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Validation of the Taiwanese Version of ACE-III (T-ACE-III) to Detect Dementia in a Memory Clinic

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Abstract

Objective: The Addenbrooke's Cognitive Examination III (ACE-III) is a 100-points cognitive test used in detecting dementia in many countries. There has been no validation study of the ACE-III in patients with suspected dementia in a Taiwanese population, where the language is traditional Chinese. We aimed to culturally adapt and validate the ACE-III as a cognitive assessment tool for differentiating between people with and without dementia presenting to healthcare professionals in Taiwan with possible dementia.
Methods: We culturally adapted the ACE-III for Taiwan (T-ACE-III) and tested it with consenting patients with suspected dementia in northern Taiwan who had been through the diagnostic process. We calculated receiver operating characteristic (ROC) curves to test the ability of the T-ACE-III to differentiate between dementia and non-dementia cases using clinician diagnosis as the gold standard. We generated the Youden Index to determine the best cut-off score.
Results: We recruited 90 Taiwanese individuals aged 49–93 years: 24 males and 33 females had dementia and 12 males and 21 females did not. The area under the ROC curve was 0.99 for distinguishing dementia from non-dementia. The T-ACE-III had a sensitivity of 100% and specificity of 78.8% when the cut-off score was 86/87. With a cut-off value of 73/74, the specificity was 100.0%, and sensitivity 89.5%. The highest Youden Index was 0.895, indicating the best overall cut-off point to be 73/74.
Conclusions: The T-ACE-III is an acceptable cognitive test with excellent psychometric properties for discriminating dementia from non-dementia in Taiwanese populations in memory clinic settings.

Keywords: Dementia; Cognitive assessment; Cross-cultural/minority

Introduction

Dementia affects around 5% of people over the age of 60 (Prince et al., 2015) worldwide and 7.19% of those over the age of 65 in Taiwan (Ministry of Health and Welfare in Taiwan, 2020), which has become an aging society particularly in the past 20 years. Studies mostly conducted around two decades ago found that the prevalence of dementia in Taiwan was 3.4% in the age-range of 65–69 years, increasing to 36.9% for the over 90s age range (Sun et al., 2014). A more recent Taiwanese national study between 2011 and 2013, found the data of very mild dementia was less reported and addressed in some early studies

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(Lin et al., 1998; Liu et al., 1998a; Liu et al., 1996; Liu et al., 1995; Liu et al., 1998b; Liu et al., 1997), indicating possible challenges in diagnosing very mild dementia (Chen, Wang, Ma, & Yang, 2014). There is a pressing need for validating rapid and accurate tests for timely detection of possible dementia among Taiwanese populations.

Early diagnosis of dementia is one of the main aims of the World Health Organization (WHO) for the period from 2017 to 2025 (Alzheimer's disease International, 2019; World Health Organization, 2017). But data collected between 1992 and 2016, found internationally only approximately half of individuals who met dementia diagnostic criteria were formally diagnosed (Amjad, Roth, Samus, Yasar, & Wolff, 2016; Connolly, Gaehl, Martin, Morris, & Purandare, 2011; Lang et al., 2017; Savva & Arthur, 2015). The project of the Ministry of Health and Welfare in Taiwan aimed to increase the diagnosis rate of dementia from 30% to 50% by 2020 and to 70% by 2025 (Ministry of Health and Welfare in Taiwan, 2020). Clinical assessments to precisely identify those individuals can be time-consuming but if only brief cognitive assessments are used, suspected dementia is often misclassified, because scores differ across factors such as age, education, and ethnicity (Ranson et al., 2019). And, screeners often do no adjust for these demographic factors. Therefore, it is important to select an appropriate brief assessment in order to achieve accurate timely detection of dementia.

Taiwan is a mix of ethnic groups, such as Southern Min, Hakka and Taiwanese Aboriginal, and many Chinese dialects are spoken. One of the most commonly spoken Chinese dialects is Taiwanese Hokkien (also called Taiwanese), spoken by approximately 70% of the population. Taiwanese speakers tend to have a low educational level, with a cut-off stage of senior high school (from 16 to 18 years old). A study of 252 patients at a hospital in South Taiwan found that 95.4% of the older group used Taiwanese and all nonliterate people spoke Taiwanese. They also discovered that people who are older are more likely to use Taiwanese Hokkien as their main language (Tsao & Lu, 1999).

