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·Original Article·

Application study of quick cognitive screening test in identifying mild cognitive impairment

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Abstract: Objective To assess whether quick cognitive screening test (QCST) could quickly identify mild cognitive impairment (MCI). **Methods** QCST and a full set of standardized neuropsychological tests, including mini-mental state examination (MMSE) and montreal cognitive assessment (MoCA) were performed. A total number of 121 cases of MCI [41 cases of amnestic MCI-single domain (aMCI-s); 44 of amnestic MCI-multiple domain (aMCI-m); 36 of nonamnestic MCI (naMCI)], 79 cases of mild Alzheimer's disease (AD) and 186 healthy elderly volunteers were employed in the present study. All the participants (55-85 years old) had an educational level no less than 5 years. QCST subtests included word list recall, naming test, animal fluency test, similarity test, color trail-1min, clock drawing test, finger construction test, and digit span test. The total score of QCST was 90 points, 10 points for each index of subtests. **Results** The total scores of QCST in MCI, AD and the control groups were (58.13±8.18), (44.53±10.54) and (72.92±6.85) points, respectively. According to the educational level, the cut off scores of participants with an educational level of 5-8 years, 9-12 years and more than 13 years were 63, 65 and 68 points, respectively. The sensitivity and specificity of QCST in detection of MCI were 87.6% (85.7% for aMCI-s, 90.1% for aMCI-m and 89.5% for naMCI) and 84.3%, respectively. The area under the curve was 0.923 (95% CI: 0.892-0.953). Delayed memory, color trail-1min and similarity test could help distinguish between aMCI and naMCI. **Conclusion** QCST may have a good sensitivity and specificity for MCI detection, which warrants its further clinical application.

Keywords: mild cognitive impairment; Alzheimer's disease; neuropsychological test; cognition

1 Introduction

Mild cognitive impairment (MCI) is an intermediate clinical state between normal cognitive aging and dementia, and is of significant value for early diagnosis and intervention of dementia. Rapid screening of MCI is usually based on the neuropsychological characteristics, diagnosis criterion and classification. The first diagnostic criterion was proposed by Petersen *et al*. in 1999[1]. The general MCI diagnostic criteria were later proposed by MCI international working group[2] and European Alzheimer's Disease Collaboration (EADC)[3] in 2004 and 2006, respectively. MCI could be classified into several subtypes on the basis of cognition performance: amnestic MCI-single domain (aMCI-s), characterized by isolated memory dysfunction; amnestic MCI-multiple domain (aMCI-m), manifested as impairment in multiple cognition domains besides the memory, such as language and execution impairment; nonamnestic MCI-single domain (naMCI-s), manifested as single non-memory MCI impairment, including simple language or other cognitive impairment; and nonamnestic MCI-multiple domain (naMCI-m), manifested

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as multiple non-memory cognitive impairment with completely reserved memory function. aMCI-s and aMCI-m are referred to as amnestic MCI (aMCI) while naMCI-s and naMCI-m as nonamnestic MCI (naMCI). Jungwirth *et al.* conducted a community investigation in the elderly aging 75-76 years and have identified 141 patients with MCI (23.8% of the total), including 53 with aMCI (8.9%) and 88 with naMCI (14.9%)[4,5]. Another community investigation by Busse *et al.* shows that the occurrence frequency of aMCI is the same as that of naMCI[6]. In terms of neuropsychological profile, these subtypes are hypothesized to be associated with distinct outcome. While aMCI-s may be a pre-dementia stage of Alzheimer's disease (AD), multiple-domain MCI may be a precursor of both AD and vascular dementia, and naMCI-s domain non-amnestic MCI may be found in the prodromal phases of frontotemporal dementia, vascular dementia, dementia with Lewy bodies, or even depressive disorders[7]. These studies demonstrate that naMCI detection is as important as aMCI detection in the elderly.

