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The validity and reliability of the Turkish version of Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) in patients with mild and moderate Alzheimer's disease and normal subjects

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SUMMARY

Objectives The cognitive subscale of the Alzheimer's Disease Assesment Scale (ADAS-Cog) is the most widely used test in clinical trials dealing with Alzheimer's disease (AD). The aim of this study was to investigate the validity and reliability of the Turkish version of ADAS-Cog.

Methods Twenty-nine patients with AD, fullfilling NINCDS-ADRDA criteria of probable AD, who were in stage 3–5 according to the Global Deterioration Scale (GDS), and 27 non-demented control subjects with similar age, gender and educational status were recruited for the study. The Turkish version of ADAS-Cog, Standardized Mini Mental Status Examination (MMSE) and Short Orientation-Memory-Concentration Test (SOMCT) were applied to both of the groups. Inter-rater reliability, internal consistency, test–retest reliability; face validity, differential validity and convergent validity were statistically analyzed.

Results Both MMSE and ADAS-Cog have significantly differentiated patients with AD and control subjects ($p < 0.001$). A significant correlation was established between MMSE and ADAS-Cog scores in AD group (r: -0.739). ADAS-Cog was also highly significantly correlated with GDS (r: 0.720) and SOMCT (r: 0.738). For the group with AD, control and whole cohort coefficients of internal consistency, Cronbach's α: 0.800, 0.515, 0.873 were found respectively. Inter-rater reliability for total ADAS-Cog score was found as ICC: 0.99 and 0.98 and test–retest reliability was found as ICC: 0.91 and 0.95 for demented and nondemented subjects, respectively.

Conclusion The Turkish version of ADAS-Cog has been found to be highly reliable and valid in differentiating patients with mild and moderate AD from nondemented subjects. Copyright © 2006 John Wiley & Sons, Ltd.

KEY WORDS — Alzheimer's disease; ADAS-Cog; validity; reliability

INTRODUCTION

The Alzheimer's Disease Assesment Scale (ADAS), which was developed by Rosen *et al.* (1984) has become the most widely used instrument in the follow-up of Alzheimer's Disease (AD), including assessment of the efficacy of dementia drug trials, since its publication in 1984. ADAS consists of two major scales : ADAS-Cog for cognitive; and ADAS-noncog for noncognitive functions. ADAS-Cog is the more extensively used portion of the test. ADAS-Cog itself contains 11 subtests. These subtests are: word recall; naming (objects and fingers); following commands; constructions (drawing); ideational praxis; orientation; word recognition; recall of test instructions; spoken language ability; word-finding difficulty and comprehension of spoken language; assessing memory; praxis and language.

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It is important to validate cognitive tests in different cultures and languages for those tests to be scientifically acceptable. This requirement has led to the adaptation of ADAS and ADAS-Cog to many languages and cultures including standardization and/or validity-reliability studies. These communities are Hong Kong (Chu *et al*., 2000), Iceland (Hannesdottir *et al*., 2002), Japan (Homma, 1992), Italy (Inzitara *et al*., 1999), Slovakia (Kolibas *et al*., 2000), China (Liu *et al*., 2002), Spain (Manzano *et al*., 1994; Pena-Casanova J *et al*., 1997), France (Puel *et al*., 1996), Brazil (Schultz *et al*., 2001), Greece (Tsolaki *et al*., 1997), Germany (Weyer *et al*., 1992; 1997) and Korea (Youn *et al*., 2002). Recently, a study analysing descripitive statistical values of ADAS-Cog in normal Turkish subjects has been reported (Kalem Akca *et al*., 2003). In this study; the aim was to establish validity and reliability of ADAS-Cog scale in Turkish patients with AD.

