

Validation of Brain Health Test-7 for Detecting Patients with Mild Cognitive Impairment and Early Dementia

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Abstract

Objectives: We intended to develop a simple dementia screening tool to help primary care physicians identify patients with mild cognitive impairment (MCI) and early dementia. **Methods:** The brain health test-7 (BHT-7) was developed based on the original BHT study. Study patients aged 50 years and above with normal cognition, MCI, and dementia were recruited. All patients received evaluation with the BHT-7, mini-mental state examination (MMSE), Montreal cognitive assessment (MoCA), and clinical dementia rating (CDR) for cognitive function. The performance of BHT-7 in identifying cognitive impairment was compared with that of MMSE and MoCA. **Results:** We enrolled 376 study participants. The mean BHT-7, MMSE, and MoCA scores showed significant differences among the three groups. Compared to MMSE and MoCA, the BHT-7 (sensitivity = 86%, specificity = 76%, area under curve = 88%) showed better sensitivity in differentiating MCI from the normal group, with a cutoff value of 17/18. The scores of the three tests were all affected by educational level. **Conclusion:** The BHT-7 is a simple and easy-to-use cognitive screening tool that may be useful in primary care settings to identify patients with MCI or early dementia.

Key words: Mini-Mental State Examination, Montreal Cognitive Assessment, screening, the elderly
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Introduction

Dementia that is a progressive condition of brain diseases, displays many cognitive deficits and affected daily function. According to Taiwan's Ministry of the Interior, Taiwan has become an "aged society" as the total population of older people over 65 years surpassed 14% at the end of March 2018, with about 18% of them diagnosed with mild cognitive impairment (MCI) and 7% with dementia [1]. The rate of Taiwanese older population is estimated to exceed 21% and enters a "super-aged society" in 2026. The size of the dementia population is increasing years by years. Thus, early detection and prevention are helpful in giving timely intervention and saving medical expenses.

Dementia is under-diagnosed in community and medical settings, especially those with mild dementia [2]. Although

many factors are affecting the diagnosis of dementia, a simple cognitive screening tool can help primary care physicians detect patients with cognitive impairment [3]. Many cognitive assessment tools exist in screening patients with dementia. The most widely used cognitive tests are mini-mental state examination (MMSE)[4] and Montreal cognitive assessment (MoCA) [5]. MMSE is commonly given for assessing cognitive impairment but is remarkably influenced by age and educational level and is not sensitive for the identification of MCI [6, 7]. MoCA is a sensitive screening tool to detect MCI and early dementia, but the cutoff values vary cross-culturally and even within the same region [8-11].

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Meanwhile, it needs a longer time of up to 10–15 minutes for administration [10–12]. Moreover, the above-mentioned cognitive assessment tools have been developed in Western countries.

Due to a lack of cognitive assessment tools specially designed for the broad ethnic Chinese population, experts from the tripartite psychogeriatric meeting (including Hong Kong, Taiwan, and China) decided to develop a cognitive tool that is suitable for ethnic Chinese people. In recent studies, two new cognitive tests were developed for screening cognitive impairment in Hong Kong and Taiwan. In its first report, Hong Kong brief cognitive (HKBC) test has shown promising results (area under the curve [AUC] = 95.5%) in detecting mild neurocognitive disorder (NCD) and major NCD in Chinese elders, including those with low educational level [13]. Meanwhile, the brain health test (BHT) has been developed in Taiwan and has shown good sensitivity (91.5%) for differentiating dementia from the cognitively normal (CN) group but is not effective in separating the CN from the MCI group [14].

In this study, we intended to develop a simple cognitive screening tool with further modification of the original BHT to help primary care physicians identify patients with MCI and early dementia among patients with memory complaints or at risk for dementia.

Methods

Study design

This study was carried out in the Department of Psychiatry of National Taiwan University Hospital (NTUH). CN subjects, subjects with MCI, and subjects with dementia were enrolled to test the sensitivity and specificity of a newly developed 7-item cognitive screening tool, the BHT-7. Most of the subjects were recruited from the NTUH psychiatry clinics, with a few CN subjects recruited from a community center.

