

The Reliability and Validity of the Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS-Cog) among the Elderly Chinese in Hong Kong

L W Chu,*^{MBBS (HK), FRCP (Edin), FHKAM (Med)}, K C Chiu,**^{MBBS (HK), MRCP (UK)}, S L Hui,***^{B Nurs Studies (Hons)},
G K K Yu,****^{MBBS (HK), FHKAM, FRCPsych (UK)}, W J C Tsui,†^{MSocSc (Clin Psych)},
P W H Lee,‡^{BSocSc, MSocSc (Clin Psych), PhD (Clin Psych)}

Abstract

Introduction: The Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog) was reported to be a sensitive cognitive function assessment scale for Alzheimer's Disease (AD). The English, Greek, Spanish but not Chinese versions had been validated previously. **Objectives:** The objectives of the present study were to investigate the reliability and validity of an adapted Chinese version of the ADAS-cog among Chinese elderly AD patients in Hong Kong. **Materials and Method:** Thirty-nine subjects were recruited during the period July to December 1998. Twenty were AD patients while 19 were non-demented normal subjects. Two raters administered the ADAS-cog scale thrice on different occasions. **Results:** The internal consistency (Cronbach's alpha) of the ADAS-cog were 0.91, 0.88 and 0.65 for the whole group, the AD and normal (i.e. non-demented) subjects respectively. The test-retest reliability as measured by the Spearman's rho correlation coefficients were 0.96, 0.86 and 0.86 for the whole group, AD and normal subjects, respectively, (all $P < 0.001$). The Spearman's rho correlation coefficients for inter-rater reliability were 0.95 ($P < 0.001$), 0.91 ($P < 0.001$) and 0.65 ($P = 0.003$) for the whole group, AD and normal subjects, respectively. The ADAS-cog score was inversely related to the Mini-Mental Status Examination (MMSE) score (Spearman's rho = -0.91 ; $P < 0.001$). The ADAS-cog score was directly proportional to the Clinical Dementia Rating (CDR) (rho = 0.89; $P < 0.001$). Forward stepwise discriminant function analysis between AD and normal subjects yielded a canonical discriminant function with 3-question items (i.e. word recall test, orientation and comprehension of speech; $P < 0.001$). This short version had a sensitivity of 90%, specificity of 94.7% and overall accuracy of 92.3%. **Conclusion:** The Chinese version of ADAS-cog subscale is both reliable and valid among the elderly Chinese in Hong Kong.

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Key words: Alzheimer's disease, Assessment, Cognitive impairment, Elderly

Introduction

The Alzheimer's Disease Assessment Scale (ADAS) is a 21-item scale designed to assess the severity of cognitive and non-cognitive impairment in patients with Alzheimer's disease (AD).¹⁻⁴

The cognitive subscale (ADAS-cog) consists of 11 items to assess memory, orientation, language and praxis function. The ADAS-cog score is the sum of the 11-question items with a maximum score of 70. The score is proportional to the severity of cognitive impairment in AD. The ADAS or its subscales is not designed for use as a diagnostic tool.

However, scores on the scale discriminates patients with clinically diagnosed AD from non-demented subjects.⁵ Its sensitivity to detect change has been documented by longitudinal follow-up data. On average, AD patients show an increase in ADAS-cog scores of approximately 7 to 8 points per 12-month interval.⁶ It is much more sensitive to change than other dementia rating scales like the Folstein Mini-Mental Status Examination (MMSE). The latter is known for the drawback of floor and ceiling effects. Because of its sensitivity to change, the ADAS-cog is commonly employed as a primary outcome measure to

* Consultant

** Medical Officer

*** Registered Nurse

Division of Geriatrics, University Department of Medicine, Queen Mary Hospital

**** Chief of Service (Psychiatry)

† Clinical Psychologist

‡ Professor, Clinical Psychology Unit

Department of Psychiatry

The University of Hong Kong, Queen Mary Hospital

Address for Reprints: Dr Leung-Wing Chu, Division of Geriatrics, University Department of Medicine, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong SAR.