METHOD

Subjects

Twenty-nine patients fulfilling DSM-IV criteria (American Psychiatric Association,1994) for dementia and NINCDS-ARDRA criteria (McKhann *et al*., 1984) for probable AD and 27 nondemented age, sex and education matched controls were recruited for the study. The patients with dementia were selected from our dementia outpatient clinic; controls were selected from the relatives of our patients or health services staff. All subjects in both groups were older than 50 years of age and had an education of minimum reading and writing (RW) level. Patients with cerebrovascular disorders, Parkinson's and other neurodegenerative diseases, major depression and other psychiatric diseases, alcohol abuse, serious metabolic abnormalities affecting mentation, and any sistemic disorders leading to hypoxia were excluded from the study. The demented patients were scored according to the Global Deterioration Scale (GDS) (Reisberg *et al*., 1982). All control subjects and most of the demented patients were administered the Hamilton Depression Scale (Hamilton, 1960; Akdemir *et al*., 1996) or the Geriatric Depression Scale (Yesavage *et al*., 1983, Ertan *et al*., 2000) for exclusion of depression.

Blood tests including fasting blood glucose, liver and kidney function tests and complete blood count were applied to all subjects if they had not already been performed within the last month. Thyroid function tests, vitamin B12 and folic acid levels were measured in all of the patients and most of the controls. The Venereal Disease Research Laboratory (VDRL) test was given to most of the patients and also a test for HIV was performed in suspected cases. All demented patients had neuroimaging (CT or MRI) study. If dementia patients received acetylcholinesterase inhibitors, nootropics and/or gingko biloba preparations, they were withdrawn at least 10, preferably 15 days before administration of ADAS-Cog test. Atypical antipsychotics and SSRIs were allowed. No subject in the control group received any drug affecting cognitive functions. However, drugs for cardiac diseases, diabetes and hypertension were continued. All patients underwent a neurological examination. Written consent was obtained from each patient or a close relative before test administration.

Adaptation of the ADAS-Cog to the Turkish community

Permission from authors was received to adapt the ADAS-Cog to the Turkish language and to use it. Forward translation of the test from English to Turkish was made by two medical professionals, one neurologist (HM) and one medical doctor with excellent acquisition of English. The translated text was further reviewed and reconcilled by an expert of English who is a native English speaker with an excellent Turkish acquisition. During adaptation, generally the text of original scale was followed. However, under advisory supervision of a Turkish linguistic professional, some words have been switched with new ones fitting better to Turkish culture. For example, in word recall task which is composed of ten words with high image, the word 'ocean' was replaced by the word 'sea' which has a higher image for Turkish people. In the naming task in which four objects with high, medium and low frequency values are exposed, the object 'table' was used instead of 'bed' and 'thermometer' instead of 'stethescope'. In the original version 'flower, bed, whistle, pencil' were chosen as high frequency objects, 'rattle, mask, scissors, comb' as medium frequency objects and 'wallet, armonica, stethescope, tweezers' as low frequency objects. For the Turkish community, 'flower, pencil, table, comb' were regarded as objects with high frequency, 'whistle, scissors, wallet, tweezers' with medium frequency and 'rattle, mask, armonica, thermometer' with low frequency. In the word recognition test, 'lobster' was switched to 'fish'. The scale was first administered to three subjects. Some troublesome instructions which were hard to comphrend and administer, and which led to hesitation during scoring were modified

to more understandable. This final form of the scale in parallel with some other previously well-known scales were applied to Alzheimer's patients and controls ($n = 29 + 27$) in order to test the validity and reliability of the ADAS-Cog on Turkish patients.

Test Administration

In order to examine convergent validity, the subjects were first administered the MMSE (Folstein *et al*., 1975), which has been validated and shown to be reliable for the Turkish community (Güngen *et al*., 2002). In the second step, the ADAS-Cog was administered. The scale was scored by two of the authors independently. Furthermore, patients with AD were given SOMCT (Katzman *et al*., 1983).

While one of the independet raters both administered the test and did the scoring, the other only rated the scale at the same session. These two seperate scores were used to examine inter-rater reliability.

The ADAS-Cog scale was administered twice within a period of 1–1.5 months to 14 patients with AD and 14 control subjects in order to test the test–retest reliability of the scale.

Analysis

The data were processed with SPSS-10 statistical pack program.

Comparison of groups for age and year of education were analyzed by means of Mann–Whitney *U* test. Also, the subjects were divided into two groups: subjects who had education between reading-writing and five years of education and subjects with more than five years of education. Comparison of groups according to educational groups and sex were made by chi-square statistical test.