Study participants

The general inclusion criteria were patients with (a) age ≥ 50 years, (b) no evidence of major surgery, obvious neurological diseases, or major psychiatric disorders (such as schizophrenia, bipolar disorder, and obsessive-compulsive disorder), (c) no obvious brain injury, and (d) no substance (including alcohol) abuse or dependence within one year. Excluded were those (a) with major physical illness (such as acute coronary syndrome, cancer, and acute stroke) or major psychiatric disorders in recent two months, (b) having major depressive disorder within one year, and (c) having severe visual or hearing impairment.

For subjects with dementia and MCI, they should have subjective or objective memory complaints, and the diagnosis had to be made by specialists according to the *DSM-5* criteria, but subjects with a score of clinical dementia rating (CDR) = 3 were excluded. Subjects in the dementia group should meet the criteria of major NCD, showing an obvious cognitive decline from previous level of performance

in any cognitive domains which affected daily activities. While the MCI group should fit in diagnostic criteria of mild NCD with the modest cognitive decline from previous cognitive function, their instrumental activities of daily living (IADL) function could be preserved. For the CN group, subjects should meet CDR = 0 or subjective memory complaints but should not have any objective impairment in all cognitive domains, while ADL and IADL are fully independent.

The institutional review board of the NTUH approved this study (IRB protocol number = 201708078RINA and date of approval = October 9, 2017), and all subjects signed informed consent. For patients with dementia, informed consent was also signed by their proxy. The study participants were enrolled between November 2017 and February 2020.

Assessment tools

Brain health test-7

BHT-7 is based on the original BHT cognitive test [14]. We have added visuospatial construction and frontal lobe function tests in the BHT-7. The cognitive test includes the orientation to time, immediate and delayed recall of five items, categorical verbal fluency test (listing four-legged animals in 1 min), visuospatial construction (cube drawing and clock drawing test), and frontal lobe function test (Luria's hand test) (Table 1). The total score of BHT-7 is 23, and it takes 5–7 min to administer.

Montreal cognitive assessment

MoCA test [5, 10] includes the visuospatial/executive functions, naming verbal memory registration and learning, attention, abstraction, delayed recall, and orientation. The MoCA takes about 10–15 min to administer, and the total score is 30 points.

Mini-mental state examination test

MMSE [4, 6] includes orientation, immediate memory, short-term memory, and language. The MMSE takes about 10 minutes to administer, and the total score is 30 points.

Clinical dementia rating

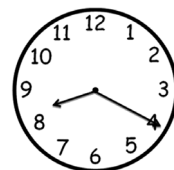
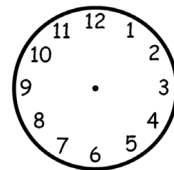
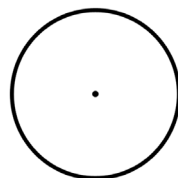
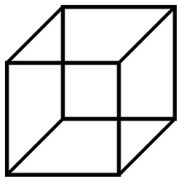
CDR [15, 16] is a structured, clinician-rated interview that evaluates cognitive function by collecting information from the patient and caregiver. The six domains include memory, orientation, judgment and problem-solving, community affairs, home and hobbies, as well as personal care. Besides the BHT-7, the MMSE, MoCA, and CDR were assessed for all subjects.

Statistical analysis

Demographic data (age, gender, and education levels) and the scores of the BHT-7, MoCA, and MMSE were described for the overall sample as well as individual groups. Continuous data were presented as means \pm standard deviation and categorical data shown as number (%). Analysis of variance was done for continuous variables among the three groups, and the Chi-square test was used for categorical variables. We analyzed the receiver operating characteristic (ROC) curve with logistic regression. The AUCs, optimal cutoff values,

