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Cognitive test battery for evaluating elderly Chinese Americans

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Abstract

Objectives: This study aimed to determine the diagnostic utility of a Chinese test battery for evaluating cognitive loss in elderly Chinese Americans.

Methods: Data from a pilot study at the Mount Sinai Alzheimer's Disease Research Center was examined. All participants were > 65 years old, primarily Chinese speaking, with adequate sensorimotor capacity to complete cognitive tests. A research diagnosis of normal mild cognitive impairment (MCI) or Alzheimer's disease (AD) was assigned to each participant in consensus conference. Composite scores were created to summarize test performance on overall cognition, memory, attention executive function, and language. Multivariable logistic regression models were used to assess the sensitivity of each cognitive domain for discriminating three diagnostic categories. Adjustment was made for demographic variables (i.e., age, gender, education, primary language, and years living in the USA).

Results: The sample included 67 normal, 37 MCI, and 12 AD participants. Performance in overall cognition, memory, and attention executive function was significantly worse in AD than in MCI, and performance in MCI was worse than in normal controls. Language performance followed a similar pattern, but differences did not achieve statistical significance among the three diagnostic groups.

Conclusions: This study highlights the need for cognitive assessment in elderly Chinese immigrants.

Keywords

cognitive function; elderly; Chinese immigrants; cognitive testing; cognitive battery; Chinese elders

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Description of authors' roles

C. Li designed the study, formulated the research questions, supervised the data collection, collected the data, and wrote the paper. J. Neugroschl designed the study, formulated the research questions, supervised the data collection, collected the data, and assisted with writing the article. C. W. Zhu analyzed the data and assisted with writing the article. M. Umpierre and J. Martin assisted in carrying out the study and writing the article. X. Zeng and Q. Huang collected the data and assisted in carrying out the study. H. Grossman designed the study and assisted with writing the article. D. Cai collected the data and assisted with writing the article. M. Sano designed the study, formulated the research questions, and assisted with writing the article.

Conflict of interest

The authors have no conflicts of interest to declare. The study was funded by the Alzheimer's Disease Research Center P50AG05138.

Introduction

The Chinese population in the United States, who are primarily Mandarin or Cantonese speakers, is one of the fastest-growing ethnic minorities in the nation (Zheng *et al.*, 2012), and the number with dementia is expected to triple in the next 30 years (Brennan *et al.*, 2009). Many elderly Chinese may be at high risk for cognitive loss due to a high prevalence of vascular risk factors (He *et al.*, 2010), low levels of formal education (Salmon *et al.*, 1995), and limited access to clinical services (Nguyen and Bornheimer, 2014). Because of the growing numbers of Chinese immigrants in the United States, there is a need to ensure that adequate cognitive assessment tools are available for early diagnosis and management of dementia in this elderly population. The use of cognitive tests for identifying mild cognitive impairment (MCI) and Alzheimer's disease (AD) is dependent upon normative data distinguishing expected performance in normal elders from that of elders with MCI and AD. Several reports have described the needs of translated tests to determine the cognitive performance of non-English speakers in countries of the developed world (Benson *et al.*, 2014; Stricks *et al.*, 1998). Therefore, it is important to determine if a translated battery of cognitive tests can be used to identify cognitive impairment in elderly Chinese Americans. This paper examined the utility of a Chinese test battery for identifying MCI and AD in a cohort of elderly Chinese immigrants in the USA Specifically, we examined different cognitive domains within the battery to determine if they are sensitive in detecting diagnostic categories of normal aging, MCI, and AD as they have been shown to do in other demographic groups. Demographic covariates were taken into consideration to further assess the sensitivity of different cognitive domains.