E-mail: lwchu@hkucc.hku.hk

assess the effects of cognitive enhancing drugs in clinical trials of new drug treatment (e.g., tacrine, aricept, rivastigmine) for AD.⁷⁻¹⁶ Its reliability and validity have been established in the original English version. The test-retest and inter-rater reliability of the original English ADAS scale, ADAS-cog and non-cognitive subscales are good. The inter-rater reliability of the ADAS-cog is 0.989. Its test-retest reliability is 0.915, which is much better than that of the non-cognitive subscale of 0.588.^{1,2} Subsequently, Spanish, Greek and Japanese adaptations of the original ADAS have also been validated.¹⁷⁻¹⁹

The objectives of the present study were to investigate the reliability and validity of an adapted Chinese version of the ADAS-cog among elderly Chinese AD patients in Hong Kong.

Materials and Methods

The original English version of ADAS-cog was translated directly into Chinese. The face validity of the translated version was assessed by a multidisciplinary group which consisted of a geriatrician, psychogeriatrician and 2 clinical psychologists. All members were experienced in the area of AD and related dementia. They were the core-members of our Queen Mary Hospital's Memory Clinic.

The ADAS-cog subscale was administered to a group of AD patients and a group of normal non-demented subjects. AD patients were recruited from our Memory Clinic. Normal subjects were recruited from the following sources: members of community elderly social centres, healthy non-demented patients from our Queen Mary Hospital's Geriatric Assessment Clinic and healthy elderly parents of our hospital staff. Baseline demographic data (i.e., sex, age, education) were obtained in all subjects. A full history on general health and cognitive functioning was taken from an informant who was living with the subject (usually a family member). A full physical examination including a detailed neurological examination was performed on every subject. All AD patients received the following investigations: full blood counts, renal and liver function tests, serum B₁₂ assay, syphilis serology and a computed tomographic (CT) brain scan. These investigations were performed to exclude secondary causes of dementia as well as vascular dementia. Subjects with vascular dementia were excluded. The diagnosis of probable AD in the AD patients group was established according to National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria.²⁰ All subjects were rated an overall Clinical Dementia Rating (CDR) as described by Hughes et al.²¹

Thirty-nine subjects were recruited during the period July to December 1998. Twenty were AD patients while 19

were non-demented normal subjects. Each subject underwent the ADAS-cog test thrice on 3 different occasions within a 2-week period. Two raters (KC and SL) administered the scale to them. One rater (KC) administered the scale twice on 2 different occasions within 2 weeks to evaluate the test-retest reliability while the second rater (SL) administered the scale only once on another occasion. The locally validated Cantonese MMSE²² was administered to all subjects.

Statistical Analysis

The internal consistency of the ADAS-cog subscale was assessed by the Cronbach's alpha. Test-retest and inter-rater reliability were analysed using the Spearman's rho non-parametric correlation coefficient. Concurrent validity of ADAS-cog with MMSE was analysed using the Spearman's rho correlation coefficient. The effect of sex on the ADAS-cog was analysed using the chi-square tests. The effects of age and education on ADAS-cog were analysed using the Spearman's rho correlation coefficient. Finally, discriminant function analysis was performed.

Results

Sample Characteristics

Thirty-nine subjects were included in the study. Twenty subjects fulfilled probable AD (National Institute of Neurological and Communicative Disorders and Alzheimer's Disease and Related Disorders Association) criteria. Nineteen subjects were non-demented normal controls. The AD patients had a higher proportion of female subjects, were older in age and less well educated than the normal subjects (Table I). By CDR staging, 25%, 45%, 25% and 5% of AD patients belonged to CDR 0.5, 1, 2 and 3, respectively. Overall, 70% of our AD patients were

TABLE I: CHARACTERISTICS OF SUBJECTS

	AD (n = 20)	Normal (n = 19)	P value
Age (mean $\pm$ SD y)	74.55 $\pm$ 6.61	67.26 $\pm$ 6.44	0.001*
Sex (% female)	75	36.8	0.016**
Education [median (range) y]	2.0 (0 to 11.0)	9.0 (1.0 to 12.0)	0.001†
MMSE [median (range)]	15.5 (7 to 25)	29.0 (24 to 30)	0.001†
CDR [median (range)]	1.0 (0.5 to 3.0)	0.0 $\pm$ 0.0 (0 to 0)	0.001†
ADAS-cog [median (range)]	24.00 (12.33 to 59)	3.66 (1.0 to 10.0)	<0.001†

* unpaired *t*-test

** χ^2 statistics

† Mann-Whitney U test

AD: Alzheimer's disease; ADAS-cog: Alzheimer's Disease Assessment Scale Cognitive Subscale; MMSE: Mini-Mental State Examination; CDR: Clinical Dementia Rating

mildly demented (i.e. CDR 0.5 and 1). Only 5% of them were severely demented (i.e. CDR 3).

