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Utility of the AD8 as a Self-Rating Tool for Cognitive Impairment in an Asian Population

Rowena Chin, BA[1], Amanda Ng, MSc[1], Kaavya Narasimhalu, PhD[1], and Nagaendran Kandiah, MRCP[1]

Abstract

Background: AD8 is a brief informant interview used to detect early cognitive change. This study evaluated the diagnostic performance of the participant-rated AD8 (p-AD8) in a predominantly Chinese population. **Methods:** Data on demographics, clinical, and cognitive features were collected from 73 participants with no cognitive impairment (NCI), 27 participants with mild cognitive impairments, and 78 participants with Alzheimer's disease–informant dyads. Agreement and discriminative properties of p-AD8 were assessed. **Results:** AD8 scores were associated with dementia severity. Participant and informant AD8 scores were moderately correlated within dementia dyads. The p-AD8 showed good diagnostic performance in differentiating between participants with NCI and participants with cognitive impairment (sensitivity = 85.0%, specificity = 74.0%, and area under the curve = 0.80), with a cutoff score of $\geq$1. Combination of impairment in Mini-Mental State Examination and p-AD8 is more useful in detecting cognitive impairment than using the AD8 alone. **Conclusion:** Within a transcultural setting, the p-AD8 demonstrated good discriminative validity and can be used to gain a preliminary understanding of an individual's cognitive status.

Keywords

Alzheimer's disease, cognitive disorders, MCI (mild cognitive impairment), screening

Introduction

The global prevalence of Alzheimer's disease (AD) is expected to dramatically increase by 2050, with Asia estimated to account for 59% of the worldwide cases.[1] The increasing prevalence of cognitive impairment in the general population demands the need for early intervention and treatment. However, the disease remains underdiagnosed due to the lack of sensitive and reliable clinical tools.

In most clinic settings, performance-based assessments are typically administered to evaluate the cognitive status of the patient. However, limitations exist. The Mini-Mental State Examination (MMSE)[2] has a ceiling effect that makes it less sensitive in detecting early cognitive impairment,[3] particularly in highly educated individuals.[4] Other tests such as the Montreal Cognitive Assessment (MoCA)[5] may be more time intensive and therefore inappropriate for use in primary care settings.

Informant-based assessments are shown to be more sensitive to early cognitive change than performance-based tests. They possess longitudinal perspective and face validity, and its usage has been well established in AD clinical trials.[6-9] Confounding factors that may influence interpretation of results, such as practice effects, educational, and sociocultural influences, are kept minimal.[8,9] However, most informant-based assessments are lengthy and require interpretation by an experienced clinician, making it difficult to use in community practice. Given the limited duration of visits available to physicians in primary care centers, a brief screening tool capable to screen dementia, especially in its early stages, is necessary to meet wider needs of the community.

It is crucial to note that in general practice, a reliable informant may not always be available, especially in cases of lesser severity of impairment. Hence, with the use of a brief informant-based interview, we aimed to investigate the capability of patients to rate changes in their own cognitive abilities.

The AD8 interview[10] is a brief dementia screening tool that is shown to be sensitive to early cognitive change. The informant-rated AD8 (i-AD8) has been translated and validated in Asian populations belonging to Korea and Taiwan.[11,12] However, an informant may not be present during visits, especially in cases of milder impairment. The participant-rated AD8 (p-AD8) is shown to be useful in a Western study,[13] although not investigated in an Asian population. In this study,

[1] Department of Neurology, National Neuroscience Institute, Singapore

Corresponding Author:
Nagaendran Kandiah, MRCP, National Neuroscience Institute, 11 Jalan Tan Tock Seng, Singapore 308433.
Email: Nagaendran_Kandiah@nni.com.sg

we examine the application of p-AD8 in an Asian population for the detection of early dementia.

