

The cognitive subscale of the “Alzheimer’s Disease Assessment Scale” in a Brazilian sample

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Abstract

The cognitive subscale of the “Alzheimer’s Disease Assessment Scale” (ADAS-Cog) is widely used for the evaluation of dementia and is very popular in dementia drug trials because of the characteristics of the scale. The objective of the present study was to adapt the ADAS-Cog for use for the Brazilian population. A major problem is that education is variable, a fact that may influence performance in cognitive evaluation. This study was conducted on a control group (CG) of 96 subjects (25 males and 71 females aged 68 ± 8.6 years) and on 44 Alzheimer’s disease (AD) patients (19 males and 25 females aged 72 ± 6.4 years) with mild dementia (Clinical Dementia Rating score 1). For statistical analysis groups were divided into three educational levels: I, 0-4 years of schooling (65 CG/20 AD); II, 5-11 years of schooling (19 CG/7 AD), and III, 12 or more years of schooling (12 CG/17 AD). The battery was applied according to original instructions. Total mean score for CG and AD was 10.9 and 22.9 for level I, 7.8 and 22.4 for level II, and 6.2 and 15.4 for level III, respectively. These results indicate that our version of the ADAS-Cog is useful to identify mild dementia, though there may be an overlapping when comparing high education demented with low education non-demented subjects.

Key words

- Dementia
- Alzheimer’s disease
- Neuropsychological evaluation
- Education

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Introduction

Although Alzheimer’s disease (AD) has a great variety of symptoms, progressive memory loss and decline in other cognitive functions are its main characteristics. As the pathophysiology of the disease is becoming better understood, a strong interest in evaluating new drugs for treatment has also arisen. Therefore, efforts have been made to improve and standardize a methodology for the evaluation of different clinical trials (1-3).

The “Alzheimer’s Disease Assessment Scale” (ADAS) was developed with the ob-

jective of evaluating the intensity of cognitive and noncognitive changes which are characteristic of this disease. The scale is composed of two parts with a maximum score of 120 points. One is cognitive (ADAS-Cog) and includes items 1-11, with a maximum score of 70, while the other is noncognitive and assesses behavior disturbances, including items 12-21 with a maximum score of 50 (4,5). The ADAS-Cog requires approximately 30 to 45 min to administer, according to the degree of cognitive impairment (6,7). The main areas of the cognitive domains evaluated are memory (50%), lan-

guage (28%), praxis (14%) and command understanding (8%) (8). A high score indicates a poor performance. The ADAS-Cog was not originally designed for use as a diagnostic instrument, but it was later proven that its scores clearly distinguished clinically diagnosed AD patients from non-dementia control subjects (7).

It was observed that the ADAS-Cog total score and its items are sensitive to the severity and degree of AD. For each 2.5 points, one point of worsening was observed in the Mini-Mental State Examination, for scores between 23 and 11 (7).

Longitudinal studies indicate that AD patients show an increase in the ADAS-Cog total score of 7 to 11 points per year (9).

After being successfully introduced as a primary evaluation instrument in the first double-blind multicenter study with tacrine (10), the ADAS-Cog has been used as the primary instrument to monitor the response to treatment of AD patients. Consequently, the scale has been adapted to several languages (11-17).

The objectives of the present study were to obtain a national ADAS-Cog standard by adapting it to the Portuguese language and to analyze the performance of a Brazilian sample in terms of gender, age and educational level, and the influence of these variables on the different ADAS-Cog items and on its total score.

Subjects and Method

Subjects

A total of 140 subjects who took part in an open and prospective study were divided into two groups: 96 control subjects (CG), 25 males and 71 females aged 68 ± 8.6 years (range, 50 to 87 years), and 44 AD patients, 19 males and 25 females aged 72 ± 6.4 years (range, 54 to 83 years). Each group was subdivided into three educational levels: I, subjects with 0 to 4 years of schooling; II, subjects with 5 to 11 years of schooling, and III, 12 or more years of schooling (Table 1). The AD group consisted of individuals older than 50 years who met the criteria for the probable presence of AD according to the DSM-IV (18) and NINCDS-ADRDA (19). They were free of other neurological diseases and took no drugs which could interfere with the cognitive evaluation.