In Taiwan, the Clinical Dementia Rating (CDR), is used for both staging and diagnosis (Morris, 1993) as it is internationally. The Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), is the most commonly used cognitive test which, on average, takes 10–15 min to administer, but does not test memory and executive functioning extensively, has ceiling effects, a major influence of education, and a copyright-protection issue (Carnero-Pardo, 2014). The Cognitive Abilities Screening Instrument (CASI) (Lin et al., 2002), which takes around 15–20 minutes, but up to 30 minutes in patients with dementia (Teng et al., 1994), gives particularly low scores in those who can only speak Taiwanese, after accounting for age and education (Chen, 1996). So far, there has been no validated short (around 20 min or less) assessment that covers a wide range of cognitive domains to detect dementia in the Taiwanese population.

The ACE-III assesses cognitive domains including attention, orientation, fluency, memory, language, visual perceptual function, and visuospatial skills. It takes a short time (<20 min) to administer. There were simplified Chinese, Japanese, and Korean language versions on the official website but not a traditional Chinese version for Taiwan. In China, it has high validity in detecting all types of dementia (sensitivity: 94.0%, 91.1%; specificity: 83.0%, 83.1%; cut-off score: 74/75, 83) (Li, Yang, Yin, Yu, & Ye, 2019; Wang et al., 2017) and is helpful in distinguishing subtypes of dementia in other countries (Elamin, Holloway, Bak, & Pal, 2016; Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013; Matias-Guiu et al., 2017).

The primary aim of this study was to culturally adapt and validate the Taiwanese version of ACE-III (T-ACE-III) in patients with dementia in clinical settings in Taiwan. The secondary aim was to explore the acceptability of other supplementary tests in this population.

Method

This prospective study was approved by the UCL Research Ethics Committee (REC) in the UK (16845/001) and the Office of Human Research of Taipei Medical University in Taiwan (NO:N202004089), including Data Protection Registration (NO:Z6364106/2020/01/48) in the UK. The data collection process was carried out through convenience sampling in Taiwan from June 2020 to October 2020.

We obtained permission to translate, adapt, and use the cognitive tests from the original authors or the relevant institutions.

Participants

Eligible participants were people, aged 45–100, referred to a neurological clinic in the north of Taiwan in the previous 6 months with memory problems or suspected dementia. Individuals who had in the past been diagnosed with severe psychiatric disorders, or with visual, hearing, or motor impairments which significantly interfered with comprehension or execution of cognitive tasks were excluded.

Dementia Diagnosis

The four neurologists based in the clinic diagnosed the participants as having or not having dementia according to the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) prior to their recruitment for the study (American Psychiatric Association, 2013) using their medical history, daily functioning, reported cognitive symptoms, laboratory results, and neuroimaging findings. Clinical observation on significant cognitive decline in one or more cognitive domains and the interference with independence in everyday activities were judged by the clinicians at consultation. The study only had access to examine their CDR, MMSE, and CASI scores, but not other tests. They also classified dementia subtypes, based on the International Classification of Diseases, Tenth Revision (ICD-10). Neuropsychological assessments were conducted by three psychologists.

Cultural Adaptation

The term China we use here refers to the People's Republic of China, excluding the Special Administrative Regions of Hong Kong and Macau. Mandarin Chinese is officially spoken in Taiwan and China, whereas the written form of Simplified Chinese is used in China and Singapore and Traditional Chinese is used in Taiwan, Hong Kong, and Macau. The most significant difference between the two written forms of Chinese is the form of the individual characters. Simplified Chinese was implemented by the Chinese government between 1956 and 1964 in order to improve literacy but is often not understood in Taiwan especially by older people. We used the Cross-Cultural Adaptation Process (Beaton, Bombardier, Guillemin, & Ferraz, 2000) to guide the appropriate procedures for cultural adaptation of psychometric tests for the Taiwan population. This is used when assessments in one language are used in other populations with the same language, but differing cultures or language characters. So, for example, the terms used for the leaders of state differ (chairman in China and president in Taiwan). The form of characters (simplified Chinese in China, traditional Chinese in Taiwan) and the culture and history between two populations also differ. In particular, the influence of different Chinese dialects is relevant when culturally adapting neuropsychological assessments (Chen, 1996). Further details are outlined below.