Methods

Patient Population

Data from healthy controls and patients with Mild Cognitive Impairment (MCI) and AD were studied. Participants with no cognitive impairment (NCI) were recruited from a community screening event in September 2011, while patients with MCI and AD were recruited from the Memory and Dementia Clinic at the National Neuroscience Institute between January and September 2011. Data on demographics and cognitive scores were collected. Approval from the Centralized Institutional Review Board was received, and written consent was obtained from the patients or his/her legal guardians.

Cognitive Assessment

Cognitive assessments including locally validated MMSE[14] and the MoCA[15] were administered to all participants. The Clinical Dementia Rating (CDR)[6] was used to quantify dementia severity, and the Instrumental Activities of Daily Living Scale (IADL)[16] measured functional status of the participants. The Geriatric Depression Scale (GDS)[17] score of $\geq$5 was used to exclude patients with depression, in both the clinic and the community cohorts.

The participant with NCI had a CDR score of 0 and a MMSE score of 27 to 30 (inclusive). In addition, participants with NCI had to be deemed cognitively normal based on the absence of significant impairment in cognitive functions or IADL, following review by a clinician. Patients with MCI were diagnosed based on Peterson's criteria.[18,19] They had subjective memory complaints, and their cognitive symptoms were corroborated by a reliable caregiver. They also had impaired memory function for age and education, a CDR of 0.5, and preserved activities of daily living. They did not fulfill National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA)criteria[20] for dementia. No patients with nonamnestic single domain MCI were included in this study. Patients with AD fulfilled the NINCDS-ADRDA criteria and had a CDR of 1 or more. Collateral history was obtained from a reliable caregiver. In this study, participants with AD were also categorized into dementia severity groups (mild, moderate, and severe), utilizing scores from the CDR and IADL. The clinician had access to scores of the MoCA, CDR, and GDS but was blinded to AD8 and MMSE scores for all groups of patients.

The AD8 was administered in English. For non-English speaking patients, appropriate translation was performed utilizing cross-cultural adaptation measures.[21] The only non-English speaking group was the Mandarin speakers. The same version of AD8 was used for the Mandarin-speaking patients, and direct verbal translation into Mandarin was done by the same rater to ensure consistency. The participants with NCI and MCI had the AD8 administered to the participant alone (p-AD8), while patients with AD had the AD8 administered to both the participant (p-AD8) and to their primary caregiver (i-AD8).

Statistical Analyses

Statistical analyses were performed using Stata 11.0 (StataCorp, College Station, Texas). Due to heterogeneity in the variances, the Kruskal-Wallis' test was used in comparing AD8 scores between participants with NCI, MCI, and AD. Post hoc Wilcoxon's rank-sum with Bonferroni's correction was performed to assess comparisons in a group-by-group basis. Agreement between the patient and the caregiver was measured with intraclass correlation coefficients. Correlations between pAD8 and iAD8 scores with performance-based tests (MMSE and MoCA), and the GDS was determined using Spearman's ρ correlation coefficients. Significance was determined as a 2-tailed α of 0.05. Receiver–operator characteristic curves were used to determined cutoff points for the AD8 as well as to compare the AD8 with the MMSE and the MoCA. Logistic regression analyses were performed to determine the additive benefit of AD8 to the MMSE.

Results

A total of 73 participants with NCI, 27 patients with MCI, and 78 patients with AD–informant pairs were recruited into this study. The mean age for the participants was 66.7 $\pm$ 10.8 years with a mean educational attainment of 8.77 $\pm$ 4.9 years. Females made up 66.9% of the sample. The sample consisted of 87.1% Chinese, 6.7% Indian, 3.4% Malay, 1.1% Eurasian, and 1.7% listed as others. The participants were categorized according to cognitive status ranging from NCI (41%), MCI (15%), mild AD (26%), and moderate to severe AD (18%).

The top 3 items from the p-AD8 which constituted as the most common complaints for the cognitively impaired group (MCI and AD) were: "Daily problems with thinking and/or memory" (55.8%), "Forgets correct month or year" (52.5%), and "Trouble learning how to use a tool, appliance or gadget" (49.2%).