There are a variety of short or long screening methods for MCI and mild dementia currently, such as AB cognitive screen (ABCS)[8], memory alteration test[9], the short cognitive performance test[10], montreal cognitive assessment (MoCA)[11], the short test of mental status (STMS)[12], Cambridge cognitive test (CAMCOG)[13,14], Dem test[15], and 7-min dementia screening test[16]. These tests show high sensitivities and specificities to identify aMCI or AD, but the identification of naMCI and discrimination diagnosis of dementia remain controversial. To our knowledge, it has never been investigated or reported whether the non-memory cognitive tests, which are usually brief and simple, could be utilized for early diagnosis of naMCI suffering from simple executive function impairment or simple language impairment. naMCI screening tests with low sensitivities might lead to the under-estimation of MCI incidence or incomparability between screening results of different regions in epidemiological investigations.

The design of quick cognitive screening test (QCST) was aimed at rapidly identifying both aMCI and naMCI, and providing preliminary evidence for further studies.

2 Participants and methods

2.1 Participants Patients in the MCI group and the AD group were chosen from successive patients of the "Memory Clinic", Department of Neurology, Huashan Hospital from Aug 2008 to May 2009. Healthy elderly in the normal control group were chosen from two communities in Shanghai (Huashan Hospital and Ganquan Hospital) by cluster sampling. Informed consents were obtained from all the participants.

All the participants in the MCI group, the AD group and the normal control group were strictly selected according to the following criteria: (1) They show normal results of cranial CT or MRI detection, or only cerebral atrophy of various degrees, without definite structural lesions in the brain; (2) They have neither obvious medical, neurological or psychiatric disease, nor psychological dysfunction including anxiety and depression within the previous 1 month; (3) They have normal audition and visual acuity; (4) They are corporative in cognitive testing; (5) They are aged 55-85 years with an educational level no less than 5 years.

There were totally 186 participants in the control group, including 87 male and 99 female, aged (67.58±6.87) years, with an average educational level of (12.18±3.24) years and a mini-mental state evaluation (MMSE) score of (28.39±1.49). The control group was further divided into 3 groups by the educational level. Group A included 63 participants with an educational level between 5 and 8 years (including 5 and 8). They have completed curricula of primary school and completed at least partially scholastic curricula of middle school. Group B included 65 participants with an educational level between 9 and 12 years (including 9 and 12). They have completely or partially finished senior high school scholastic curricula. Group C included 68 participants with an educational level no less than 13 years. They have finished scholastic curricula of junior college or higher.

MCI was diagnosed according to the previously established criteria[1-3,17,18], including (1) subjective complaints of gradual cognitive loss for over 6 months reported by the patient and/or confirmed by an family member; (2) cognitive impairment objectively measured by neuropsychological tests

(the score should be lower by 1.5SD compared with health population with matched age and educational level); (3) with general cognitive function preservation measured by the Chinese version MMSE[19]; (4) preserving basic activities of daily living/minimal impairment in complex instrumental functions; (5) does not meet the clinical criteria of dementia in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).

In the MCI group, 121 patients (58 male and 63 female, 41 with aMCI-s, 44 with aMCI-m and 36 with na-MCI) received the neuropsychological tests. These patients were aged (68.35±7.20) years, with an education level of (11.75±3.54) years. The total MMSE score was (27.09±1.80).

The mild AD group included 83 participants (40 male and 43 female) with a diagnosis of probably AD, meeting the criteria in the DSM-IV[20] and in National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association[21]. These participants were all mildly demented, with a total MMSE score of (21.35±2.53) (ranging 17-27). The participants were aged (68.68±8.73) years, with an education level of (12.35±3.51) years.

There were no statistical differences among the 3 groups in age, gender distribution or educational level ($P > 0.05$), however, MMSE scores were significantly different among the 3 groups ($F = 184.42$, $P = 0.000$).

2.2 Principles for item selection in QCST Principles for item selection in QCST were listed as follows. (1) The items should reflect the corresponding cognitive function domains; (2) The range of cognitive abilities covered should be as broad as possible; (3) The time consumption should be as little as possible (time consumed for each question should be less than 1 min and the total time should be within 8-12 min); (4) The subtests should have a good applicability with a high completion rate; (5) The tests and scoring method that had already been confirmed to have high MCI-identifying effect should be adopted in priority.

2.3 Subtests of QCST A total number of 9 items of subtests were included in QCST. The total score of QCST equaled 90 points.

