Improvement of Dementia Screening Accuracy of Mini-Mental State Examination by Education-Adjustment and Supplementation of Frontal Assessment Battery Performance

Jee Wook Kim,[1] Dong Young Lee,[2,3]
Eun Hyun Seo,[3] Bo Kyung Sohn,[2]
Shin Young Park,[4] IL Han Choo,[2]
Jong Chul Youn,[5] Jin Hyeong Jhoo,[6]
Ki Woong Kim,[7] and Jong Inn Woo[2,3]

[1]Department of Neuropsychiatry, Hallym University
Dongtan Sacred Heart Hospital, Hwaseong;
[2]Department of Neuropsychiatry, Seoul National
University Hospital, Seoul; [3]Interdisciplinary Program
in Cognitive Science, Seoul National University,
Seoul; [4]Department of Neuropsychiatry, Daelim
Saint Mary's Hospital, Seoul; [5]Department of
Neuropsychiatry, Gyeonggi Provincial Hospital for
the Elderly, Yongin; [6]Department of Neuropsychiatry,
Kangwon National University Hospital, Chuncheon;
[7]Department of Neuropsychiatry, Seoul National
University Bundang Hospital, Seongnam, Korea

Address for Correspondence:
Dong Young Lee, MD
Department of Neuropsychiatry, Seoul National University
Hospital and Seoul National University College of Medicine,
101 Daehak-ro, Jongno-gu, Seoul 110-744, Korea
Tel: +82.2-2072-2205, Fax: +82.2-744-7241
E-mail: selfpsy@snu.ac.kr

This study aimed to investigate whether the demographic variable-adjustment and supplementation of Frontal Assessment Battery (FAB) score can improve the screening ability of Mini-Mental State Examination (MMSE) for dementia and its subtypes. Five hundred forty-one non-demented comparison (NC) and 474 dementia (320 Alzheimer's disease [AD]; 139 non-Alzheimer's disease dementia [NAD]; and 15 mixed AD-NAD dementia) individuals living in the community were included. Education-adjusted MMSE (MMSE-edu) score showed significantly better screening accuracy for overall dementia, AD, and NAD than MMSE raw score. FAB-supplemented MMSE (MMSE-FAB) score had significantly better screening ability for NAD, but not for overall dementia and AD, than MMSE raw score alone. Additional supplementation of FAB to MMSE-edu further increased the ability for overall dementia or NAD screening, but not for AD screening. Further education adjustment of MMSE-FAB also improved its ability for overall dementia, AD, and NAD screening. These results strongly support the usefulness of education-adjustment and supplementation of frontal function assessment to improve screening performance of MMSE for dementia and its subtypes, NAD in particular.

Key Words: Mini-Mental State Examination; Frontal Assessment Battery; Education; Dementia; Screening Accuracy

INTRODUCTION

The Mini-Mental State Examination (MMSE) (1) is the most commonly used instrument for the assessment of cognitive function in both clinical and research settings. It is usually used as a screening test for dementia and cognitive impairment or as a brief cognitive assessment that takes about 10 min to complete.

In spite of its briefness and practical usefulness, it has a couple of important limitations related with its interpretation and test items. First, demographic variables, such as educational level, age, and gender, are known to have strong influences on MMSE score (2-8). Demographic variables may cause a bias of MMSE scores leading to a misclassification of cognitive status

of individuals (9). In terms of dementia screening, for example, people with low education tend to get false positive results, while well-educated people tend to get false negative results (2, 9). For the effect of education or other demographic variable-adjustment, however, there is still controversy. While Kittner et al. (10) provided a good rationale for adjusting demographic variables in dementia screening with MMSE, Kraemer et al. (11) had not demonstrated an advantage of education- or age-adjustment of MMSE score.