Measures

The ACE-III takes 15–20 min and has a maximum score of 100—a higher score indicates better cognitive function. R-CY, a researcher with a clinical background in dementia who is bilingual and literate in Traditional and Simplified Chinese and English, adapted the Simplified Chinese version of the ACE-III into Traditional Chinese. C-CY who is a clinical neuropsychologist and linguistics expert is also a bilingual researcher, read the draft adapted version and discussed the changes with R-CY. It was adapted for Taiwanese culture after a series of discussions with two neurologists specializing in dementia, C-JH and C-TH, resulting in a consensus. Lastly, after pretesting in a small sample of Taiwanese colleagues and adapting it in line with their feedback, we generated the final version of the Taiwanese ACE-III (T-ACE-III). The main changes include replacing phonemic fluency with semantic fluency (from generating Chinese words starting with the word "car" to "naming vegetables and fruits"), using local Taiwanese name and addresses for memory, using pictures frequently seen in daily life in Taiwan (from pencil, panda, harp, barrel to spoon, kangaroo, drum, bulb) instead of in China for language and understanding, using traditional Chinese words for reading in language, and replacing English letters with numbers for visuospatial abilities. More importantly, alterations were made to language subtest items (asking them to repeat the phrases or proverbs) for Taiwanese language users and Taiwanese language was used throughout the assessments. The validated T-ACE-III is now available online (The University of Sydney, 2021).

In addition to the T-ACE-III, we administered several neuropsychological tests for acceptability. These included: *The Brixton Spatial Anticipation Test from Hayling and Brixton tests* (Burgess & Shallice, 1997) for assessing cognitive flexibility/set shifting, one aspect of executive function—it takes 15–20 min and is a visual test where people follow a rule to position a blue circle from two rows of five circles numbered 1–10 in each page, evaluating the ability to detect a rule, to follow it, and to switch to a new rule. It does not require a verbal or complex motor response by the patient and has no time restriction. The maximum number of errors is 54—higher scores mean worse performance. We directly translated the brief instructions from English to Chinese. R-CY who used this test discussed with N-K (a neuropsychology expert) to ensure the procedure was in line with guidance.

Processing Speed Index from the Wechsler Adult Intelligence Scale IV—(WAIS-IV-PSI) (Wechsler, 2008) measures processing speed through a series of tasks of symbol search, cancelation and coding. It takes less than 10 min. The Taiwanese version of the WAIS-IV was released in 2015 (Wechsler, 2015a; Wechsler, 2015b), and we used it, without it requiring changes for cultural adaptation and translation.

The Coin-in-the Hand (CIH) test (Kapur, 1994), a two-choice memory test, takes 5 min and measures cognitive effort. It has been used for differentiating malingerers from those with true memory impairment (Schroeder, Peck, Buddin Jr., Heinrichs, & Baade, 2012) including in a pilot study in Taiwan (Yeh et al., 2018), which achieved a high AUC of 0.79 with a cut-off value of 8.27. R-CY translated the administration instructions from English to Chinese for this study.

Apart from the assessments above, we also collected the demographic information including age, sex, language spoken, years of education, the last employment (types and position: managerial/ nonmanagerial), and medical history from the case report form.

Power Calculation

We calculated the numbers of participants needed in each group through "easyROC" (http://www.biosoft.hacettepe.edu.tr/easyROC/). With setting power 90%, type I error 0.05, area under the ROC 0.7, and allocation ratio 0.5, the numbers of participants required in dementia group and non-dementia group were 48 and 24, respectively. For better understanding the influence of languages used on the T-ACE-III scores, we recruited nine more participants in each group.

Statistical Methods

We analyzed data using SPSS (version 26). We first described the demographic characteristics; sex, age, education, language, and raw cognitive test scores in the dementia and non-dementia groups. We also described cognitive tests results, including the mean with standard deviation (SD) for parametric data and median with interquartile range (IQR) for nonparametrically distributed data.

We recorded the time taken for assessments from participant 47 onwards when R-CY experienced in the interview.