Internal consistency was analysed with Cronbach alpha test. An alpha valued over 0.7 was regarded sufficient for AD. Inter-rater and test–retest reliabilities were examined with Intraclass Correlation Coefficient (ICC).

Face validity was evaluated by the neurologist (HM). Discriminant validity and sensitivity was evaluated by comparing test scores of patients with AD and control subjects with Mann–Whitney U test. Convergent validity was found by correlating ADAS-Cog and MMSE scores with Spearman-rank order correlation test. Also, the relationships between ADAS-Cog and GDS and SOMCT were analyzed by Spearman-rank order correlation test.

The responsiveness of the Total ADAS-Cog score to different severity (stages) of dementia were analyzed by using Kruskal Wallis ANOVA and post hoc comparisons were made by Bonferroni test by taking critical *p*-value as 0.0167 (0.05/3). The relationships between ADAS-Cog score and age, education and disease stage were analyzed by Multipl Linear Regression analysis.

RESULTS

There was no statistically significant difference between AD and control subjects regarding age, educational status and gender distribution (Table 1).

According to GDS, 48.3% of patients with AD had mild (stage 3), 27.6% had mild-moderate (stage 4) and 24.1% had moderate (stage 5) dementia.

Validity

Scores of MMSE and ADAS-Cog in AD and control groups were compared in order to test the discriminant validity. Both tests could differentiate patients with AD and nondemented subjects succesfully ($p < 0.001$) (Table 2). ADAS-Cog also differentiated patients with mild AD (stage 3) from controls ($p < 0.001$). Kruskal Wallis ANOVA and post hoc comparisons which were made by Bonferroni test showed that ADAS-Cog could discriminate patients with mild AD (stage 3) from patients with mild-moderate (stages 4) (*p*: 0.015) and moderate AD (Stage 5) (*p*: 0.009). Total scores of ADAS-Cog of patients with mild-moderate AD (stage 4) was lower than patients with moderate AD (stage 5), although this difference wasn't significant (Table 3). The effect of education on the ADAS-Cog scores were analyzed by controlling age and disease stage by

Table 1. The distrubition of Alzheimer Disease and control groups according to age, sex and education

Group	*n*	Age	Sex		Education status		
			Female(%)	Male (%)	Mean year	RW-5 year(%)	6 year ↑ %
Alzheimer	29	70.55 ± 7.05	48.3	51.7	7.00 ± 3.67	62.1	37.9
Control	27	68.41 ± 7.69	40.7	59.3	6.96 ± 3.98	63.0	37.0
		p: 0.16*	*p*: 0.57**		*p*: 0.95*	*p*: 0.95**	

*Mann–Whitney-*U*.
**Chi square.

Table 2. The discriminant validity of ADAS-Cog and MMSE between patients and controls

	Alzheimer	Control	*p*-value (*)
Word recall	6.68 ± 1.75 (3.50–10.00)	4.28 ± 1.16 (0.67–6.67)	0.000
Naming	0.91 ± 0.76 (0.00–3.00)	0.11 ± 0.32 (0.00–1.00)	0.000
Following commands	1.36 ± 1.23 (0.00–4.00)	0.28 ± 0.51 (0.00–2.00)	0.000
Constructional praxis	1.50 ± 0.80 (0.00–3.00)	0.59 ± 0.62 (0.00–2.00)	0.000
Ideational praxis	1.66 ± 1.00 (0.00–5.00)	0.48 ± 0.73 (0.00–2.00)	0.000
Orientation	2.69 ± 2.11 (0.00–7.00)	0.07 ± 0.27 (0.00–1.00)	0.000
Word recognition	7.34 ± 2.95 (2.33–12.00)	2.86 ± 1.62 (0.67–7.34)	0.000
Recall of test instructions	2.69 ± 1.95 (0.00–5.00)	0.91 ± 1.14 (0.00–4.00)	0.000
Spoken language ability	0.19 ± 0.43 (0.00–2.00)	0.04 ± 0.19 (0.00–1.00)	0.035
Word -finding difficulty	0.88 ± 0.80 (0.00–3.00)	0.15 ± 0.33 (0.00–1.00)	0.000
Comprehension of spoken language	1.33 ± 0.98 (0.00–3.00)	0.07 ± 0.21 (0.00–1.00)	0.000
Total score of ADAS-Cog	27.23 ± 9.67 (13.17–53.00)	9.85 ± 3.57 (3.00–18.67)	0.000
Total score of MMSE	17.31 ± 5.44 (2.00–26.00)	26.12 ± 1.83 (23.00–29.00)	0.000

*Mann–Whitney-*U*.