The aim was to study only patients with mild dementia, or dementia in its initial stages, who had a Clinical Dementia Rating (CDR) score of 1.0 (20) because they present a more difficult diagnostic challenge, may have a larger range of therapeutic alternatives and, consequently, present a greater possibility for improvement.

The CG consisted of subjects aged 50 years or older, spouse control volunteers and also other healthy elderly individuals from the community, who were free of neurological or psychiatric diseases and took no drugs which could interfere with the cognitive evaluation. Informed consent was obtained from CG subjects, all of whom had a CDR equal to 0.

All subjects were free of severe and uncorrected visual or auditory deficits that could interfere with test performance.

Method

The ADAS-Cog was translated directly into Portuguese from the original English version. The structured evaluation was pre-

Table 1. Educational level for the control group and Alzheimer's disease patients.

Educational level (years of schooling)	CG	AD
0-4	65 (68%) - 17 illiterate subjects 13 males/52 females	20 (45%) - 4 illiterate subjects 7 males/13 females
5-11	19 (20%) 6 males/13 females	7 (16%) 2 males/5 females
12 or more	12 (12%) 6 males/6 females	17 (39%) 11 males/6 females

CG, control group; AD, Alzheimer's disease.

ceded by an open-ended conversation with the objective of assessing various aspects of both expressive and receptive speech (5,7, 12,21). The scores of this evaluation were determined after the end of the test session, and they concern the following items: spoken language ability, word-finding difficulty in spontaneous speech, and comprehension. The ADAS-Cog scoring method is not difficult, but experience is needed for its application, especially for these three items (8).

Statistical analysis

Since data obtained for each variable were a skewed curve, it was not possible to use parametric tests. The following tests were applied to analyze the results: the Mann-Whitney test (22) was used to analyze the sex and age variables and the influence of education, comparing the AD patients with CG. Kruskal-Wallis (22) analysis of variance was used for comparison of the different educational levels in each group for similar items and age. When significant for items, this analysis was complemented by the multiple comparison test of Miller-Dunn (23).

Battery

The ADAS-Cog scale was applied by a neurologist according to the original instructions. The words for the items "immediate word recall" and "word recognition task" were modified for adaptation to the Portuguese language (see Appendix). Since, as far as we know, there is no frequency study for Brazilian Portuguese, we used a study on "familiarity and complexity" (24) with the following criteria: pairing low/high frequency words with low/high familiarity words, pairing for word extension, and preferably pairing for the same semantic category.

Results

No significant difference was observed

for gender among AD patients and CG subjects for the different items or for the total score and further analysis did not consider this variable. A significant difference was observed for age in total subjects between groups and among AD patients and CG subjects for educational level between 5 and 11 years of schooling. No significant difference was observed for the age variable for other educational levels within or between groups. The influence of education was studied independently with comparisons between and within groups with reference to the items and corresponding educational levels (Table 2). Since we used only CDR 1.0 AD patients, for some items there was a ceiling effect in the sense that CG and AD patients did not make mistakes. No floor effect was observed. The total mean score for CG and AD was 10.9 and 22.9 for level I, 7.8 and 22.4 for level II, and 6.2 and 15.4 for level III, respectively. For all subitems the means, standard deviation and medians for each educational group are shown in Table 2. The high standard deviations observed for some subitems indicate the possibility of an overlap between groups. It should be noted that for the immediate word recall and total score subitems the performance within both groups was more homogeneous. In the AD patient group, considering the different educational levels, significant results were observed for the items commands, constructional praxis, comprehension and total score. For the CG, significance was observed in the items naming of objects and fingers, commands, constructional praxis, ideational praxis, remembering test instructions and total score. Between CG and AD subjects, when comparing the corresponding items in terms of the respective educational levels, the existence of significant differences was noted for educational level of 0 to 4 years of schooling in the items immediate word recall, constructional praxis, ideational praxis, orientation, word recognition and total score, with a better performance for CG. For 5 to 11 years

of schooling, significance was noted in the items immediate word recall, ideational praxis, orientation, word recognition, comprehension and total score, with a better performance for CG; while for 12 or more years of schooling significance was noted in the items immediate word recall, ideational praxis, orientation, word recognition, remembering test instructions and total score, with a better performance for CG.