Table 1. Brain health test-7

Items	Questions	Score
Orientation	“What is the year? Date? Day of the week?” _____ year, _____ month, _____ day, _____ week	/4
Immediate memory	“Please repeat the five words that I said” (<i>only allocate scores for each word the subject responses on first trial, you can only teach it four times if the subject cannot repeat five words correctly</i>)	/5
	Tooth Wool School Daisy Red	
Verbal fluency	“Say as many four-legged animals as you can” (1 minute)	≥ 9 words 2
	_____	5-8 words 1
	_____	< 5 words 0
Delayed recall	“Earlier I told you the names of five things. Can you tell me what those were?”	/5
	Tooth Wool School Daisy Red	
Cube	“Copy this drawing as accurately as you can in the space below”	Time: _____
		≤ 15 s 2
		> 15 s 1
Clock	“I would like you to draw a clock, put in all the numbers, and set the hands for 10 after 11”	/2
	“Please tell me what time it is?”	/1
Luria’s hand	“Pay attention and look carefully at what I am doing”	/1
	→Palm-edge-fist	
	“Now, with your hand do the same series, first with me, then alone”	
	“Now, do it on your own in three times”	/1
	Total score	/23



sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were provided using the

ROC curve module. We also did correlation analyses for the criterion validity of BHT-7.

All study variables were computed using Statistical Analytic System software version 9.4 (SAS Institute Inc., Cary, North Carolina, USA). The differences between the groups were considered significant if p (two-tailed) < 0.05 .

Results

In this hospital-based study, we recruited 376 study participants. Among them, 305 were patients from outpatient clinics of the Department of Psychiatry, NTUH, and the other 71 were recruited from the community outside of NTUH. Table 2 presents the demographic variables in all the three groups. The participants were female predominant (66%). The mean age was 70 years, and only 98 (26%) of the total participants were with a low educational level (equal or less than six years). In dementia group, 29% of the patients were with CDR 0.5, 60% of the patients CDR 1, and 11% of the patients CDR 2. Significant difference existed in age ($p < 0.001$) and years of education ($p < 0.001$), as well as the scores of BHT-7 ($p < 0.001$), MMSE ($p < 0.001$), and MoCA ($p < 0.001$) among the three groups. The dementia group was significantly older ($p < 0.05$) and with a lower educational level ($p < 0.05$). The total scores of BHT-7, MMSE, and MoCA were significantly lower in the dementia group, compared with that of the other two groups ($p < 0.05$).

Table 3 shows the comparison of BHT-7, MMSE, and MoCA performance among those three groups. With the cutoff value set to 17/18, the BHT-7 had the best sensitivity in differentiating MCI from the CN group (sensitivity = 86%, specificity = 76%, AUC = 88%, PPV = 63%, NPV = 92%) and the highest AUC value = 0.881, but the specificity was slightly lower. Meanwhile, BHT-7 had the highest sensitivity and AUC in differentiating MCI from the dementia group with a cutoff score of 11/12 (sensitivity = 90%, specificity = 81%, AUC = 89%, PPV = 86%, NPV = 85%). Overall, the BHT-7 was a promising cognitive assessment tool for both MCI and dementia. No much difference existed in differentiating dementia from the CN group among the three tests.

Table 4 shows the results of the subgroup analysis of high and low education levels. The optimal cutoff value of BHT-7

in differentiating MCI subjects from CN and the dementia group showed a one-point difference between the two different educational levels. But education level was to influence the BHT-7 optimal cutoff value more in differentiating dementia from the CN group, with a difference of three of the cutoff value. Besides, the cutoff scores of MoCA were also markedly affected by the educational level, with a difference of 3–5 of the cutoff value between the high and low educational levels. In contrast, MMSE was less influenced by educational level, with a difference of 1–2 of the cutoff value between the high and low educational levels.

We further examined the correlations between BHT-7, MMSE, and MoCA scores as a way to verify the criteria validity of the BHT-7. A high correlation existed between BHT-7 and MMSE score ($r = 0.833$, $p < 0.001$) and between BHT-7 and MoCA score ($r = 0.908$, $p < 0.001$).

Discussion

A simple and effective cognitive screening tool warrants the ability to detect early-phase dementia. Early detection and diagnosis allow an opportunity for timely intervention by providing proper education, psychosocial support, appropriate healthcare, and financial plan. The main findings of this study were (a) BHT-7 performed relatively better than MoCA or MMSE in differentiating MCI from CN and (b) education had significant effect on the scores of those three tests.

BHT-7 was sensitive in detecting MCI. Although the original BHT had good sensitivity (91.5%) for differentiating dementia from the CN group, it was not effective to separate the CN from the MCI group, with an AUC of 0.721. After the revision of the original BHT by adding cube drawing, clock drawing, and Luria's hand test, the BHT-7 showed improved sensitivity (86%) and AUC (88%) in differentiating the CN from MCI group. The total administration time was about 5–7 minutes, which is slightly longer than that of the original BHT cognitive test (about 4 minutes) [14].