Table 3. The responsiveness of the total ADAS-Cog score to different severity (stages) of dementia determined by Global Deterioration Scale

	Stage 3	Stage 4	Stage 5	*p*-value
Total ADAS-Cog score	20.28 ± 6.35	31.36 ± 4.89	36.60 ± 9.41	0.001*
Percentage of patients(n)	48.3(14)	27.6(8)	24.1(7)	

*Kruskal-Wallis.
post hoc (Bonferroni) Comparison: stage 3 < stage 4 (p: 0.015); stage 3 < stage 5 (p: 0.009); stage 4 = stage 5 ($p > 0.05$).

utilizing a multiple linear regression analysis where ADAS-Cog score was the dependent variable and age, years of education and disease stage (all as numeric variables) were the independent variables. The results of this analysis indicated that, while ADAS-Cog score was significantly sensitive to age (p: 0.026) and disease stage ($p < 0.001$) variables, it was not affected by level of education (p: 0.150).

The satisfactory correlation (r: −0.739) between ADAS-Cog and MMSE scores in AD group indicated an acceptable convergant validity. On the other hand, ADAS-Cog was also found to correlate with GDS (r: 0.720) and SOMCT (r: 0.738)(Table 4).

Reliability

Internal consistency was 0.800 for AD, 0.515 for control and 0.873 for whole group.

Inter-rater reliability for total ADAS-Cog score was found as ICC: 0.99 and 0.98 in demented and nondemented subjects, respectively. All subtests had acceptable levels of inter-rater reliability, with coefficients ranging from 0.71 to 0.99 for AD and from 0.62 to 1.00 for control subjects (Table 5).

Test–retest reliability for total score was ICC: 0.91, 0.95 for AD and control subjects, respectively. For the patients with AD, all subtests except for ideational praxis and spoken language ability had significant test-retest reliability, with correlations ranging from 0.60 to 0.96. For controls, other subtests except naming objects and fingers, following commands and comprehension of spoken language had significant test–retest reliability, with correlations ranging from 0.62 to 1.00 (Table 6).

Table 4. The correlation of ADAS-Cog with the other tests (convergent validity)

	SMMT	Global Deterioration Scale	Short orientation- memory-consentration test
ADAS-Cog	−0.739	0.720	0.738
p-value(*)	0.000	0.000	0.000

*Spearman rank-order correlation.

Table 5. Inter-rater reliability of ADAS-Cog (*)

	Alzheimer's Disease		Control	
	ICC (*p*-value)	(95%CI)	ICC	(95%CI)
Total score of ADAS-Cog	0.99 (0.000)	(0.988–0.998)	0.98 (0.000)	(0.955–0.992)
Word recall	0.96 (0.000)	(0.912–0.985)	0.99 (0.000)	(0.987–0.998)
Naming	0.98 (0.000)	(0.945–0.991)	1.00	
Following commands	0.98 (0.000)	(0.962–0.994)	0.84 (0.000)	(0.602–0.931)
Constructional praxis	0.89 (0.000)	(0.739–0.957)	0.93 (0.000)	(0.839–0.972)
Ideational praxis	0.94 (0.000)	(0.857–0.976)	0.92 (0.000)	(0.813–0.968)
Orientation	0.99 (0.000)	(0.987–0.998)	1.00	
Word recognition	0.99 (0.000)	(0.996–0.999)	0.99 (0.000)	(0.983–0.997)
Recall of test instructions	0.93 (0.000)	(0.832–0.972)	0.88 (0.000)	(0.701–0.949)
Spoken language ability	0.71 (0.004)	(0.288–0.883)	1.00	
Word-finding difficulty	0.77 (0.001)	(0.433–0.907)	0.62 (0.016)	(0.086–0.842)
Comprehension of spoken language	0.92 (0.000)	(0.792–0.966)	0.62 (0.016)	(0.086–0.842)

*Intraclass Correlation Coefficient (ICC).