Kruskal-Wallis analysis of variance showed differences between educational levels within groups in some items, i.e., commands and ideational praxis for CG; constructional praxis for CG and AD; CG in total score of ADAS-Cog, subjects between 0 and 4 years of educa-

tion were more significant than subjects between 5 and 11 and more than 12 years of education. For CG in items naming objects and fingers and remembering test instructions and AD patients in item commands, subjects between 0 and 4 years of education were more significant than subjects more than 12 years of education. For AD patients in item comprehension, subjects between 5 and 11 years of education were more significant than subjects between 0 and 4 years and more than 12 years of education. For AD patients in total score, subjects between 0 and 4 years and between 5 and 11 years of education were more significant than subjects with more than 12 years of education.

Table 2. Scores for the items of the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-Cog) obtained for a control group and for Alzheimer's disease patients with educational levels between 0 and 4 years of schooling (0-4 Edu), 5 and 11 years of schooling (5-11 Edu) and 12 or more years of schooling (12+ Edu).

Item	Control group [mean \pm SD (median)]			Alzheimer's disease [mean \pm SD (median)]		
	0-4 Edu	5-11 Edu	12+ Edu	0-4 Edu	5-11 Edu	12+ Edu
Immediate word recall	3.9 \pm 1.4 (4.0)*	3.9 \pm 1.3 (3.0)*	3.4 \pm 0.8 (4.0)*	6.1 \pm 1.1 (6.0)*	6.4 \pm 1.4 (7.0)*	5.4 \pm 1.2 (6.0)*
Naming objects and fingers	0.7 \pm 0.6 (1.0)#	0.4 \pm - (0)	0.3 \pm - (0)#	1.0 \pm 0.8 (1.0)	1.0 \pm - (1.0)	0.4 \pm - (0)
Commands	0.8 \pm - (0)#	0.3 \pm - (0)#	0.1 \pm - (0)#	1.1 \pm 1.0 (1.0)#	0.7 \pm - (0)	0.4 \pm - (0)#
Constructional praxis	1.0 \pm 0.7 (1.0)*#	0.6 \pm - (0)#	0.3 \pm - (0)#	2.0 \pm 1.3 (1.5)*#	0.7 \pm 0.5 (1.0)#	0.4 \pm - (0)#
Ideational praxis	0.8 \pm 0.7 (1.0)*#	0.3 \pm - (0)*#	0.1 \pm - (0)*#	1.7 \pm - (1.5)*	1.3 \pm - (1.0)*	0.8 \pm - (1.0)*
Orientation	0.5 \pm - (0)*	0.5 \pm - (0)*	0.3 \pm - (0)*	2.7 \pm 1.7 (2.5)*	3.7 \pm 0.8 (4.0)*	2.1 \pm 1.7 (2.0)*
Word recognition	2.4 \pm 2.1 (2.0)*	1.7 \pm 1.6 (1.0)*	1.8 \pm 1.3 (1.0)*	6.7 \pm 2.9 (6.5)*	6.1 \pm 2.0 (7.0)*	4.9 \pm 3.2 (4.0)*
Remembering test instructions	0.7 \pm - (0)#	0.3 \pm - (0)	0 \pm - (0)*#	1.8 \pm - (1.0)	1.3 \pm - (1.0)	0.7 \pm - (0)*
Spoken language ability	0 \pm - (0)	0 \pm - (0)	0 \pm - (0)	0.1 \pm - (0)	0.3 \pm - (0)	0.1 \pm - (0)
Word-finding difficulty in spontaneous speech	0 \pm - (0)	0 \pm - (0)	0 \pm - (0)	0.1 \pm - (0)	0.4 \pm - (0)	0.1 \pm - (0)
Comprehension	0.1 \pm - (0)	0 \pm - (0)*	0 \pm - (0)	0.1 \pm - (0)#	0.4 \pm - (0)*#	0.1 \pm - (0)#
Total score of ADAS-Cog	10.9 \pm 6.2 (10.0)*#	7.8 \pm 2.8 (8.0)*#	6.3 \pm 2.4 (5.5)*#	23.0 \pm 7.5 (22.5)*#	22.4 \pm 5.0 (21.0)*#	15.4 \pm 5.0 (16.0)*#