Table 1 is an overview of the participant demographics and test scores according to a classification based on dementia severity. Among patients with AD, the difference between mean p-AD8 scores and mean i-AD8 scores were greater in patients with moderate to severe AD compared to patients with mild AD. The p-AD8 was significantly different across groups (chi-square [3, N = 178] = 44.2, P =.0001). The p-AD8 was able to differentiate between participants with NCI and MCI (P < .0001), but no significant differences were found between MCI and mild AD or between mild and moderate to severe AD. However, the i-AD8 was able to differentiate between mild AD and moderate to severe AD groups (P < .0001, r = .62).

There was adequate agreement in p-AD8 and i-AD8 for all patients with AD (intraclass correlation coefficient, 0.54; 95% confidence interval [CI], 0.43-0.66). This agreement was stronger in patients with mild AD (intraclass correlation coefficient, 0.76; 95% CI, 0.58-0.87). Table 2 shows the correlations

Table 1. Demographics and Cognitive Scorings by Classification of Cognitive Impairment.

	NCI (n = 73)	MCI (n = 27)	Mild AD (n = 46)	Moderate to severe AD (n = 32)	*P* value
Females (n, %)	47, 64.4%	16, 59.3%	32, 70.0%	24, 75.0%	.304
Age (mean ± SD) years	58.6 ± 4.8	61.9 ± 9.0	74.3 ± 8.0	77.9 ± 7.8	<.0001
Education (mean ± SD) years	11.5 ± 3.2	11.4 ± 3.5	5.93 ± 4.7	4.39 ± 3.8	<.0001
MMSE	28.9 ± 1.5	28.2 ± 2.0	22.7 ± 4.5	12.4 ± 3.9	<.0001
MoCA	27.8 ± 2.5	27.2 ± 2.6	21.0 ± 5.1	9.0 ± 2.8	<.0001
p-AD8	1.20 ± 1.7	2.70 ± 1.9	2.91 ± 1.4	2.69 ± 1.4	<.0001
i-AD8	NA	NA	4.37 ± 1.8	6.81 ± 1.3	<.0001

Abbreviations: MMSE, Mini-Mental State Examination; MoCA, Montreal cognitive assessment; p-AD8, participant-rated AD8; i-AD8, informant-rated AD8; NA, not available; SD, standard deviation.

Table 2. Correlations Between Both Informant- and Participant-Rated AD8 and Assessment Variables in Patients With Mild and Moderate to Severe AD.

	Informant AD8		Participant AD8	
Variable	Spearman's ρ	*P* value	Spearman's ρ	*P* value
MMSE	−0.63	<.0001	−0.32	.006
MoCA	−0.68	<.0001	−0.42	.001
GDS	0.14	.36	0.11	.48

Abbreviations: MMSE, Mini-Mental State Examination; MoCA, Montréal cognitive assessment; GDS, geriatric depression scale.

Table 3. Psychometric Properties of the Participant-Rated AD8 Using Different Cutoffs to Discriminate Between Participants With NCI and Cognitive Impairment and Participants With NCI and MCI.

NCI vs CI p-AD8 Score	Sensitivity, %	Specificity, %	PPV, %	NPV, %
1	85	74	82	78
2	73	80	84	67
3	59	85	85	59
NCI vs MCI p-AD8 score	Sensitivity, %	Specificity, %	PPV, %	NPV, %
1	84	65	78	74
2	67	78	81	62
3	55	83	82	56

Abbreviations: p-AD8, participant-rated AD8; NCI, no cognitive impairment; MCI, mild cognitive impairment; CI, cognitively impaired; NPV, negative predictive value; PPV, positive predictive value.

between both p-AD8 and i-AD8 scores with the MMSE and the MoCA. The i-AD8 showed stronger correlation with the MMSE and the MoCA. No significant correlation was found between AD8 and GDS.