2.3.1 Word lists The examiner read 5 two-character words with unrelated meaning. Right after the auditory presentation of the whole list, the participants recalled these words. The test was conducted twice, and the score of immediate memory was the sum of the 2 immediate memory correct scores. Then the participant took an 8-min non-verbal test. He or she then freely recalled the 5 words again and cued recall after given a category cue. The score of delayed memory was the sum of the 2 delayed memory scores.

2.3.2 Naming test Oral naming 10 lines of drawing (chosen from Boston naming test[22]), 1 point for each drawing.

2.3.3 Animal Fluency test[23] For this test, each participant was allowed 1 min to generate the names of animals. Each correct name was indicated for 0.5 points, and when more than 20 animals were listed, the total score was 10 points.

2.3.4 Similarity test Items of similarity test came from Cognitive Abilities Screening Instrument (CASI)[24]. The task is to point out the similarities between 2 words, including train-bicycle, watch-ruler, hand-foot, cry-smile, and eat-sleep. Each pair had 2 points. Two points were indicated when the answer was correct, while 1 point was indicated for a partially correct answer. When the answer was wrong, 0 point was indicated.

2.3.5 Color Trail test-1 min (CTT1m)[25] This test was designed to mark trail that alternates between numbers chosen from complete CTT-partB materials (numbers from 1 to 24) following red-yellow sequence. Scoring method: numbers trailed by first 1min minus 5; 10 points when more than 15 numbers; 0 points when less than 5 numbers. In our previous study, discriminability of item of CTT1m was slightly better than index of time consumed in completing total length, and significantly better than abbreviate CTT-partB (numbers from 1 to 8).

2.3.6 Clock Drawing test (CDT)[26] Participants were required to draw a clock that reads at 1:50. Scoring was as follows: 1 point for the cycle, 3 points for anchoring the scales (first determining the 4 key scale: 12-3-6-9), 3 points for the correct number, and 3 points for pointer.

2.3.7 Finger Construction test In this test, participants should finish 5 meaningless actions by left and right hands, respectively. These actions included making a circularity by thumb and forefinger, just straightening forefinger and little

finger, putting fist at forehead and putting open hands at mouth, drawing a cross (most Chinese elderly are not accustomed to draw a cross and they do not know the exact sense), and a sequential of making fist–edge of palm down –prostrate palm actions. Each correct action was scored as 1 point.

2.3.8 Digit Span Items of the Digit Span subtest came from the Chinese revision of the Wechsler Adult Intelligence Scale (WAIS-RC)[27]. The task is to recite 6 digits (from 3 numbers to 8 numbers) and recite 4 digits in a reverse order (from 2 numbers to 5 numbers). The score was the sum of the 2 tasks.

2.4 Neuropsychological evaluations Besides QCST, all participants were asked to complete a set of standardized comprehensive neuropsychological evaluations, including MMSE, Mattis dementia rating scale–Chinese version[28], MoCA[29], Auditory verbal learning test[18], Logical memory test[30], Rey-Osterrich complex figure test[31], Stroop color word test–Chinese version[32], Trail-making test (TMT-B, the Arabic digits are surrounded by either squares or circles and the participant is asked to connect the digit in sequence while alternating between the two surrounding shapes), Similarity test (13 questions chosen from WAIS-RC[27]), Category fluency test (including Supermarket, fruit and vegetables), Boston naming test (30 items), Center for epidemiological studies depression scale (CESD), Alzheimer's disease Cooperative Study scale for ADL in MCI (ADCS-MCI-ADL) for the assessment of impairments of complex ADL[33] and clinical dementia rating scale (CDR)[34]. These cognitive tests have been applied by the Neuropsychological Research Group of Huashan Hospital since 2002 and validated in reliability and validity tests. The neuropsychological test battery and QCST did not overlap each other. The assessment was conducted by 2 full-time examiners (ZY and CXY) after strict training.

2.5 Statistical analysis Chi-square test was used for the analysis of ordinal data, bivariate correlation, and One-way ANOVA was used for three-group comparisons. LSD analysis was used for pair-wise post-hoc comparisons.

3 Results

3.1 Psychometric properties of QCST Test-retest reliability data were collected from a subsample of 30 tested participants (patients and controls), with an interval of (32.1±6.9) d in average. The mean change in QCST scores from the first to the second evaluation was (2.05±5.21) points, and the correlation between the scores of the two evaluations was high ($r = 0.93$, $P < 0.001$).