In our study, BHT-7 was slightly superior as an MCI screening tool (AUC = 0.88, sensitivity = 0.86) compared to MMSE (AUC = 0.80, sensitivity = 0.62) and MoCA (AUC = 0.86, sensitivity = 0.76). The sensitivity and

Table 2. The demographic and cognitive characteristics of the three groups

	CN [§] ($n = 205$) Mean \pm SD	MCI ($n = 99$) Mean \pm SD	Dementia ($n = 72$) Mean \pm SD	P	Post hoc analysis*
Age, years	65.9 \pm 10.6	72.8 \pm 7.9	78.3 \pm 9.3	< 0.001	CN $<$ M $<$ D
Gender, n (%)					
Male	72 (35.1)	33 (33.3)	23 (31.9)		
Female	133 (64.9)	66 (66.7)	49 (68.1)	NS	
Years of education	12.2 \pm 3.8	9.2 \pm 4.6	9.1 \pm 5.1	< 0.001	CN $>$ M, CN $>$ D
≤ 6	28 (13.7)	42 (42.4)	28 (38.9)		
> 6	177 (86.3)	57 (57.6)	44 (61.1)	< 0.001	
BHT-7 score	18.8 \pm 2.2	14.8 \pm 2.8	8.1 \pm 4.4	< 0.001	CN $>$ M $>$ D
MMSE score	28.0 \pm 1.7	25.1 \pm 3.3	18.8 \pm 5.1	< 0.001	CN $>$ M $>$ D
MoCA score	26.3 \pm 2.6	21.5 \pm 3.9	13.3 \pm 5.5	< 0.001	CN $>$ M $>$ D

* $p < 0.05$ using ANOVA.

[§]CN, Cognitively normal; MCI, Mild cognitive impairment; D, Dementia; BHT-7, Brain health test-7; MMSE, Mini-mental state examination; MoCA, Montreal cognitive assessment; SD, Standard deviation; NS, Not significant; ANOVA, Analysis of variance

Table 3. Comparison of brain health test-7 score with mini-mental state examination and Montreal cognitive assessment score between different groups

	AUC	Cutoff	SEN	SPE	PPV	NPV
MCI versus CN						
BHT-7	0.881	≧ 17	0.86	0.76	0.63	0.92
MMSE	0.801	≧ 26	0.62	0.85	0.66	0.82
MoCA	0.859	≧ 24	0.76	0.78	0.63	0.87
MCI versus dementia						
BHT-7	0.889	≧ 12	0.90	0.81	0.86	0.85
MMSE	0.869	25	0.66	0.93	0.93	0.66
MoCA	0.891	≧ 18	0.88	0.76	0.84	0.82
Dementia versus CN						
BHT-7	0.983	≧ 13	0.88	0.99	0.97	0.96
MMSE	0.982	≧ 24	0.93	0.96	0.89	0.98
MoCA	0.988	≧ 20	0.93	0.97	0.92	0.98

CN, Cognitively normal; MCI, Mild cognitive impairment; AUC, Area under the curve; SEN, Sensitivity; SPE, Specificity; PPV, Positive predictive value; NPV, Negative predictive value; BHT-7, Brain health test-7; MMSE, Mini-mental state examination; MoCA, Montreal cognitive assessment

AUC were quite similar between BHT-7 and MoCA test in detecting MCI from dementia group. The reasons that both BHT-7 and MoCA tests are sensitive in detecting MCI may be due to their having more items sensitive to detect frontal lobe and memory dysfunctions, which are associated with a better discriminative ability in identifying MCI [10]. But BHT-7 is less time-consuming than MoCA and MMSE.

Table 1 shows that the mean MMSE score was 25.1 for the MCI group and 18.8 for the dementia group, and the mean MoCA score was 21.5 for the MCI group and 13.3 for the dementia group. These mean scores are higher than those of the three recent studies in Hong Kong and Taiwan on the validation of the Chinese version of MoCA [10-13]. The findings may be related to the different mean educational levels in our study and the other three studies. The current study was based mainly on the NTUH sample, which was composed of subjects with higher socioeconomic status, and the proportion of subjects with an educational level higher than six years was 74%.

