole predictors of the re-

Table 8. Example of z scores calculation for a 73 years old person with 4 years of education

	Formula	Expected Result	Obtained Result	SD	*z* Score
ACE-III (total)	103,762 + 0,791 * **4** - 0,255 *73	88	78	6,48	-1,5
Attention	16,705 + 0,127 * **4**	17	15	1,42	-1,4
Memory	30,476 - 0,107 * **73**	23	22	2,42	-0,4
Fluency	16,522 - 0,054 * **73**	13	12	1,82	-0,6
Language	24,503 + 0,078 * **4**	25	24	1,43	-0,7
Visuospatial	15,873 + 0,305 * **4** - 0,068 * **73**	16	14	2,27	-0,9

sults. This observation is in accordance to the study of the original version (Hsieh et al., 2013), the Spanish (Matias-Guiu et al., 2014) and the Egyptian- Arabic (Qassem et al., 2015) versions. ACE- III is heavily weighted with verbal tasks and language items(Hsieh et al., 2013), therefore age and education must be considered for the interpretation of the results. In fact, most of the neuropsychological screening tests like the Mini-mental State Examination (Morgado, Rocha, Maruta, Guerreiro, & Martins, 2009), the Montreal Cognitive Assessment (Freitas et al., 2011) and the Phototest (Dias et al., 2014), are highly influenced by these two variables. Age and education alone or in combination were also predictors for the ACE-III domains. Attention domain was predicted by education and Memory domain was predicted by age. These findings are in line with the idea that factors related to memory are sensitive to age, whereas those related to attention sensitive to education(Gómez-Pérez & Ostrosky-Solís, 2006). Verbal Fluency it is a very common domain in cognitive assessment and its known that age but not education, has a differential effect on the tasks of verbal fluency(Mathuranath et al., 2003). In fact, the relation of ACE-III domains to age and education reflects a complex interaction between these variables in normal aging (Ardila, Ostrosky-Solis, Rosselli, & Gómez, 2000).

The obtained data from the healthy sample enabled the extraction of normative equations. Hence, to compare the performance of an individual to the present sample it is necessary to compute the formulas in order to obtain the expected results according to age and years of complete education. Afterwards, the z scores for the total of ACE-III and each domain it is calculated according to the following formula:

$$z\ Score = \left(\frac{Obtained\ result - Expected\ result}{Standard\ Deviation}\right)$$

In table 8, an example of a 73 years old subject with 4 years of education it is given.

In conclusion, the Portuguese version of ACE-III has proved to have acceptable internal reliability reinforced by validity evidence pertaining to the internal

structure and it has convergent and divergent validity. The performance of the healthy sample was highly influenced by age and education, with some variations in each domain. The availability of ACE-III normative equations based on a healthy sample according to age and education enables the use of a brief screening tool for cognitive functioning. However, future studies should consider the increment of the sample and must determine the validity in several types of dementia, establish cut-off scores and values of sensitivity and specificity and test the utility in different clinical settings (e.g. primary care, general neurology or memory clinics).

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