For the control group, QCST score was not correlated with age ($r=-0.08$, $P > 0.05$) but correlated with educational level ($r=0.23$, $P < 0.001$). Among the 9 subtests, only Color Trail test was in correlation with age ($r=-0.18$, $P < 0.05$) and the Similarity test had a most significant correlation with educational level ($r=0.45$, $P < 0.001$). In participant groups, QCST score was significantly correlated with MMSE score ($r=0.68$, $P < 0.001$), CDR score ($r=-0.39$, $P < 0.001$), DRS score ($r=0.72$, $P < 0.001$) and MoCA score ($r=0.89$, $P < 0.001$). Scores of the 9 subtests were all significantly correlated with the total QCST score ($r=0.40$~0.69, $P < 0.001$).

3.2 Comparisons of QCST scores among the MCI group, the AD group and the normal control group As shown in Table 1, in the control group, subtest with the lowest score was Similarity test, while scores of Naming test, immediate memory, Finger Construction and Animal Fluency were the highest.

There were statistically significant differences when scores of all the subtests were compared between the control group and the MCI group. Besides, there were significant differences in any of these items and in the total score among the 3 groups (Table 1).

Upper limit of the QCST score was 90 points and lower limit was 0 point. In the present study, the highest total score of QCST in control group was 87 points and the lowest was 48 points. In the MCI group, the highest score was 75 points and the lowest score was 40 points. In the mild AD group, the highest score was 63 points and the lowest score was 20 points. All these scores were between the upper and lower limits of QCST, without any ceiling or floor effects.

3.3 Cut off score of total QCST score Cut off score, sensitivity and specificity of the total QCST score were listed in Table 2. Sensitivity of the QCST score to identify MCI was 87.6% (85.7% for aMCI-s; 90.1% for aMCI-m; 89.5% for naMCI) and the specificity was 84.3%, with an area under curve of 0.923 (95% CI: 0.892-0.953), while the area of MoCA was 0.856 (95% CI: 0.814-0.898), and the area of MMSE was

Table 1. QCST scores in control, MCI and AD groups (Mean±SD)

Index	Control group (n=186)	MCI group (n=121)	Mild AD group (n=79)	F(P)
Immediate Memory	8.76±1.14	7.67±1.39$^{\#\#}$	5.89±1.60$^{\wedge\wedge}$	129.03$^{\$\$}$
Delayed Memory	7.30±1.98**	3.78±2.79$^{\#\#}$	1.57±2.09$^{\wedge\wedge}$	198.08$^{\$\$}$
Naming	8.93±.99**	7.89±1.51	7.31±1.86$^{\wedge\wedge}$	44.83$^{\$\$}$
Animal Fluency	8.66±1.48**	7.18±1.81$^{\#\#}$	5.48±2.14$^{\wedge\wedge}$	95.83$^{\$\$}$
Similarity test	6.72±2.01*	6.02±2.42$^{\#\#}$	4.71±2.52$^{\wedge\wedge}$	21.98$^{\$\$}$
Color Trail-1min	7.96±2.36**	5.22±3.18$^{\#\#}$	3.51±3.25$^{\wedge\wedge}$	78.43$^{\$\$}$
Clock Drawing	7.88±1.63**	6.39±2.27$^{\#\#}$	4.33±2.57$^{\wedge\wedge}$	83.02$^{\$\$}$
Finger Constructions	8.66±1.46**	7.07±1.77$^{\#\#}$	5.74±2.10$^{\wedge\wedge}$	87.22$^{\$\$}$
Digit Span	8.03±1.39**	6.88±1.78$^{\#\#}$	5.97±1.43$^{\wedge\wedge}$	54.63$^{\$\$}$
Total score	72.92±6.85**	58.13±8.18$^{\#\#}$	44.53±10.54$^{\wedge\wedge}$	360.08$^{\$\$}$

There were significant differences in any of the items and in the total score among the 3 groups ($^{\$\$}P < 0.01$). $^{**}P < 0.01$ *vs* MCI group, $^{\#\#}P < 0.01$ *vs* AD group, $^{\wedge\wedge}P < 0.01$ *vs* control group.