The effect of education level was also reflected in significantly higher cutoff values ($p < 0.001$) in our study (Table 2) versus the other studies. For example, the cutoff value of MMSE in our study was 24/25 in detecting dementia from CN group. This finding in MMSE is higher than that in the study of Chiu et al. [13]. Moreover, the cutoff value of MoCA in our study (24/25) in differentiating the MCI from CN group is higher than that of the other Taiwanese study [10]. The results of our study are similar to previous studies as educational level had a remarkable effect on the scores of MoCA and MMSE [6, 10]. The effect of education level is more evident in MoCA as the sensitivity and AUC of MoCA for differentiating dementia from the CN and MCI groups improved significantly after education-adjusted cutoff values were applied. Although education level only had a slight effect on the cutoff score of

Table 4. Comparison of the performance of brain health test-7, mini-mental state examination, and Montreal cognitive assessment among subjects with different education level

	AUC	Cutoff	SEN	SPE	PPV	NPV
≧ 6 years						
MCI versus CN						
BHT-7	0.842	≧ 16	0.83	0.75	0.83	0.75
MMSE	0.810	≧ 25	0.64	0.86	0.87	0.62
MoCA	0.872	≧ 20	0.71	0.89	0.91	0.68
MCI versus dementia						
BHT-7	0.932	≧ 12	0.86	0.93	0.95	0.81
MMSE	0.880	≧ 22	0.79	0.86	0.89	0.73
MoCA	0.907	≧ 16	0.93	0.86	0.91	0.89
Dementia versus CN						
BHT-7	0.983	≧ 11	0.93	1.00	1.00	0.93
MMSE	0.997	≧ 23	1.00	0.93	0.93	1.00
MoCA	0.984	≧ 18	0.96	1.00	1.00	0.97
> 6 years						
MCI versus CN						
BHT-7	0.869	≧ 17	0.81	0.79	0.55	0.93
MMSE	0.767	≧ 26	0.53	0.88	0.58	0.85
MoCA	0.830	≧ 25	0.79	0.70	0.46	0.91
MCI versus dementia						
BHT-7	0.878	≧ 13	0.88	0.80	0.85	0.83
MMSE	0.895	≧ 24	0.84	0.82	0.86	0.80
MoCA	0.925	≧ 21	0.84	0.91	0.92	0.82
Dementia versus CN						
BHT-7	0.981	≧ 14	0.86	0.98	0.93	0.97
MMSE	0.974	≧ 24	0.89	0.97	0.87	0.97
MoCA	0.988	≧ 21	0.93	0.97	0.89	0.98

CN, Cognitively normal; MCI, Mild cognitive impairment; AUC, Area under the curve; SEN, Sensitivity; SPE, Specificity; PPV, Positive predictive value; NPV, Negative predictive value, BHT-7, Brain health test-7; MMSE, Mini-mental state examination; MoCA, Montreal cognitive assessment

BHT-7 in detecting MCI, it should be adjusted for the optimal cutoff values in differentiating dementia group from CN group. The HKBC test has been found to have less educational bias for detecting Chinese elders with cognitive impairment in Hong Kong, but the finding has not been replicated in Taiwan or other countries [13].

Our BHT-7 and the HKBC test are both effective in detecting MCI patients [13]. When the cognitive domains of the two tests are compared, both have similar cognitive tests, and the BHT-7 contains 6 out of 9 questions of the HKBC test. This may explain why the two newly developed screening tools performing well in identifying subjects with MCI.

Study limitations

The study results should be interpreted with caution because our study has three limitations:

- Most of our participants were recruited from the NTUH.
- The sample size was relatively small compared to previous

studies.

- The assessment tool was not designed to differentiate different kinds of dementia subtypes.

Summary

In this study, the BHT-7 was shown to be a simple and easy-to-use cognitive screening tool that may be useful in primary care settings to identify patients with MCI or early dementia. Future studies with a larger sample size to further validate our findings and test its generalizability are warranted.

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Conflicts of Interest

None.

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