The primary analysis was area under the curve (AUC) with receiver operating characteristic (ROC) curve analysis, which we used to calculate the diagnostic accuracy for the T-ACE-III to distinguish between dementia and non-dementia groups. To consider the optimal cut-off point, providing the best measure of sensitivity and specificity combined, we used the Youden Index, which can range between 0 and 1, with 1 indicating no false positives or false negatives. We estimated the reliability using the domain-total internal consistency of the T-ACE-III (Cronbach's α-coefficient). We also examined the convergent validity by calculating correlation using a two-tailed Spearman's test between the scores of the T-ACE-III and the tests previously administered in the neurology clinic (CDR, MMSE, CASI).

To examine the influence of demographic factors on the T-ACE-III scores, we used linear regression analysis, with the T-ACE-III scores as the dependent variable and the independent variables of age, years of education, sex, SES (managerial/ nonmanagerial), and language. We then considered independent predictors of diagnosis of dementia by entering demographic factors (age, years of education, Socioeconomic Status (SES), and sex) and T-ACE-III scores into logistic regression analysis with dementia diagnosis as the outcome. In a post hoc analysis suggested by referees we also explored the relationship of education and age on language (speaking only Taiwanese compared to speaking both Mandarin and Taiwanese) as the outcome in logistic regression analysis. $p < .05$ was considered statistically significant. Lastly, we examined the convergent validity of the supplementary tests with the T-ACE-III using a two-tailed Spearman's correlation analysis.

Results

Demographic and Clinical Profile

We invited 110 participants to take part in this study, of whom 91 (82.7%) consented and 90 (81.8%) completed the neuropsychological assessments. Reasons for refusal included having appointments with other doctors, impaired attention due to bad sleep, and not wanting to take part in this research. There were 57 participants with complete data in the dementia group, including 21 patients with Alzheimer's disease (AD), 15 with vascular dementia (VaD), 6 with Parkinson's disease dementia (PDD), 3 with frontotemporal dementia (FTD), 1 with dementia with Lewy bodies (DLB), 2 patients with unspecified dementia, 9 with mixed-type dementia (3 VaD + PDD, 4AD+VaD, 1AD+FTD, 1AD+Trauma), and 33 in the non-dementia group. All participants completed the T-ACE-III. Overall, 35 (61.4%) participants in the dementia and 32 (97.0%) in the non-dementia groups completed WAIS-IV symbol search, 33 (57.9%) with dementia and 32 (97.0%) without completed WAIS-IV symbol coding, 38 (66.7%) with dementia and 33 (100.0%) without completed Brixton spatial anticipation test, 56 (98.2%) with dementia and 33 (100.0%) without completed the CIH test.

The demographic information of the participant groups, and their scores on neuropsychological assessments and the short cognitive battery are shown in Table 1. Those who had been diagnosed with dementia were older (74.2 vs. 66.4), and with less

Table 1. Demographic and neuropsychological characteristics of participant groups

Variable (number)	Dementia($N = 57$)	Non-dementia ($N = 33$)
Male	24 (42.1%)	12 (36.4%)
Female	33 (57.9%)	21 (63.6%)
Education, years*	7.70 ± 4.4	11.24 ± 4.0
Illiterate	6 (10.5%)	1 (3.0%)
Elementary school	25 (43.9%)	5 (15.2%)
Junior high school	9 (15.8%)	6 (18.2%)
Senior high school	12 (21.1%)	11 (33.3%)
College	5 (8.8%)	9 (27.3%)
Higher education	0 (0.0%)	1 (3.0%)
Age, years*	74.2 ± 8.4	66.4 ± 7.5
<60	5 (8.8%)	7 (21.2%)
61–70	13 (22.8%)	17 (51.5%)
71–80	23 (40.4%)	7 (21.2%)
81–90	15 (26.3%)	2 (6.1%)
>90	1 (1.8%)	0 (0.0%)
Language used		
Taiwanese only	14 (24.6%)	0 (0.0%)
Chinese only or Chinese and Taiwanese	43 (75.4%)	33 (100.0%)
CDR 0	0 (0.0%)	28 (84.9%)
0.5	36 (63.2%)	5 (15.2%)
1	15 (26.3%)	0 (0.0%)
2	6 (10.5%)	0 (0.0%)
MMSE	18.4 ± 5.2	27.7 ± 1.9
CASI	60.8 ± 16.3	91.2 ± 4.9
Total T-ACE-III scores	55.0 ± 15.8	90.8 ± 6.6
Orientation/attention*	11.3 ± 4.0	17.4 ± 1.1
Memory*	11.7 ± 5.3	23.5 ± 2.3
Verbal fluency*	4.6 ± 3.2	10.5 ± 2.2
Language*	16.6 ± 5.1	24.2 ± 2.3
Visuospatial*	10.8 ± 4.0	15.3 ± 1.3
WAIS-IV-PSI-Symbol search (35/32)*	6.6 ± 2.4	10.7 ± 3.4
WAIS-IV-PSI-Digit symbol coding (33/32)*	6.9 ± 3.0	9.5 ± 2.6
Brixton spatial anticipation test*(38/33)	2.2 ± 1.6	4.3 ± 2.2
The Coin-in-the-hand test*(56/33)	9.7 ± 0.7	9.9 ± 0.3