Internal Consistency of the Scale

Cronbach's alpha of the ADAS-cog were 0.91, 0.88 and 0.65 for the whole group, the AD and normal (i.e. non-demented) subjects, respectively.

Test-retest Reliability

The test-retest reliability was measured using the Spearman's rho correlation coefficients, which were 0.96, 0.86 and 0.86 for the whole group, AD and normal subjects, respectively. All *P* values were <0.001.

Inter-rater Reliability

The Spearman's rho correlation coefficients for inter-rater reliability were 0.95, 0.91 and 0.65 for the whole group, AD and normal subjects, respectively. The *P* values were <0.001, <0.001 and 0.003, respectively.

Concurrent Validity with MMSE and CDR

The ADAS-cog score was inversely related to the MMSE score. The Spearman's rho was -0.91 (*P* <0.001). The ADAS-cog score was directly proportional to the CDR. The Spearman's rho was 0.89 (*P* <0.001).

Effect of Age, Sex and Education on the ADAS-cog

The ADAS-cog score was directly related to age (Spearman's rho = 0.42; *P* = 0.008) and inversely related to educational level (Spearman's rho = -0.53; *P* = 0.01). Female subjects had a higher ADAS-cog score than male subjects [median (range): 18.83 (2.33 to 59.0) versus 5.66 (1.0 to 42); *P* = 0.009, Mann-Whitney U test].

Effect of AD on the ADAS-cog score

AD subjects had a higher ADAS-cog score compared with normal non-demented subjects [median (range): 24.0

(12.33 to 59.0) versus 3.66 (1.0 to 10.0); *P* <0.001, Mann-Whitney U test].

Individual Question Items in the ADAS-cog

The individual item scores in AD and non-demented subjects for question items 1, 2, 3, 4, 5, 6, 7 and 8 were statistically different for the 2 groups. For question items 9, 10 and 11, the item scores in AD subjects showed a higher but statistically insignificant trend than the non-demented subjects (Table II).

Discriminant Function Analysis

Forward stepwise discriminant function analysis between AD and normal subjects yielded a canonical discriminant function with 3 of the 11-question items, namely question items 1 (word recall test), 6 (orientation) and 11 (comprehension of speech). The *P* value was <0.001 (Wilks' lambda 0.197; chi-square 57.7, df = 3). This function correctly classified 90% AD (sensitivity = 90%) and 94.7% normal non-demented subjects (specificity = 94.7%). The overall classification accuracy was 92.3%. The equation representing the overall classification function was as follows:

$$AD - N = -3.72 + 0.591 \times Q \text{ item 1} + 0.502 \times Q \text{ item 6} - 0.739 \times Q \text{ item 11}$$

If the result of *AD - N* was greater than 0, the subject had AD. If the result was less than 0, the subject was non-demented.

Discussion

The ADAS scale was originally designed to be a tailored-made scale for patients with AD. Following the report of the English version, the ADAS has been adapted for Greek, Spanish and Japanese languages.¹⁷⁻¹⁹ The reliability and validity of the original English, Greek and Spanish versions