Methods

Participants

A total of 122 elderly Chinese Americans were recruited for the Alzheimer's Disease Research Center (ADRC) pilot study at the Icahn School of Medicine at Mount Sinai (ISMMS) using community-based recruitment procedures explained in depth elsewhere (Li *et al.*, 2016). The pilot study was conducted to evaluate the feasibility of recruiting elderly Chinese Americans in clinical studies for aging and dementia and to evaluate a cognitive battery that had been used in mainland China for detection of dementia. Inclusion criteria were 65 years old or above and primarily Chinese speaking, with adequate sensorimotor capacity to complete the cognitive test battery. All were required to have a study partner, usually a relative who attended the session or provided information by phone. All participants received the 3-hour standard clinical research dementia evaluation used by the ADRC at ISMMS. This consisted of the National Alzheimer's Coordinating Center Uniform Data Set (NACC UDS) evaluation, which included a clinical interview, functional assessment, medical examination, brief mental status examination, and blood collection for apolipoprotein E ε4 (APOE ε4)genotyping. A battery of Chinese cognitive tests that is a close match to the UDS cognitive battery was used in the study and is described later. Institutional review board approval was obtained at ISMMS. Informed consent was signed by either the participants or their legally authorized representatives.

Chinese cognitive test battery

Cognitive function was evaluated with a subset of cognitive tests that were translated into Mandarin and adopted by Peking Medical Union College Hospital in Beijing for use in dementia evaluation. The following measures were selected to cover the most common domains in aging and dementia.

Memory—Logical Memory (Wechsler, 1981) is a task in which participants are read two short stories and then asked to recall the information (immediate recall). After 20 minutes, the participant is again asked to recall the stories (delayed recall). The score is the total bits of information from the stories that are recalled immediately and after the 20-minute delay interval (maximum score of 50 for both immediate and delayed recall). The Philadelphia Verbal Learning Test is a task in which participants are read a 12-item word list over five trials (Garrett, 2013) and asked to recall the words after each of the five trials (immediate recall). The immediate word recall score is the total number of correct responses (range = 0 to 60). After 20 minutes, the participant is asked to recall the words (delayed recall). Delayed word recall score is the number accurately recalled after this time lag (range = 0 to 12).

Attention executive function—The digit span subtest from the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1981) requires the participant to repeat sequences of single-digit numbers that are read aloud by the examiner. In the forward condition, the participant must repeat the digits in the same order; in the backward condition, the digits must be repeated in reverse order. The sequence length increases from three to eight digits in the forward condition, and from two to seven digits in the backward condition, with two trials presented for each sequence length. A point is awarded for each sequence correctly produced. The maximum score for each condition is 12 points. The Trail Making Test is a widely used instrument for assessing attention and executive function (Karimpoor *et al.*, 2017). Part A consists of 25 circles numbered 1 through 25 and distributed over a white sheet of 81/2” × 11” paper. The participant is instructed to connect the circles by drawing a line as quickly as possible in ascending numerical order. Part B also consists of 25 circles, but these are either Arabic numbers (1 through 13) or Chinese numbers (一 through 十二). Now the participant must connect the circles while alternating between Arabic and Chinese numbers in ascending order (e.g., 1 to 一; 一 to 2; 2 to 二; 二 to 3). The time (in seconds) required to complete each trial is recorded, as well as the number of errors of commission and omission. The maximum time for Part A is 150 seconds and for B is 300 seconds. The Digit Symbol subtest from the WAIS consists of a number (e.g., nine) of digit-symbol pairs (e.g., 1/-, 2/⊥ … 7/Λ, 8/X, 9/=) followed by a list of 135 digits (Fleisher *et al.*, 2007). Under each digit, the participants are asked to write down the corresponding symbol as quickly and accurately as they can within 90 seconds (maximum raw score = 135).

Language—Category fluency is a measure of verbal fluency in which the participant is asked to generate unique examples of the “animal” category in a 1-minute trial (Diesfeldt *et al.*, 2009). The primary performance measure is the number of correct, unique animals generated. The Boston Naming Test is a measure of visual confrontation naming (Katsumata *et al.*, 2015). It requires the participant to name 30 objects depicted in outline drawings. The

number of spontaneous correct responses (maximum score = 30) and spontaneous plus semantically cued correct responses (maximum score = 30) are recorded.