Table 3 summarizes the results of receiver–operating curve analysis to determine the optimal cutoff. The p-AD8 had the best combination of sensitivity = 85%, specificity = 74%, and area under the curve (AUC) 0.80, with a cutoff score of 1.

The p-AD8 was also effective in discriminating individuals without dementia from those with MCI (sensitivity = 84%, specificity = 65%, and AUC = 0.76). The p-AD8 was a more sensitive tool as compared to cognitive tests such as the MMSE (AUC = 0.62) or the MoCA (AUC = 0.59) in earlier stages of cognitive impairment (Table 4). When utilized to discriminate between stages of severity in patients with dementia (eg, between mild AD and moderate AD), the p-AD8 was not as effective as the use of the MMSE or MoCA. However, the i-AD8 was shown to be a relatively good discriminative tool in differentiating between mild AD and moderate to severe AD (AUC = 0.86).

In multivariate analyses adjusting for age and education, the combination of impairment in both the AD8 and the MMSE (odds ratio [OR], 223.12; CI, 38.73-1285.33) was significantly better at detecting any cognitive impairment than impairment in AD8 only (OR, 8.99; CI, 2.90-27.80) but not better than impairment in MMSE alone (N = 3, all 3 impaired).

Discussion

In the absence of an informant, the p-AD8 has shown to be effective in differentiating individuals with MCI from individuals without dementia. The current study demonstrates that as previously depicted in a Western population,[13] the self-rated AD8 is a valid tool for self-rated cognitive status in an Asian population. When administered to patient with dementia–caregiver dyads, the self-rated AD8 showed adequate agreement with that of the informant's AD8 ratings. The self-rated AD8 also corresponded to global cognitive assessments such as the MMSE. Consistent with the original study,[13] the optimal cutoff value of the self-rated AD8 was found to be 1.

The top 3 items from the p-AD8 which constituted as the most common concerns for the cognitively impaired group (MCI and AD) were found to be memory-related components of the AD8. Such subjective memory complaints have been postulated as early precursors of future cognitive decline and may also be associated with negative effect.[22,23]

The consistency of results obtained in this study suggests that the self-rated AD8 was not overly influenced by the difference in cultural backgrounds. This similarity may be due to the objective nature of the AD8 which is not likely to be influenced by age, education, or cultural differences.[24] Its usefulness also lies in the neutrality of questions which is unlikely to incite distress. Although the i-AD8 has been validated in both Korean and Taiwanese populations, to our knowledge, this is the first study of the p-AD8 within an Asian population. The usefulness of the AD8 in an Asian population is important and different from previous studies in Western populations as it involves

Table 4. Sensitivity, Specificity, and AUC for the MMSE, the MoCA, and the p-AD8.

Variable	Categorization	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV
MMSE	Cognitively Impaired	0.86 (0.80-0.92)	0.91	0.73	0.83	0.85
	MCI	0.62 (0.50-0.74)	0.33	0.84	0.75	0.47
MOCA	Cognitively Impaired	0.78 (0.70-0.86)	0.89	0.62	0.77	0.80
	MCI	0.59 (0.45-0.73)	0.80	0.36	0.64	0.55
p-AD8	Cognitively Impaired	0.80 (0.74-0.86)	0.85	0.74	0.82	0.78
	MCI	0.76 (0.67-0.85)	0.84	0.65	0.78	0.74

Abbreviations: MMSE, Mini-Mental State Examination; MoCA, Montréal cognitive assessment; p-AD8, participant-rated AD8; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; AUC: area under the curve; MCI, mild cognitive impairment.

cultural differences between Western and Asian populations. The structured nature of the AD8 might help in circumventing this problem as the test gives scaffolding for the caregiver to accurately relate cognitive and functional deficiencies to the clinician.