TABLE II: INDIVIDUAL ADAS-cog QUESTIONS

		AD (n = 20)	Normal (n = 19)	<i>P</i> value*
Q item 1 (Word recall test)	median (range)	6.66 (5.0 to 10.0)	3.0 (1.0 to 6.33)	<0.001
Q item 2 (Name objects and fingers)	median (range)	1.0 (0.0 to 4.0)	0.0 (0.0 to 1.0)	0.002
Q item 3 (Commands)	median (range)	1.0 (0.0 to 4.0)	0.0 ± 0.0 (0.0 to 0.0)	0.003
Q item 4 (Constructional praxis)	median (range)	2.0 (0.0 to 3.0)	0.0 (0.0 to 1.0)	<0.001
Q item 5 (Ideational praxis)	median (range)	2.0 (0.0 to 3.0)	0.0 (0.0 to 1.0)	<0.001
Q item 6 (Orientation)	median (range)	4.5 (1.0 to 7.0)	0.0 (0.0 to 1.0)	<0.001
Q item 7 (Word recognition)	median (range)	7.66 (0.0 to 12.0)	0.66 (0 to 2.33)	<0.001
Q item 8 (Remember test instructions)	median (range)	1.5 (0.0 to 5.0)	0.0 (0.0 to 0.0)	<0.001
Q item 9 (Spoken language ability)	median (range)	0.0 (0.0 to 5.0)	0.0 (0.0 to 0.0)	0.184
Q item 10 (Word finding difficulty)	median (range)	0.0 (0.0 to 4.0)	0.0 (0.0 to 0.0)	0.061
Q item 11 (Comprehension of speech)	median (range)	0.0 (0.0 to 4.0)	0.0 (0.0 to 0.0)	0.113

* Mann-Whitney U test

AD: Alzheimer's disease; Q: Question

TABLE III: COMPARISONS OF THE RELIABILITY OF CHINESE, ENGLISH, GREEK AND SPANISH ADAS-cog IN AD PATIENTS

	Chinese ADAS-cog*	English ADAS-cog ²	Greek ADAS-cog ¹⁹	Spanish ADAS-cog ¹⁸
Internal Consistency (Cronbach's alpha)	0.88	Not reported	0.93	Not reported
Test-retest reliability	0.86	0.915	Not reported	0.901
Inter-rater reliability	0.91	0.989	Not reported	0.975

* Present study

AD: Alzheimer's disease; ADAS-cog: Alzheimer's Disease Assessment Scale Cognitive Subscale

have previously been reported.^{1-6,18,19} The cognitive subscale of ADAS was useful to measure the change or improvement after specific AD drug treatment. The ADAS-cog was one of the key outcome measures employed in major clinical drug trials in AD. In Hong Kong, several new drugs (i.e. tacrine, donepezil and rivastigmine) for AD are available recently. A sensitive cognitive assessment measure is greatly needed locally to help the clinicians monitor the improvement in cognitive function. Prior to the present study, the MMSE and Abbreviated Mental Test (AMT) were the only two locally validated cognitive assessment scales in Hong Kong.^{22,23} However, these 2 scales are not sensitive to change and have the shortfall of "ceiling" and "floor" effects.

In the present study, we found that the Chinese ADAS-cog had good internal consistency, test-retest and inter-rater reliability in our Chinese elderly population. The reliability of the Chinese ADAS-cog in AD patients was similar to the original English scale (Table III).¹⁻³ Thus, it was suitable for clinical and research use in Hong Kong. In univariate analysis, female gender, older age and lower educational level were associated with high ADAS-cog scores. Our finding on the effect of education was also reported previously.²⁴

The ADAS-cog score was inversely related to the MMSE and directly proportional to the CDR. Thus, the ADAS-cog score increases with the severity of AD. Similar findings were reported from other studies.^{25,26}

Although the ADAS-cog was not designed as a diagnostic instrument, it was also valid in discriminating AD and normal elderly subjects. Amongst the 11 individual question items, 3 of them (i.e. word recall test, orientation and comprehension of speech) were found to be important by canonical discriminant analysis. The model has a discriminant sensitivity of 90%, specificity of 94.7% and an overall accuracy of 92% for AD and normal subjects. These 3 questions might serve as a short version of the ADAS-cog subscale. However, further study into this aspect is needed in the future.

Our sample size of 39 subjects is small. This is the main limitation of the present study. In future, a bigger sample than the present one is suggested to confirm our results. Despite this limitation, our study has been able to

demonstrate that the Chinese ADAS-cog has a high internal consistency, reliability and validity in Chinese elderly AD patients. This is not due to any bias towards having severely demented AD patients. In fact, 70% of our AD subjects in this study had mild dementia (i.e. CDR of 0.5 or 1).

In conclusion, the Hong Kong Chinese version of ADAS-cog subscale is both reliable and valid. It can serve as a sensitive cognitive assessment measure for use in our Chinese AD population. This is particularly important during treatment with the new cognitive "enhancers" or AD medications.

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