Test administration and scoring were completed by English-Chinese (i.e., Mandarin and Cantonese) bilingual research coordinators who were trained and supervised by an English-Chinese bilingual neuro-psychologist. Cognitive tests were administered in participants' preferred language (either Mandarin or Cantonese).

Cognitive composites

Cognitive status was assessed using seven cognitive measures in three separate domains: memory (Logical Memory task and Philadelphia Verbal Learning Test), attention executive function (Digit Span, Trail Making Test, and Digit Symbol), and language (category fluency in animals and Boston Naming Test). Following similar methodology from earlier studies (Cosentino *et al.*, 2010; Nandipati *et al.*, 2012), a normalized cognitive composite (CC) score and sub-scores in each of the three cognitive domains were constructed to summarize neuropsychological measures by dividing item scores by the maximum possible scores and summing across items. Trail Making Test scores were reversed; therefore, a higher CC score and individual cognitive subscores indicate better cognitive performance. A language composite was created by combining naming and category fluency for animals. Because category fluency does not have a maximum, we explored using naming alone as a measure for language.

Clinical and demographic measures

The Montreal Cognitive Assessment (MoCA) is a brief cognitive screening tool designed to assist clinicians in detecting cognitive impairment (Nas-reddine *et al.*, 2005). It assesses global cognition and cognitive domains of memory, visuospatial skill, language, attention, and abstract reasoning (score range 0–30). The Chinese version of MoCA is available at http://www.mocatest.org/pdf_files/test/MoCA-Test-Chinese_Beijing.pdf.

The Clinical Dementia Rating (CDR) is a semi-structured global dementia measurement rated by a clinician who was blinded to cognitive scores following interviews with participant and informant (Morris, 1997). It assesses daily functioning in the areas of memory, orientation, judgment, hobbies, community affairs, and personal care. CDR Sum of Boxes (SOB) is a simple aggregate of scores in the six clinical domains. CDR-SOB scores range from 0 to 18, with higher scores indicating worse clinical status. The Chinese version of CDR was provided by Peking Medical Union College Hospital in Beijing.

The Geriatric Depression Scale (GDS) is a 15-item self-administered inventory (Yesavage *et al.*, 1982). It provides a reliable assessment of depression. One point is assigned to each positive answer, and the cumulative score is rated on a scoring grid. The grid sets a range of 0–4 as "normal," 5–8 as "mildly depressed," 9–11 as "moderately depressed," and 12–15 as "severely depressed." The Chinese version of GDS is available at https://web.stanford.edu/~yesavage/Chinese2.html.

The Functional Activity Questionnaire (FAQ) measures instrumental activities of daily living (IADLs) such as preparing balanced meals and managing personal finances (Gold, 2012). Sum scores range from 0 to 30, with higher scores indicating worse function.

Participants' demographic variables, including age, gender, education, years living in the USA, and primary language, were collected using the UDS evaluation and local instruments.

APOE exists as three major alleles: ε2, ε3, and ε4 (Wang *et al.*, 2014). APOE genotype analysis was done using Qiagen kits and blood tubes. Participants were defined as ε4 allele carriers (with one or two ε4 alleles) or non-carriers.

Diagnostic criteria

All participants were assigned a research diagnosis at a clinical consensus conference using criterion sheets developed at the ADRC at ISMMS ("NACC Uniform Data Set (Version 3.0, March 2015) Coding Guidebook") for normal aging, MCI (Albert *et al.*, 2011), and dementia (McKhann *et al.*, 2011). Dementia was further categorized by etiology and the types of dementia as described by the UDS ("NACC Uniform Data Set (Version 3.0, March 2015) Coding Guidebook"). The consensus conference was run by a dementia-expert physician and a neuropsychologist, who conducted the clinical interview, functional assessment, medical exam, and brief mental status examination. Whereas qualitative observations of the participants' test-taking behaviors and presentations (e.g., distractibility, impulsivity, articulation, mood, frustration tolerance, motivation, test cooperativeness/refusals, need for redirection) were interpreted when formulating impressions about the participants' cognitive status, diagnostic categories of normal cognition, MCI, and AD were not determined by the cognitive test scores because there were no normative data available.