The p-AD8 has also shown to be a more sensitive tool as compared to the MMSE and the MoCA in discriminating between cognitively normal and those with very MCI. This could be attributed to possible ceiling effects[3] in patients with advanced education,[4] with the usage of performance-based tests such as the MMSE. The AD8, unlike these cognitive tests, is unlikely to be influenced by education levels as it compares the participant's current cognitive status to his previous cognitive status. However, as the AD8 was designed to be a screening tool sensitive to early cognitive impairment, it may not differentiate as well between mild, moderate, and severe dementia. This is particularly relevant in the p-AD8, because patients in more severe stages of dementia are unlikely to identify more dementia symptoms due to diminishing insight.[25] Due to the development of cognitive anosognosia[26] as the disease progresses, denial of cognitive deficits[27] may lead to widening discrepancies between self-assessment and information provided by the informants. Hence, it has been reflected in this study that as severity of dementia increases, the MMSE and the MoCA become more effective than the p-AD8 in classifying individuals. Thus, the utility of the AD8 as a self-reporting measure may be greater in individuals with very mild impairment as compared to more individuals with dementia.[13] In addition, when the AD8 was combined with the MMSE, a significant increase in the ability to detect MCI was observed. This increase in detection rate reflects the usefulness of combining subjective symptoms with objective cognitive evaluation.

A comparison within the participant with AD –informant dyads revealed that the i-AD8 was found to have stronger correlations with the MMSE and the MoCA as compared to the p-AD8, suggesting that participants may have underestimated their cognitive deficits. The i-AD8 was also found to possess sensitivity in differentiating between early dementia and later stages of dementia. This emphasizes the role of caregivers in providing reliable accounts of memory and functional changes in patients.

There are limits to this study. The sample is a convenience cohort recruited from both a screening event and a memory clinic. Hence, it may not be representative of the general population. In addition, almost all the cognitively normal and participants with MCI in our study were unaccompanied by an informant during their visit. Due to the resulting absence of i-AD8 data for the above-mentioned group, the effectiveness of i-AD8 cannot be excluded and needs to be investigated in future studies. Data on informant AD8 ratings were only available for patients with dementia presenting with greater cognitive impairment. However, we were still able to assess the general utility of the self-rated AD8 in comparison with other frequently utilized cognitive measures like the MMSE. In addition, agreement between self-rated AD8 and i-AD8 could still be assessed within patient with dementia–caregiver dyads. The effectiveness of the i-AD8 has also been well established in other Asian populations.[11,12]

Informant interviews are still preferable as they provide better reliability in determining cognitive and functional change in patients with dementia. However, in reality, informants are not always present at clinic visits. This is especially the case in patients with little cognitive impairment and who are still able to function independently. In the absence of an informant, the AD8 has been shown to be able to offer useful information regarding the patients' cognitive abilities. The demonstration of the effectiveness of the self-rated AD8 within a local Asian population supports its utility in cross-cultural settings. The AD8 may be a good preliminary screening tool for the early detection of dementia in both primary and community health care settings.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

1. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement*. 2007;3(3):186-191.