CDR, Clinical Dementia Rating Scale; MMSE, mini-mental state examination; T-ACE-III, Taiwanese version of Addenbrooke's Cognitive Examination III; WAIS-IV-PSI, Processing Speed subtests of the Wechsler Adult Intelligence Scale-IV.
*Represents the results presented with Mean ± SD.

education than those in the non-dementia group (7.7 and 11.2 years of education). Fourteen (24.6%) participants in the dementia group could speak only Taiwanese language. But all of those in the non-dementia group could speak at least Mandarin Chinese (15.2%) or both (84.8%).

Time to Administer on Average

We measured time taken for testing in 43 participants, of whom 16 did not complete the supplementary tests. The T-ACE-III took a mean (SD) of 24.0 ± 6.1 and 16.3 ± 4.6 min in the dementia group and non-dementia group, respectively. With the supplemental tests, the mean total time taken was 41.1 ± 4.8 and 32.0 ± 5.3 min to administer in the dementia group and non-dementia group, respectively.

The T-ACE-III Scores for Discriminating Dementia from Non-Dementia

Figure 1 shows the ROC analysis. The area under the ROC curve (AUC) was 0.990 for the T-ACE-III ($p < .001$, 95% confidence interval (CI) = 0.977–1.000). As shown in Table 2, when the cut-off score was 86/87, the T-ACE-III had a specificity of 0.788 and a sensitivity of 1, with a value of 0.788 on the Youden index; when the cut-off score was 73/74, the T-ACE-III had a specificity of 1 and a sensitivity of 0.895, with the highest value of 0.895 of Youden index, indicating the best cut-off point.

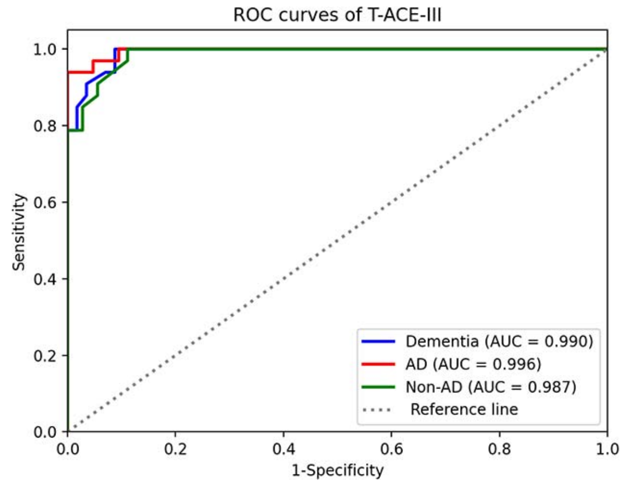

Fig. 1. ROC curves of T-ACE-III.

Table 2. Cut-off scores for the T-ACE-III in differentiating dementia from non-dementia

Cut-off scores	Sensitivity	Specificity	Youden Index
73/74	0.895	1.000	0.895
74/75	0.895	0.970	0.865
75/76	0.912	0.970	0.882
76/77	0.930	0.939	0.869
77/78	0.947	0.939	0.886
80	0.965	0.909	0.874
82/83	0.965	0.879	0.844
83/84	0.982	0.848	0.830
84/85	0.982	0.818	0.800
85/86	0.982	0.788	0.770
86/87	1.000	0.788	0.788

The T-ACE-III Scores for Discriminating AD and Other Dementia Subtypes from Non-Dementia

The AUCs for distinguishing either AD or other dementia subtypes from the non-dementia group were calculated. As shown in Figure 1, the AUCs of T-ACE-III for detecting AD and other dementia subtypes versus no dementia, were 0.996 ($p < .001$, 95% CI = 0.986–1.000) and 0.987 ($p < .001$, 95% CI = 0.969–1.000), respectively, which suggested that the high diagnostic accuracy was not influenced by the type of dementia.