Data analysis

The current report included a cohort of 116 Chinese-speaking elders with a research diagnosis of normal cognition, MCI, or AD. Four participants with other types of dementia were excluded from this report. Demographic and clinical variables were first compared by diagnostic categories. Categorical variables were compared using chi-squared tests. Continuous variables were compared using Kruskal-Wallis tests. Statistical significance was set *a priori at* $p = 0.05$.

To assess the utility of the test battery for diagnostic discrimination of normal, MCI, and AD, a generalized ordered logistic regression model was initially estimated. Results showed that the parallel lines (or proportional odds) assumptions were not violated, so ordered logistic regressions are sufficient. In these models, the odds ratios (OR) estimate the odds for cases belonging in the combined MCI/AD groups compared to normal and belonging in the AD group compared to combined MCI/normal groups for a one-unit change in the predictor variable, given that the other variables in the model are held constant. For example, the estimated OR for the cognitive composite is interpreted as the proportional odds ratio for a one-unit increase in the cognitive composite score on the diagnostic group, controlling for other variables. Thus, for a one-unit increase in the cognitive composite score, the odds of the AD diagnostic group versus the combined MCI/normal groups, given the other variables, are held constant in the model. An odds ratio greater than 1 indicates a higher likelihood of

being in a worse diagnostic group, and an odds ratio less than 1 indicates a lower likelihood of being in a worse diagnostic group. Two sets of models were estimated. In Model 1, the main independent variable is the cognitive composite scores. In Model 2, the main independent variables are the attention executive function, memory, and language domain scores. Both models controlled for age, gender, education, primary language, and years living in the USA Exploratory models tested for whether the effects of education differed by gender by adding an interaction term, and also the effects of APOE ε4, but these variables were dropped in the final models because they were statistically nonsignificant.

Results

Sample characteristics

Demographic, cognitive, and clinical characteristics for samples in three different diagnostic categories are compared and presented in Table 1. Using the research diagnosis, the sample was categorized into 67 normal cognition, 37 MCI, and 12 AD. Participants were primarily females (69%) and Man-darin speaking (56%) with a mean age of 73.9 ±7.02, 12.75 ± 4.41 years of education, and having lived in the USA for 33.74 ± 15.39 years. Of the 116 participants, APOE data were available for 73 participants. There was no difference in the rate of missing data between diagnostic groups ($p = 0.86$). Among the 73 participants who had APOE data, 17(23.2%) participants were APOE ε4 carriers. Specifically, 12 participants (29.2%) with normal cognition, 2 participants (8%) in the MCI group, and 3 participants (42.9%) in the AD group were APOE ε4 carriers. Three diagnostic groups were significantly different in age and education. The MCI diagnostic group tended to be older and less educated compared to the normal cognition group, but younger and more educated than the AD group. There were no differences in gender, primary language, years living in the USA, and APOE ε4 status between the diagnostic groups. The average MoCA score in the overallsamplewas21.54±5.32andtheotherscoresas follows: CDR-SOB 1.2 ± 2.76, GDS 3.41 ± 3.8, and FAQ 2.79 ± 6.83. The MCI group tended to show worse performance on the MoCA, CDR, and FAQ assessments compared to the normal cognition group but better than the AD group. On the GDS assessment, the normal cognition group was less likely to report depressive symptoms than was the MCI group, but more likely than the AD group.

Cognitive composite scores for the overall sample and by diagnostic categories are also presented in Table 1. The average composite scores for overall cognition, memory, attention executive function, and language were 4.81–1.44, 2.04–0.92,3.05–0.92, and 1.07–0.24, respectively. Composite scores across cognitive domains were lower in the MCI group compared to the normal cognition group, but higher than those in the AD group.