Second, MMSE consists of test items mainly covering orientation, attention, memory and language, and is less sensitive to frontal executive dysfunction (9, 12). While memory decline is the earliest and most important cognitive deficit in Alzheimer's disease (AD), frontal executive dysfunction is frequently more

prominent than memory or other cognitive deficits in non-Alzheimer's disease dementia (NAD), especially frontotemporal dementia (FTD) (13) and vascular dementia (VD) (14). Therefore, the assessment of frontal executive dysfunction can probably make a meaningful contribution to the screening of dementia, NAD in particular. Nevertheless, the effect of supplementing executive dysfunction to MMSE score on dementia screening accuracy was poorly investigated.

In this study, we aimed to investigate whether demographic variable-adjustment and supplementation of frontal executive dysfunction, measured by the Frontal Assessment Battery (FAB) (15) can improve the screening accuracy of MMSE for dementia and its major subtypes, i.e., AD and NAD, in a large community-dwelling population.

MATERIALS AND METHODS

Subjects

Study subjects were recruited from the pool of individuals registered in a program for the early detection and management of dementia at four centers located in Seoul, Korea (two public health centers, one senior citizens welfare center, and one dementia clinic) from January 2000 to May 2011. In this study, 474 patients with dementia and 541 non-demented comparison (NC) individuals were included.

A diagnosis of dementia was made according to the criteria of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (16). AD was diagnosed according to the probable or possible AD criteria of the National Institute of Neurological and Communication Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (17). VD was diagnosed according to the probable or possible VD criteria of the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) (18). Dementia with Lewy bodies (DLB) or Parkinson disease dementia (PDD) was diagnosed according to the DLB consensus criteria (19), and FTD was diagnosed according to the FTD consensus criteria (20).

The exclusion criteria for all subjects were any present serious medical, psychiatric, and neurologic disorders that could affect the mental function; the presence of severe behavioral or communication problems that would make a clinical examination difficult; an absence of a reliable informant; and inability of reading Korean (i.e., inability of reading 10 words in Word List Memory from the Consortium to Establish a Registry for Alzheimer's Disease [CERAD] neuropsychological battery) (21, 22). All Individuals with minor physical abnormalities (e.g., diabetes with no serious complications, essential hypertension, mild hearing loss, or others) were included.

Clinical and neuropsychological assessments

All subjects were examined by neuropsychiatrists with advanced training in dementia research according to the CERAD protocol (21, 22). The CERAD clinical assessment battery included Clinical Dementia Rating (CDR) (23), Blessed Dementia Scale-Activities of Daily Living (BDS-ADL), general medical examination, neurologic examination, laboratory tests, and brain MRI or computed tomography. Standard administration of the CERAD battery was previously described in detail (21, 22). Reliable informants were necessarily interviewed to acquire the accurate information regarding the cognitive, emotional, and functional changes and the medical history of the subjects.

MMSE and other neuropsychological tests included in the CERAD neuropsychological battery (Verbal fluency, 15-item Boston naming test, Word List Memory, Word List Recall, Word List Recognition, Constructional Praxis, and Constructional Recall test) were applied by experienced clinical psychologists or nurses. FAB, a short bedside test to assess the presence and severity of dysexecutive syndrome affecting both cognitive and motor behavior (15, 24), was also applied by experienced clinical psychologists or nurses. FAB consists of six subtests: conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. Global performance on these six subtests gives a composite score summarizing the severity of executive dysfunction.

A panel consisting of 4 neuropsychiatrists with expertise in dementia research made the clinical decisions including diagnosis and CDR after reviewing all the available raw data.

Statistical analysis

Between-group comparisons for continuous data including demographic and clinical data were done by two-tailed t tests. Categorical data were analyzed by chi-square test. A stepwise multiple linear regression analysis was performed to assess the relative contribution of age, education, and sex on MMSE score in NC. Age and education were entered as continuous variables and sex was coded as zero and 1 for females and males, respectively. Based on the result of this analysis, we selected a demographic variable with the strongest influence on MMSE score for the adjustment of MMSE. A series of multiple logistic regression models for dementia, AD, and NAD screening were used to obtain new scores after adjusting the selected demographic variable or supplementing FAB to MMSE score. Receiver operating characteristic (ROC) curve analysis was used to compare dementia or its subtype screening accuracy between MMSE raw score and the new scores derived from logistic regression models. Area under the curve (AUC) of ROC curve was compared by using the method of Hanley and McNeil (25).