Reliability and Convergent Validity of the T-ACE-III

The internal consistency of the T-ACE-III was 0.895. There was negative correlation between CDR scores and total T-ACE-III scores ($r = -0.8$, $p < .01$) and a correlation between MMSE and CASI scores from psychologists and total T-ACE-III scores (both $r = 0.9$, $p < .01$).

Association of Demographic Factors with the T-ACE-III Scores in Linear Regression

Using linear regression with the T-ACE-III scores as the dependent variable, (see Table 3), we found language used (only Taiwanese compared to both Mandarin and Taiwanese, $p = .005$, 95% CIS for B = −30.868 to −5.856) and every additional year of education ($p = .009$, 95% CIS for B = 0.404–2.760) were significantly associated with the T-ACE-III scores. However, age (for every year older, $p = .213$, 95% CIS for B = −0.810 to −0.183), sex (male compared to female, $p = .292$, 95% CIS for B = −13.406 to −4.085), and employment divided into managerial/ nonmanagerial jobs ($p = .614$, 95% CIS for B = −6.864 to 11.550) were not. The variance inflation factors (VIFs) were from 1.157 to 1.798 (lower than 10), indicating there was no multicollinearity existed among the independent variables (education years, age, sex, language spoken, and SES). The model

Table 3. Association of demographic factors with T-ACE-III scores and diagnosis of dementia

Dependent variables	Independent variables						
	Coefficients	T-ACE-III (higher)	Education (increasing years)	Age (higher)	Sex (male)	SES (managerial/ nonmanage-rial)	Language (Taiwanese)
Linear regression (T-ACE-III scores)	Standardized Coefficients β	-	0.329	−0.127	−0.105	0.052	−0.300
	95% CIS for B	-	0.404–2.760	−0.810-0.183	−13.406-4.085	−6.864-11.550	−30.868 – −5.856
	T	-	2.672	−1.256	−1.060	0.506	−2.921
	p	-	.009	.213	.292	.614	.005
	R^2	0.319					
Logistic regression (outcome diagnosis of dementia)	B	−0.727	0.236	−0.163	−0.945	3.259	-
	Exp(B)	0.483	1.267	0.850	0.389	26.031	-
	95% CIS for Exp(B)	0.260–0.898	0.808–1.985	0.679–1.063	0.005–28.690	0.140–4833.824	-
	p	.021	.302	.155	.667	.221	-
	NagelkerkeR^2	0.927					
Logistic regression (language used—Taiwanese only)	B	-	−0.35	0.061	-	-	
	Exp(B)	-	0.704	1.063	-	-	
	95% CIS for Exp(B)	-	0.586–0.847	0.990–1.141	-	-	
	p	-	<.001	.094	-	-	
	NagelkerkeR^2	-	0.357	0.058	-	-	

T-ACE-III, Taiwanese version of Addenbrooke's Cognitive Examination III. SES = socioeconomic status We could not include language in logistic regression as there were no Taiwanese speakers in the non-dementia groups.

accounted for 31.9% of the variance in the T-ACE-III scores overall model (F = 7.6, $p < .001$). Further analysis on the language used (Taiwanese only) through logistic regression, the results confirmed that every decreasing year of education ($p < .001$, 95% CIS for Exp(B) = 0.586–0.847) was significantly associated. The model accounted for 35.7% of the variance in the overall model ($p < .001$). Although age was not ($p = .935$, 95% CIS for Exp(B) = 0.990–1.141). The model accounted for 5.8% of the variance in the overall model ($p < .001$).

Association of Demographic Factors with Diagnosis of Dementia on Logistic Regression

In the logistic regression model, (see Table 3), lower T-ACE-III ($p = .021$, 95% CIS for Exp(B) = 0.260–0.898) scores were associated with diagnosis of dementia. With T-ACE-III scores in the model, years of education ($p = .302$, 95% CIS for Exp(B) = 0.808–1.985), age ($p = .155$, 95% CIS for Exp(B) = 0.679–1.063), sex ($p = .667$, 95% CIS for Exp(B) = 0.005–28.690) and managerial/nonmanagerial jobs ($p = .221$, 95% CIS for Exp(B) = 0.140–4833.824) were not significantly associated. The model accounted for 92.7% of the variance ($p < .001$). We were unable to add language to the model as no one who spoke only Taiwanese was not diagnosed of dementia.