Multivariate results

Results show that a 1-point increase in the cognitive composite is associated with a decreased likelihood of being in a worse diagnostic group (e.g., normal vs. MCI/AD) as well as not having dementia (normal/MCI) versus having dementia (AD) (OR = 0.174, SE = 0.051, 95% CI = 0.097, 0.310) (Table 2, Model 1). Results from examining separate cognitive domains show that increases in the memory and the attention executive function components were associated with a decreased likelihood of being in a worse diagnostic

group: OR = 0.116 for memory component score, and OR = 0.265 for attention executive function component score (Table 2, Model 2). In both models, being male was associated with a higher likelihood of being in a worse diagnostic group, and having lived longer in the USA was associated with a lower likelihood of being in a worse diagnostic group. Using the Boston Naming Test as an alternative measure for language demonstrated similar results.

Discussion

We administered a translated battery of cognitive tests to 116 Chinese American elders with diagnoses of normal cognition, MCI, and AD at the ADRC of ISMMS. As expected, performance on the CDR, MoCA, and FAQ assessments was best in the normal cognition group, poorer in the MCI group, and poorest in the AD group. Similarly, cognitive composites were highest in the normal cognition group, lower among those in the MCI group, and lowest in the AD group. Consistent with other aging cohorts (Ganguli *et al.*, 2010), better cognitive test scores were associated with higher education and younger age in our subjects. However, results from our regression models showed that cognitive scores differed among three diagnostic groups even adjusted for age and education. Specifically, performance on overall cognition, memory, and attention executive function demonstrated differences by diagnostic categories and therefore could be helpful in distinguishing subjects belonging to diagnostic groups. Larger samples could provide a better characterization of normative scores and should be a goal of future work. The language domain demonstrated a similar trend of poor performance in MCI and AD cohorts compared to the normal cognition group, but the differences were not significant. A number of studies report language impairments in the more advanced stages of AD (Appell *et al.*, 1982) and in those with early-onset AD (Smits *et al.*, 2012), groups that are not well represented in our cohort. Language change in the early stages of the disease is typically mild and may require a larger sample to detect any effect. These results highlight the importance of establishing robust norms to characterize the full range of cognitive impairment in elderly Chinese Americans. Validation of a Chinese test battery will allow for systematic assessment of data in this population and facilitate early detection of cognitive impairment in this elderly immigrant population. In our cohorts, the prevalence of APOE ε4, a known genetic risk for AD, was not significantly different among normal cognition (29.2%), MCI (8%), and AD groups (42.9%). However, a recent report from a memory disorder clinic in Beijing with a larger sample size observed a higher prevalence of APOE ε4 among Chinese MCI and AD patients compared to those in the healthy cognition group (Wang *et al.*, 2014).

This study has several limitations. First, the sample size in this study was small, with a relatively low number of AD patients. Future study of a larger cohort with more AD subjects is warranted, to investigate the validity of the test battery. Second, results of medical laboratory studies and AD pathology biomarkers were not available, reducing some confidence in the diagnostic accuracy. Third, Chinese individuals speak a variety of dialects; however, the participants in this study were tested in either Mandarin (the most widely used dialect in Taiwan and China) or Cantonese (the most widely used dialect in Hong Kong). Little is known about whether the findings in this study can be generalized to populations who speak other dialects. Fourth, our AD group did not include patients with other types of dementia, and we therefore cannot draw conclusions about the diagnostic utility of this

battery for differential diagnosis of different dementia types. Lastly, our cohort was recruited from New York, and thus the results may not be generalized to Chinese elders from other states or countries.

To conclude, our findings confirm prior work regarding the value of cognitive tests for diagnosing dementia in English- and Spanish-speaking elders (Sayegh and Knight, 2013) and extend those findings to the elderly Chinese American community. In our study, cognitive performance distinguished between diagnostic groups of normal cognition, MCI, and AD, with sensitivity from tests of memory and attention executive function. Better cognitive scores were associated with younger age and higher education, demonstrating the predictive sensitivity of specific demographic variables to cognitive performance. Our study demonstrates the potential utility of using the Chinese versions of a common cognitive battery in assessing elderly Chinese immigrants. Future studies are needed to validate norms for these assessments and to enhance detection of early deficits and diagnostic categories.