Data are reported as means \pm SD and medians are given in parentheses.

*P<0.05 between groups for the same educational level;

#P<0.05 within each group for different educational levels (Kruskal-Wallis test).

Discussion

It is important to note that we did not examine variables such as vitamin use, estrogen replacement therapy and anti-inflammatory therapies, and it is possible that our control sample may have included patients with mild cognitive impairment.

Our data show significant differences between controls and AD patients in several items and in the total score of the ADAS-Cog (Figure 1). It is important to stress that there is a large overlap between the AD and control groups.

There were no significant differences with respect to gender, a finding similar to that obtained in other reports (13,17,25,26).

A lower educational level is related to a worse performance in the tests in most of the studies with ADAS (11,25,27-29). We observed that there is a significance in the education variable between and within groups. The items commands, constructional praxis and the total score of ADAS-Cog were equally significant in the CG and in the group with AD. The items immediate word recall, ideational praxis, orientation, word recognition and total score of ADAS-Cog were statistically significant in the three educational levels.

The literature demonstrates that the ADAS-Cog correlates well with other neuropsychological scales like the Mini-Mental State Examination (11,25,30-32), Global Deterioration Scale (11,25,30), Geriatric Evaluation of Relative's Rating Instrument (25) and CDR (8).

We also believe that the battery is very useful in differentiating between normal in-

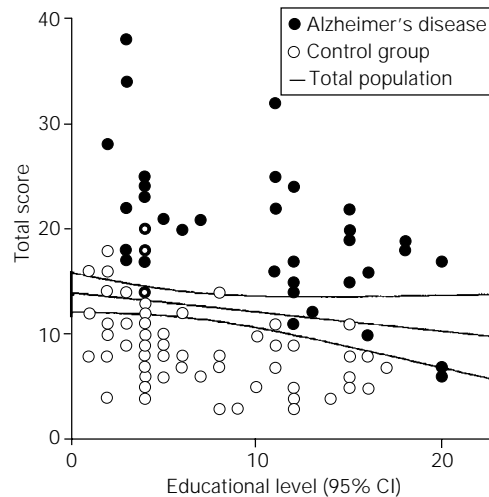


Figure 1. Performance in total score of the cognitive subscale of the "Alzheimer's Disease Assessment Scale" for years of educational level. CI, confidence interval.

dividuals and mild AD patients.

We would like to stress that the variation shown by some subitems is an indication that the ADAS-Cog should be always applied as a complete battery, the isolated result of subitems having no meaning or leading to false negative/false positive results.

Conclusions

The educational level greatly influences the ADAS-Cog performance of the CG and the AD and CDR 1.0 patient group, as observed for different items of the test.

The present results indicate that the adaptation of the ADAS-Cog is adequate for our population when analyzed together with educational level.

This performance analysis permitted the differentiation between normal elderly individuals and AD patients using the ADAS-Cog.

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Appendix. The following items were analyzed:

1. Immediate word recall

In this task, the subject is given three tries to learn a list of ten words (see below). The subject must first read the words aloud, memorize them and then reproduce them. The subject's score is the average number of words not recalled in three trials (maximum 10).