The level of statistical significance was set as two-tailed $P < 0.05$. ROC curve analyses were performed by using MedCalc for Windows, version 12.1 (MedCalc Software, Mariakerke, Belgium).

All the other analyses except ROC curve analysis were performed by using SPSS software, version 15.0 (SPSS Inc, Chicago, IL, USA).

Ethics statement

This study was approved by the institutional review board of the Seoul National University Hospital, Korea (IRB No. H-1202-110-399). All subjects or their legal representatives gave written informed consent.

RESULTS

Demographic and clinical characteristics

The demographic and clinical characteristics of subjects are summarized in Table 1. Among the patients with dementia (n = 474), 320 (67.5%) had AD; 139 (29.3%) NAD (55 VD; 21 FTD; 12 DLB; 7 PDD; 19 mixed NAD dementia; and 25 other dementia); and 15 (3.2%) mixed AD-NAD.

Selection of demographic variable for the adjustment of MMSE

Stepwise multiple regression analysis revealed that MMSE was significantly influenced by education (β = 0.505, t = 14.253, R^2 change = 0.305, P < 0.001) and age (β = -0.229, t = -6.474, R^2 change = 0.050, P < 0.001), but not by sex in subjects with NC (Model 1: predictors = education, dependent variable = MMSE, R^2 change = 0.305; Model 2: predictors = education and age, dependent variable = MMSE, R^2 change = 0.050). Education showed the most prominent influence on MMSE score in the result. Although age had significant association to MMSE score, we selected only education as a demographic variable for the adjustment of MMSE raw score owing to very small change of R^2 between the two models.

Calculation of new scores by education-adjustment or FAB-supplementation of MMSE

We mathematically yielded new scores through education-adjustment or FAB-supplementation of MMSE score by using multiple logistic regression analyses. The equations for new scores derived from multiple logistic regressions for each of dementia, AD, and NAD screening are summarized in Table 2.

ROC Analysis

ROC curve was constructed for each score as shown in Fig. 1, and AUC for each ROC curve was calculated. AUC, sensitivity, specificity, cutoff points of MMSE raw, education-adjusted MMSE (MMSE-edu), FAB-supplemented MMSE (MMSE-FAB), and education-adjusted MMSE-FAB (MMSE-FAB-edu) scores are shown in Table 3. The results of ROC curve comparisons between MMSE raw score and new scores are as follows:

Dementia screening

MMSE-edu showed significantly superior dementia screening accuracy to MMSE (z = 3.680, P < 0.001), but MMSE-FAB did not. Dementia screening accuracy of MMSE-FAB-edu was significantly better than those of MMSE (z = 4.367, P < 0.001), MMSE-edu (z = 2.121, P = 0.034), and MMSE-FAB (z = 4.073, P < 0.001) (Table 3).

AD Screening

MMSE-edu showed significantly better AD screening accuracy than MMSE (z = 3.342, P < 0.001), but MMSE-FAB did not. AD screening accuracy of MMSE-FAB-edu was significantly better than those of MMSE (z = 3.470, P < 0.001) and MMSE-FAB (z = 3.457, P < 0.001), but was not better than that of MMSE-edu (Table 3).