Table 2. Cut off score, sensitivity and specificity of total QCST score

	Education level	Cut off score (points)	Sensitivity (%)	Specificity (%)
QCST	Group A: 5-8 years	≤63	89.4	91.0
	Group B: 9-12 years	≤65	89.3	94.3
	Group C: ≥13 years	≤68	86.7	78.2
	Total		87.6	84.3
MoCA		23	79.6	72.7
MMSE		26	83.3	38.3

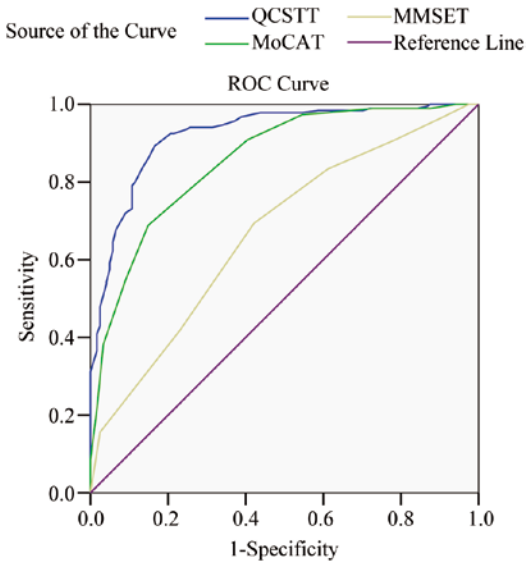

Fig. 1 An area under curve of QCST, MoCA and MMSE.

0.670 (95% CI: 0.608-0.731)(Table 2, Fig. 1).

Besides, between the MCI and the mild AD groups, the sensitivity was 75.0% and the specificity was 78.2% to detect MCI when choosing 53 points as a cut off score. QCST scores of MCI patients were between 53 and 68 points.

3.4 Comparison of QCST scores between different subtypes of MCI As shown in Table 3, patients with aMCI-s exhibited milder deficit than those with aMCI-m. Scores in 4 subtests including Naming, Similarity, Digit Span and Color Trail-1min in the aMCI-s subtype were all significantly higher than those in the aMCI-m subtype.

Besides, delayed memory scores of aMCI patients were significantly lower than that of naMCI patients ($P < 0.01$). Also, there were significant differences in scores of Naming, Similarity and Color Trail-1min between aMCI-s and naMCI

Table 3. Comparison of QCST scores between different subtypes of MCI (Mean±SD)

Index	aMCI-s (*n*=41)	aMCI-m (*n*=44)	naMCI (*n*=36)	F(P)
Immediate Memory	7.87±1.12	7.36±1.49	7.83±1.52	1.77
Delayed Memory	2.48±2.37	2.97±2.56$^{\#\#}$	6.25±1.81$^{\wedge\wedge}$	29.92$^{\$\$}$
Naming	8.49±1.16**	7.64±1.52	7.53±1.68$^{\wedge\wedge}$	5.17$^{\$\$}$
Animal Fluency	7.43±1.94	6.89±1.84	7.23±1.61	0.96
Similarities	7.29±1.70**	5.57±2.31	5.14±2.70$^{\wedge\wedge}$	10.10$^{\$\$}$
Color Trail-1min	7.29±2.46*	4.43±3.05	3.83±2.95$^{\wedge\wedge}$	16.96$^{\$\$}$
Clock Drawing	6.66±1.99	6.20±2.56	6.31±2.21	0.45
Finger Constructions	7.17±1.71	6.68±1.92	7.44±1.57	1.95
Digit Span	7.60±1.74*	6.72±1.78	6.25±1.55$^{\wedge\wedge}$	6.38$^{\$\$}$
Total Score	62.31±6.91	54.48±8.12	57.81±7.50	11.45$^{\$\$}$

$^{*}P < 0.05$, $^{**}P < 0.01$ *vs* aMCI-m, $^{\#\#}P < 0.01$ *vs* naMCI group, $^{\wedge\wedge}P < 0.01$ *vs* aMCI-s group. $^{\$\$}P < 0.01$ among the 3 groups.

patients and in delayed memory score between aMCI-m and naMCI patients. These results showed that aMCI was mainly manifested as impairment of delayed memory and naMCI as impairment of execution function.