2. Folstein MF, Folstein SE, McHugh PR. Mini-Mental State: a practical method for grading the cognitive state of patients for the clinicians. *J Psychiatr Res*. 1975;12(3):189-198.
3. Lawrence J, Davidoff D, Katt-Lloyd D, Auerbach M, Hennen J. A pilot program of improved methods for community-based screening for dementia. *Am J Geriatr Psychiatry*. 2001;9(3):205-211.
4. Lorentz W, Scanlan J, Borson S. Brief screening tests for dementia. *Can J Psychiatry*. 2002;47(8):723-733.
5. Smith T, Gildeh N, Holmes C. The Montreal cognitive assessment: validity and utility in a memory clinic setting. *Can J Psychiatry*. 2007;52(5):329-332.
6. Morris JC. The Clinical Dementia Rating (CDR)—current version and scoring rules. *Neurology*. 1993;43(11):2412-2414.
7. Jorm A, Christensen H, Korten A, Jacomb PA, Henderson AS. Informant ratings of cognitive decline in old age: validation against change on cognitive tests over 7 to 8 years. *Psychol Med*. 2000;30(4):981-985.
8. Morris JC, Berg L, Coben LA, et al. Clinical dementia rating (CDR). In: Bergener M, Finkel SI, eds. *Treating Alzheimer's and Other Dementias: Clinical Applications of Recent Research Advances*. New York, NY: Springer, 1995:338-346.
9. Tierney MC, Herrmann N, Geslani DM, Szalai JP. Contribution of informant and patient ratings to the accuracy of the Mini-Mental State Examination in predicting probable Alzheimer's disease. *J Am Geriatr Soc*. 2003;51(6):813-818.
10. Galvin JE, Roe CM, Powlishta KK, et al. The AD8: a brief informant interview to detect dementia. *Neurology*. 2005;65(4): 559-564.
11. Ryu HJ, Kim HJ, Han SH. Validity and reliability of the Korean version of the AD8 informant interview (K-AD8) in dementia. *Alzheimer Dis Assoc Disord*. 2009;23(4):371-376.
12. Yang YH, Galvin JE, Morris JC, Lai CL, Chou MC, Liu CK. Application of AD8 questionnaire to screen very mild dementia in Taiwanese. *Am J Alzheimers Dis Other Demen*. 2011;26(2):134-138.
13. Galvin JE, Roe CM, Coats MA, Morris JC. Patient's rating of cognitive ability: using the AD8, a brief informant interview, as a self-rating tool to detect dementia. *Arch Neurol*. 2007;64(5):725-730.
14. Yeo D, Gabriel C, Chen CP, Lee SH, Loenneker T, Wong MC. Pilot validation of a customized neuropsychological battery in elderly Singaporeans (abstract). *Neurol J South East Asia*. 1997;2:123.
15. Ng A, Chew I, Narasimhalu K, Kandiah N. Montreal Cognitive Assessment is effective for the diagnosis of Mild Cognitive Impairment and Mild Alzheimer's disease in Singapore. *Singapore Med J*. In Press.
16. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS). Recent evidence and development of a shorter version. In: Brink TL, ed. *Clinical Gerontology: A Guide to Assessment and Intervention*. New York, NY: The Haworth Press, Inc, 1986:165-173.
17. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9(3):179-186.
18. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Kokmen E, Tangelos EG. Aging, memory, and mild cognitive impairment. *Int Psychogeriatr*. 1997;9(suppl 1):65-69.
19. Petersen RC. Mild cognitive impairment as a diagnostic entity. *J Intern Med*. 2004;256(3):183-194.
20. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34(7):939-944.
21. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. *J Clin Epidemiol*. 1993;46(12): 1417-1432.
22. Schmand BB, Jonker C, Hooijer C, Lindeboom J. Subjective memory complaints may announce dementia. *Neurology*. 1996; 46(1):121-125.
23. Jorm AF, Christensen H, Korten AE, Jacomb PA, Henderson AS. Memory complaints as a precursor of memory impairment in older people: a longitudinal analysis over 7-8 years. *Psychol Med*. 2001;31(3):441-449.
24. Galvin JE, Roe CM, Xiong C, Morris JC. Validity and reliability of the AD8 informant interview in dementia. *Neurology*. 2006; 67(11):1942-1948.
25. Akai T, Hanyu H, Sakurai H, Sato T, Iwamoto T. Longitudinal patterns of unawareness of memory deficits in mild Alzheimer's disease. *Geriatr Gerontol Int*. 2009;9(1):16-20.
26. Sevush S. Relationship between denial of memory deficit and dementia severity in Alzheimer disease. *Neuropsychiatry Neuropsychol Behav Neurol*. 1999;12(2):88-94.
27. Barrett AM, Eslinger PJ, Ballentine NH, Heilman KM. Unawareness of cognitive deficit (cognitive anosognosia) in probable AD and control subjects. *Neurology*. 2005;64(4):693-699.