Trial 1		Trial 2		Trial 3	
Original list	Adapted list	Original list	Adapted list	Original list	Adapted list
Home	Creme	Library	Flor	Army	Rei
Coin	Dedo	Flag	Casa	Wheat	Chá
Railroad	Mar	Home	Creme	Coin	Dedo
Child	Carta	Railroad	Mar	Flag	Casa
Army	Rei	Ocean	Motor	Skin	Poste
Flag	Casa	Coin	Dedo	Railroad	Mar
Skin	Poste	Army	Rei	Home	Creme
Library	Flor	Child	Carta	Ocean	Motor
Wheat	Chá	Skin	Poste	Library	Flor
Ocean	Motor	Wheat	Chá	Child	Carta

2. Naming objects and fingers

For this item the subject is asked to name the 12 real objects presented randomly as well as the fingers of his/her dominant hand. The objects presented were: flower, bed, whistle, pencil, rattle, mask, scissors, comb, wallet, harmonica, stethoscope, and tweezers. The score varies from 0 to 5.

3. Commands

The subject is asked to carry out one to five commands. Score varies from 0 to 5.

4. Constructional praxis

This task assesses the subject's ability to copy four geometric forms: a circle, a superimposed rectangle, a diamond and a square. Score varies from 0 to 4.

5. Ideational praxis

This task is designed to determine whether the individual can perform a complex sequence of actions. The score varies from 0 to 5.

6. Orientation

The components of this task are person, day of the week, day of the month, month, year, season, time of day and specific place. One point is given for each incorrect answer (maximum 8).

7. Word recognition

In this task, the subject must read and memorize a list of 12 words (in bold, see next page). These words are then randomly mixed with 12 words the subject has not seen, and the subject is asked to decide whether or not the word has already been read. The subject has three tries, in each of which, the word order is changed. The score is calculated by summing up the number of errors and dividing by 3; 12 points is the maximum.

Trial 1		Trial 2		Trial 3	
Original list	Adapted list	Original list	Adapted list	Original list	Adapted list
Corn	Milho	River	Rio	Plant	Planta
Effort	Esforço	Officer	Chefe	River	Rio
Party	Festa	Thought	Plano	Amount	Total
River	Rio	Event	Fato	Event	Fato
Folly	Tolice	Queen	Dama	Queen	Dama
Locker	Cofre	Position	Posição	Industry	Indústria
Event	Fato	Camp	Campo	Position	Posição
Queen	Dama	Fate	Fim	Occasion	Ocasião
Position	Posição	Golf	Golfe	Dove	Siri
Quality	Dom	Dove	Siri	Cradle	Berço
Sunset	Entardecer	Belief	Fé	Banality	Bobagem
Dove	Siri	Permission	Permissão	Singer	Cantor
Belief	Fé	Umbrella	Sombrinha	Belief	Fé
Umbrella	Sombrinha	Hint	Dica	Umbrella	Sombrinha
Allegory	Ficção	Missile	Míssil	Hypothesis	Hipótese
Hound	Cão	Blister	Bolha	Hint	Dica
Idiom	Idioma	Concept	Noção	Missile	Míssil
Hint	Dica	Proxy	Corretor	Proxy	Corretor
Missile	Míssil	Pianist	Piano	Noose	Nó
Gem	Jóia	Lobster	Pomba	Distinction	Distinção
Proxy	Corretor	Gender	Gênero	Lobster	Pomba
Lobster	Pomba	Criterion	Critério	Tank	Tanque
Criterion	Critério	Bullet	Tiro	Criterion	Critério
Deceit	Erro	Intellect	Mente	Decree	Lei

8. Remembering test instructions

This item evaluates the individual's ability to remember the instructions of the recognition task. Score varies from 0 to 5.

9. Spoken language ability

This item is an overall rating of the quality of speech, such as clarity and capacity to make someone understand. Score varies from 0 to 5.

10. Word-finding difficulty in spontaneous speech

This task analyzes the decrease in expressive speech, but only as refers to difficulty in word choice. Score varies from 0 to 5.

11. Comprehension

This item evaluates the individual's ability to understand the examiner's speech. Score varies from 0 to 5.