Table 6. Test–retest reliability of ADAS-Cog (*)

	Alzheimer's Disease		Control	
	ICC (*p*-value)	(95%CI)	ICC (*p*-value)	(95%CI)
Total score of ADAS-Cog	0.91 (0.000)	(0.725–0.972)	0.95 (0.000)	(0.840–0.984)
Word recall	0.90 (0.000)	(0.683–0.967)	0.85 (0.001)	(0.517–0.950)
Naming	0.82 (0.002)	(0.431–0.941)	(0.500)	—
Following commands	0.91 (0.000)	(0.712–0.970)	(0.607)	—
Constructional praxis	0.76 (0.008)	(0.249–0.923)	0.64 (0.040)	(−0.133–0.883)
Ideational praxis	(0.159)	—	0.62 (0.046)	(0.187–0.878)
Orientation	0.96 (0.000)	(0.877–0.987)	0.89 (0.000)	(0.654–0.964)
Word recognition	0.60 (0.056)	(-0.251–0.871)	0.93 (0.000)	(0.621–0.953)
Recall of test instructions	0.68 (0.024)	(0.007–0.898)	0.86 (0.001)	(0.567–0.955)
Spoken language ability	(0.700)	—	1.00	
Word -finding difficulty	0.80 (0.003)	(0.381–0.936)	0.79 (0.004)	(0.336–0.932)
Comprehension of spoken language	0.76 (0.007)	(0.263–0.924)	(0.607)	—

*Intraclass Correlation Coefficient (ICC).

DISCUSSION

It is important to validate cognitive tests in different cultures and languages. During the adaptation of the ADAS-Cog to the Turkish Community, some words of word recall and word recognition items were switched with new ones fitting better to Turkish culture. Also, we changed some objects in the naming item Section. In the German (Weyer *et al*., 1997) and Italian (Inzitara *et al*., 1999) versions of ADAS which were used in an international multicentre AD trial, the words of the two memory items were not merely translated, but were choosen in agreement with imagery and frequency in their specific cultural and linguistic environment. Also, coloured pictures of objects were used instead of real objects in the naming task. Similarly, coloured photographs of objects were used in the naming item section in the Chinese version of ADAS-Cog because many Chinese elderly were illiterate (Liu *et al.*, 2002). Furthermore, the subjects were asked to write only name on the envolope without writing the address in the ideational praxis item in Chinese version. In the Brazilian version, the words for the items 'word recall' and 'word recognition' were modified to the Portuguese language (Schultz *et al*., 2001). They paired low/high frequency words with low/high familiarity words, paired for word extension and paired for the same semantic category.

This study has shown that the Turkish adaptation of ADAS-Cog is a valuable instrument for differentiating patients with mild and moderate AD from nondemented controls for elderly people over 50 years old with at least reading-writing level education. The mean score of ADAS-Cog was found as 27.23 ± 9.67 in AD group and as 9.85 ± 3.57 in the control group ($p < 0.001$). At the same time, all subscales were observed to be impaired by comparison to the control group in a similar fashion (Table 2).

Total ADAS-Cog score was highly correlated with total MMSE score (r: −0.739) and with SOMCT

score (*r*: 0.738) (Table 4). In literature, values like −0.76 (Chu *et al*., 2000), −0.85 (Doraisway *et al*., 1997), −0.91 (Liu *et al*., 2002) were reported in studies searching for correlation with MMSE. In the original study, correlations between ADAS-Cog and the Sandoz Clinical Assessment Geriatric Scale at *r*: 0.668 level, with memory-information test at *r*:−0.775 level and with dementia evaluation scale at *r*: 0.484 level were detected (Rosen *et al.*, 1984).