Correlation between the T-ACE-III and the Supplemental Tests

As shown in Table 4, there was a significant correlation between WAIS-PIS scores (including symbol search and digit symbol coding) and the T-ACE-III scores (including subdomains), and a significant correlation between Brixton spatial anticipation test scores and the T-ACE-III scores (The CIH scores were only slightly correlated with the T-ACE-III scores, including subdomains). The results suggested WAIS-PIS scores and Brixton spatial anticipation test scores increased when the T-ACE-III scores increased, whereas an increase in the CIH scores was unable to reflect the tendency of the T-ACE-III scores and its subdomains.

Discussion

To our knowledge for the first time, we have culturally adapted and validated the T-ACE-III in a Taiwan population, and established cut-off scores in differentiating patients with dementia from healthy participants. The T-ACE-III had excellent

Table 4. Correlation between T-ACE-III and the supplemental tests

	WAIS-symbol search	WAIS-digit symbol coding	Brixton spatial anticipation test	Coin-in-the-hand test
T-ACE-III total scores	0.610**	0.511**	0.563**	0.265*
Attention	0.549**	0.484**	0.533**	0.247*
Language	0.568**	0.456**	0.539**	0.137
Memory	0.511**	0.349**	0.542**	0.248*
Verbal fluency	0.416**	0.363**	0.351**	0.339**
Visuospatial	0.656**	0.717**	0.488**	0.164

*$p < .05$.
**$p < .01$.
T-ACE-III, Taiwanese version of Addenbrooke's Cognitive Examination III.

accuracy in distinguishing dementia from non-dementia in a memory clinic population with a higher ROC AUC than currently used tests (Chang et al., 2012; Chen et al., 2018; Tsai et al., 2016; Wang et al., 2013). The T-ACE-III was psychometrically robust with the total T-ACE-III scores showing a high correlation with the scores of current assessments used in differentiating dementia from those who did not have dementia in Taiwan (CDR, MMSE, CASI), pointing to good convergent validity and good internal consistency (Cortina, 1993). It had a very high acceptability and completion rate and took a relatively short time to administer compared to current assessments (CASI, CDR, and Neuropsychiatric Inventory) for diagnosing dementia in Taiwan, which usually take around an hour for each patient in a Taiwan clinic (personal communication, C-CY). Linear regression showed that sociodemographic characteristics did not account for most of the variance in the cognitive test scores.

Our secondary aim was to explore the acceptability (completion rate and administration time) of supplementary neuropsychological tests. The completion rates of Symbol Search and Coding subtests of the WAIS-IV and of the Brixton Spatial Anticipation Test were only between 57.9% and 66.7%, and so had low acceptability in the dementia group. We do not know why this was, but some patients may have been tired since the T-ACE-III was always completed first, some struggled with the physical demands of performing the WAIS subtests and others with understanding the Brixton test.

We found in multiple linear regression analysis that years of education and spoken languages of only Taiwanese were significant predictors of the T-ACE-III scores, but that there was no significant effect of age on the total scores. We found that language spoken (Taiwanese only compared to those who spoke both Mandarin and Taiwanese) was a significant predictor of ACE scores and this may be because those who only spoke Taiwanese had less education, echoing previous research that indicated education levels are negatively correlated with the choice of Taiwanese language (Tsao & Lu, 1999). People who spoke only Taiwanese had less education and this was possibly a risk factor for dementia and may have led to lower scores on the T-ACE-III. However, the clinical diagnosis was made independently of T-ACE-III scores. In terms of the potential predictors on the diagnosis of dementia, logistic regression analysis found that demographic factors had no influence over and above T-ACE-III. In summary, in the cultural context of Taiwan, although demographic factors of language and education years have some influence on the T-ACE-III scores, it is still a powerful diagnostic tool in detecting patients with dementia, with T-ACE-III scores contributing more to diagnostic classification than other factors.