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Table 1.

Participants' demographic, clinical, and cognitive variables at study entry for overall sample and by diagnosis

	DIAGNOSTIC CATEGORIES				
	OVERALL (*N* = 116)	**NORMAL (*N* = 67)**	**MCI (*N* = 37)**	**AD (*N* = 12)**	***P* VALUE**
Demographic variables					
Age, mean ± SD	73.90 ± 7.02	72.60 ± 6.65	74.89 ± 6.30	78.08 ± 9.34	0.048
Education, mean ± SD	12.75 ± 4.41	13.90 ± 3.29	11.46 ± 5.34	10.33 ± 5.05	0.0047
Male, %	31.90	25.37	40.54	41.67	0.211
Mandarin speaking, %	56.03	58.21	56.76	41.67	0.660
Years living in the USA, mean ± SD	33.74 ± 15.39	34.34 ± 16.21	35.03 ± 13.50	26.44 ± 15.38	0.1962
Clinical variables					
MoCA, mean ± SD	21.54 ± 5.32	24.28 ± 3.23	19.30 ± 3.63	11.40 ± 5.95	< 0.001
CDR SOB, mean ± SD	1.20 ± 2.76	0.03 ± 0.12	1.03 ± 0.70	8.25 ± 3.94	< 0.001
GDS, mean ± SD	3.41 ± 3.88	2.58 ± 3.34	5.16 ± 4.62	2.50 ± 1.72	< 0.001
FAQ, mean ± SD	2.79 ± 6.83	0.54 ± 2.20	1.62 ± 3.47	19.00 ± 9.84	< 0.001
Cognitive variables					
Overall cognitive composite, mean ± SD	4.81 ± 1.44	5.57 ± 0.74	4.26 ± 1.12	2.24 ± 1.66	< 0.001
Memory composite, mean ± SD	2.04 ± 0.92	2.51 ± 0.72	1.67 ± 0.62	0.53 ± 0.43	< 0.001
Attention executive composite, mean ± SD	3.05 ± 0.92	3.48 ± 0.45	2.79 ± 0.85	1.50 ± 1.12	< 0.001
Language composite, mean ± SD	1.07 ± 0.24	1.16 ± 0.11	1.01 ± 0.22	0.71 ± 0.42	< 0.001

Note: *P*-values for group differences from Kruskal-Wallis test.

Table 2.

Ordered logistic regression estimates of relationship between cognitive composites in discriminating among diagnostic groups (i.e., normal control, mild cognitive impairment, and Alzheimer's disease)

	MODEL 1	MODEL 2
	ODDS RATIO (se) [95% CI]	**ODDS RATIO (se) [95% CI]**
Cognitive composite score	0.174**	
	(0.051)	
	[0.097, 0.310]	
Memory composite score		0.116**
		(0.054)
		[0.046, 0.290]
Attention executive composite score		0.265**
		(0.130)
		[0.102, 0.692]
Language composite score		0.225
		(0.437)
		[0.005, 10.107]
Age	0.965	0.977
	(0.038)	(0.039)
	[0.894, 1.042]	[0.903, 1.057]
Gender	3.174*	2.979*
	(1.750)	(1.659)
	[1.077, 9.355]	[1.001, 8.871]
Education	1.086	1.066
	(0.072)	(0.075)
	[0.953, 1.238]	[0.929, 1.222]
Primary language	0.828	0.935
	(0.469)	(0.545)
	[0.273, 2.514]	[0.299, 2.928]
Years living in the USA	0.965*	0.956*
	(0.017)	(0.019)
	[0.932, 0.999]	[0.920, 0.993]

* $p < 0.05$,

** $p < 0.01$.