In our study, correlation with GDS was observed at *r*:0.720 level. ADAS-Cog could discriminate patients with mild AD (stage 3) from both controls and patients with mild-moderate AD (stage 4) and with moderate AD (stage 5). Although a linear trend of increase on the scale score could be observed between three stages of disease, a significant difference could not be obtained between stage 4 and 5 (Table 3). This might be attributed to the low number of subjects in these sub-categories of disease. Because of the small sample size, low number of subjects fell in these subcategories. This restriction of the study was overcome by conducting multivariate analysis. The ADAS-Cog was found to be sensitive to the disease severity in the multivariate analysis ($p < 0.001$). These findings have revealed that the Turkish version of ADAS-Cog has the potential to discriminate different levels of dementia.

Internal consistency (Cronbach alpha values) of the test was found as 0.800, 0.515 and 0.873 for AD, for controls and for whole group, respectively. The Turkish version of the test shows satisfactory levels of internal consistency. The discrepancy between the alpha values of demented patients and controls may be due to the substantially smaller variation in the control group compared to the dementia group which will tend to reduce the intercorrelations among the items. High values such as 0.86–0.96 have been reported in the tests that were adapted to the other languages and cultures (Pena-Casanova *et al*., 1997; Weyer *et al*., 1997; Chu *et al*., 2000; Liu *et al*., 2002).

Inter-rater reliability of the Turkish version was found to be quite satisfactory for both demented and control group (ICC: 0.99, 0.98 respectively). Correlation values were 0.91, 0.65 with the same order as the Hong-Kong study (Chu *et al*., 2000). They were 0.99 in the Chinese version (Liu *et al*., 2002) and 0.989, 0.986 for the demented and control group respectively in the original study (Rosen *et al*., 1984). In our study correlation coefficients differing between 0.71–0.99 for AD and 0.62–1.00 for nondemented subjects were detected for subscale scores. Consistency was more remarkable in the eight subscales using quantative evaluation. Correlation coefficients in subscales using qualitative evaluations such as spoken language ability, word-finding difficulty and comprehension were somewhat lower, especially in the control group (Table 5).

In this study, test–retest consistencies for AD and control group were found as ICC: 0.91 and 0.95 respectively (Table 6). These correlations were highly significant, although they were lower than inter-rater reliability. In the original scale, these figures were 0.915 for AD and 0.646 for controls (Rosen *et al*., 1984). In the Spanish adaptation, it was 0.93 (Pena-Casanova *et al.*, 1997), in a German multi-center study 0.93 (Weyer *et al*., 1997) and in the Chinese version 0.96 (Liu *et al*., 2002).

Our findings showed that after controlling for age and disease stage, ADAS-Cog score was not affected by the number of years of education. Usually, a relationship is expected between neuropsychometric tests and education. This expectation has been proven true in some studies (Doraisway *et al*., 1995;1997; Pena-Casanova *et al*., 1997; Schultz *et al*., 2001), although negative results have also been reported (Kolibas *et al*., 2000). ADAS-Cog was influenced by only low educational level in some studies (Liu *et al*., 2002). In a study from Turkey (Kalem Acka *et al*., 2003), descriptive statistical values of ADAS-Cog in normal subjects have been analyzed, and total ADAS-Cog score was found to be remarkably high in the group consisting of illiterate and RW subjects compared to subjects with higher education.

The results of multiple linear regression analysis indicated that ADAS-Cog score was significantly sensitive to age (*p*: 0.026). When the literature was reviewed, some relations with age were observed in the Spanish version (Pena-Casanova *et al*., 1997) and in a multicentered study (Doraisway *et al*., 1997), however none was reported in the Chinese version (Liu *et al*., 2002). In the Turkish study (Kalen Acka *et al*., 2003), 40–54 and 55–64 age groups had similar scores while the subjects over 65 showed worse scores.

In conclusion, the Turkish version of ADAS-Cog has been shown to be a valid and reliable neuropsychometric scale in discriminating patients with mild and moderate AD from the nondemented subjects and also in disease follow-up in a Turkish population. The test can be confidently used in research studies to be conducted on Turkish communities.

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