4 Discussion

The QCST has shown a high test-retest reliability and a content validity. Subtest material selection and scoring method in QCST's design can likely explain its superior sensitivity for detecting MCI. More importantly, QCST has an excellent sensitivity in detecting naMCI. Therefore, QCST as a screening tool should provide quick guidance for referral and further investigation of MCI.

Subtests that are influenced by language background such as FAS fluency, number-letter sequence test and trail-making test (alternative numbers and alphabets) have been excluded here. Chinese culture-specific tests were avoided in QCST and culturally universal items were chosen as frequently as possible so that the test could be applied in populations with different cultural backgrounds, and comparable results in populations with different languages and regions can be obtained. Among the test materials, part of them (i.e. Color Trail test and Clock Drawing test) are derived from the typical tests, and changes of analysis skill are made to get a higher sensitivity and specificity. Other part of them (i.e. Similarity test and Digit Span) share the same rationale and method with the typical tests.

Although the duration of QCST is short, only 8-15 min, the difficulty degree varys greatly and reflects functions of various cognitive domains, which could be utilized to draw profiles for manifestation of each cognitive domain. At least 2 out of 7 cognitive domains, including orientation, memory, language, praxis, attention, visual perception and ability to resolve problems, should be impaired to meet NINCDS-ADRDA criteria for diagnosing dementia[21]. DSM-IV dementia diagnostic criteria require that the patients had dysfunctions in at least 2 cognitive domains out of 5 domains, including amnesia, aphasia, apraxia, agnosia and executive dysfunction[20]. Here the 9 items included in QCST reflect memory, language, attention, visual-spatial, praxis and executive function, all of which are the target domains required in diagnosis of dementia and also the basis of MCI subtype analysis. The number of domains with cognitive impairment can not only help the diagnosis of AD, but also help to predict the transformation from MCI to AD[35]. However, up to now, it is still hard to select a best test to examine one specific non-memory function (i.e. executive function), although episodic memory is internationally recognized as a representative index for the examination of memory function. Therefore, the method we selected to test non-memory function probably has its limitations.

Other limitations of QCST are similar to those of many

tests. For example, illiterate elderly or those with low educational level could not use a pen and paper, and patients with hemiplegia can not finish the whole subtests. Therefore, educational level is an important factor that can influence the testing results, thus should be considered into result analysis and interpretation.

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快速认知筛查测验在检测轻度认知损害中的应用研究

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摘要：目的 轻度认知损害(mild cognitive impairment, MCI)可根据认知表现分为遗忘型 MCI (aMCI)和非遗忘型MCI (naMCI)。本研究旨在编制快速认知筛查测验(quick cognitive screening test, QCST)便于快速全面地识别 MCI，为进一步研究提供依据。**方法** 符合 MCI 操作性诊断标准的 MCI 组 121 例、符合 DSM-Ⅳ有关痴呆诊断标准的阿尔茨海默病(AD)组 79 例和正常老年人组 186 例，参与了 QCST 和标准化全套神经心理测验。参与者教育程度均在 5 年或以上，年龄 55-85 岁。QCST 项目包括即刻记忆、延迟回忆、命名、动物流畅性、相似性、彩色连线 B、画钟、手指结构、数字广度等 9 个分测验，每个分测验满分 10 分，总分 90 分，耗时 10-15 分钟。**结果** MCI 组、AD组和正常老年人组QCST总分分别为(58.13±8.18)、(44.53±10.54)和(72.92±6.85)分。制定教育程度在5-8年、9-12年、高于 13 年 3 个组别的 QCST 总分的划界分分别为 63、65 和 68 分。QCST 识别 MCI 的敏感性为 87.6%，其中识别 aMCI-s、aMCI-m 和 naMCI 的敏感性分别为 85.7%、90.1% 和 89.5%，特异性均为 84.3%。曲线下面积为 0.923 (95% CI：0.892-0.953)。延迟回忆、连线和相似性均有助于区分 aMCI 与 naMCI。**结论** QCST 对 MCI 具有较高的敏感性和特异性，可在临床和流行病学调查方面进行推广应用。

关键词： 轻度认知损害；阿尔茨海默病；神经心理测验；认知