A previous study validated the traditional Chinese version of ACE-III in community settings rather than a clinical setting for detecting MCI in Taiwan, and their translation did not follow cultural adaptation guidelines (Lin, Hsu, Wang, & Ouyang, 2019). However, our own study followed specific guidelines for translation and cultural adaptation (Beaton et al., 2000), incorporating opinions from a bilingual linguist, a bilingual researcher, two neurologists, one psychiatrist, and one clinician.

Most participants completed the CIH test and most participants passed it even if they had dementia. This confirms its validity as a test of cognitive effort and its acceptability (Schroeder et al., 2012; Yeh et al., 2018) in a non-Western population such as that sampled in Taiwan.

There are some limitations to the current study. Firstly, we recruited a consecutive sample of people to reduce selection bias and found that Taiwanese language users in the current study were all in the dementia group. Future research can further confirm the influence of language used on the T-ACE-III performance if necessary, enriching the sample and recruiting Taiwanese users in each group. Also, there were six participants in the dementia and one in the non-dementia groups who were illiterate. They may have led to problems in tasks with reading and writing elements which were not due to dementia, the cut-off values after adjusting the T-ACE-III scores is shown in appendix. We recommend that future research uses a larger sample size to explore different cut-off values of the T-ACE-III for participants with different educational levels and levels of literacy, so as to provide more tailored cut-off scores relating to educational and literacy needs, and thus increase the diagnostic accuracy. Secondly, we calculated internal consistency but no other forms of reliability in the analysis, such as test–retest reliability. Similarly, we did not examine discriminant validity. Thirdly, one question in the attention domain (orientation) has been replaced with the MMSE item due to the instruction of the simplified Chinese version not being clearly translated and tending to misguide the examiners during the assessing procedure. Fourth, the study could not be double-blind as the patients had been given a diagnosis as part of the routine clinical work-up. Both the patient and the researcher were aware of the diagnosis when administering psychometric tests but at that time the cutpoint for the T-ACE-III was not known. Lastly, under the threat of COVID-19, Taiwanese residents were required to wear a mask in all indoor spaces, such as hospitals and public transport. During the assessment procedures, both participants and examiners were wearing a mask, which may potentially have affected the understanding of instructions or conversations, especially for specific items, such as language tasks (asking participants to repeat a sentence, asking them to complete three actions) and attention tasks (asking participants to repeat three words). As a result, this may have contributed to a degree of variability in the T-ACE-III test performance, as well as the average time taken by individual participant to complete the T-ACE-III, which was slightly longer than 20 min in the dementia group. Apart from that, personal and environmental factors during the assessment session may also have contributed to variability in time taken to complete the T-ACE-III. However, since the T-ACE-III showed a high level of diagnostic accuracy for dementia, which was superior to those of MMSE and CASI and took shorter time to administer than CASI, the T-ACE-III would appear to be a promising screening tool for detecting dementia in a Taiwan population.

In conclusion, the T-ACE-III is a valid, reliable, and effective tool to diagnose dementia with a very high AUC in ROC analysis and is relatively quick compared to current test batteries. It has greater validity in differentiating dementia from non-dementia compared to currently used tests so it may prove to be the test of choice in clinical settings in Taiwan in view of its ease of administration and accuracy.

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Conflict of Interest

None declared.

Authors' Contributions

Ruan-Ching Yu, Naaheed Mukadam, Narinder Kapur, Joshua Stott, Gill Livingston did the conceptualization and design, analysis and interpretation of data, and preparation of manuscript. Chaur-Jong Hu, Chien-Tai Hong, Cheng-Chang Yang, Lung Chan, Li-Kai Huang did the reading and commenting on manuscript, provision of suggestion on literature review and discussion.

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University College London (UCL).

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Appendix 1. Cut-off scores for the T-ACE-III (adjusted) in differentiating dementia from non-dementia

Cut-off scores	Sensitivity	Specificity	Youden Index
73/74	0.895	1.000	0.895
74/75	0.895	0.970	0.864
75/76	0.912	0.970	0.882
76/77	0.930	0.970	0.900
77/78	0.947	0.970	0.917
78/79	0.965	0.939	0.904
80	0.965	0.909	0.874
82/83	0.965	0.879	0.844
83/84	0.982	0.848	0.831
84/85	0.982	0.818	0.801
85/86	0.982	0.788	0.770
86/87	1.000	0.788	0.788