**Table 1.** Demographic and clinical characteristics of subjects (n = 1,015)

Parameters	NC	D	AD	NAD	*P* value			
					NC vs D	NC vs AD	NC vs NAD	AD vs NAD
No.	541	474	320	139				
Age (yr)	67.7 ± 10.8	71.6 ± 9.1	71.9 ± 8.9	70.2 ± 9.5	< 0.001*	< 0.001[†],*	0.014[‡],*	0.064*
Education (yr)	9.0 ± 5.2	8.1 ± 5.4	8.0 ± 5.3	8.8 ± 5.8	0.007*	0.004[†],*	0.638[‡],*	0.143*
% Women	69.1	62.0	70.9	43.9	0.020[†]	0.592[†]	< 0.001[†]	< 0.001[†]
%CDR					< 0.001[†]	< 0.001[†]	< 0.001[†]	0.068[†]
CDR 0	43.6	0.0	0.0	0.0				
CDR 0.5	56.4	39.7	44.1	33.1				
CDR 1	0.0	46.4	42.2	53.2				
CDR 2+	0.0	13.9	13.8	13.7				
CDR-SOB	1.1 ± 0.7	5.5 ± 3.2	5.3 ± 3.3	5.7 ± 3.0	< 0.001*	< 0.001*	< 0.001*	0.324*
MMSE	24.3 ± 4.3	15.9 ± 6.0	15.6 ± 5.8	16.9 ± 6.2	< 0.001*	< 0.001*	< 0.001*	0.025*
FAB	13.4 ± 3.2	8.6 ± 4.1	8.7 ± 4.2	8.5 ± 3.8	< 0.001*	< 0.001*	< 0.001*	0.557*

Data are presented as mean ± SD or number (%). *By Student t-test, df = 1013, 859, 678, 457; [†]by chi-square test, df = 3, 3, 3, 2. NC, Non-demented comparison; D, dementia; AD, Alzheimer's disease; NAD, Non-Alzheimer's disease dementia; CDR-SOB, clinical dementia rating sum of box score; MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery. Dementia is regarded as AD, NAD, and mixed AD-NAD.

Table 2. Calculation of new scores by education-adjustment or FAB-supplementation of MMSE

Categories	Equations for new scores derived from multiple logistic regressions
Dementia screening	
MMSE-edu score	Logit (case) = 6.641-0.395 × MMSE+0.164 × education or Pr (case) = 1/ (1+exp [-6.641+0.395 × MMSE-0.164 × education])
MMSE-FAB score	Logit (case) = 6.111-0.256 × MMSE-0.086 × FAB or Pr (case) = 1/ (1+exp [-6.111+0.256 × MMSE+0.086 × FAB])
MMSE-FAB-edu score	Logit (case) = 6.894-0.322 × MMSE-0.173 × FAB+0.190 × education
	or Pr (case) = 1/ (1+exp [-6.894+0.322 × MMSE+0.173 × FAB-0.190 × education])
AD screening	
MMSE-edu score	Logit (case) = 6.623-0.420 × MMSE+0.174 × education or Pr (case) = 1/ (1+exp [-6.623+0.420 × MMSE-0.174 × education])
MMSE-FAB score	Logit (case) = 5.944-0.306 × MMSE-0.019 × FAB or Pr (case) = 1/ (1+exp [-5.944+0.306 × MMSE+0.019 × FAB])
MMSE-FAB-edu score	Logit (case) = 6.748-0.375 × MMSE-0.104 × FAB+0.191 × education
	or Pr (case) = 1/ (1+exp [-6.748+0.375 × MMSE+0.104 × FAB-0.191 × education])
NAD screening	
MMSE-edu score	Logit (case) = 4.426-0.341 × MMSE+0.163 × education or Pr (case) = 1/ (1+exp [-4.426+0.341 × MMSE-0.163 × education])
MMSE-FAB score	Logit (case) = 4.063-0.150 × MMSE-0.202 × FAB or Pr (case) = 1/ (1+exp [-4.063+0.150 × MMSE+0.202 × FAB])
MMSE-FAB-edu score	Logit (case) = 4.888-0.216 × MMSE-0.317 × FAB+0.216 × education
	or Pr (case) = 1/ (1+exp [-4.888+0.216 × MMSE+0.317 × FAB-0.216 × education])

FAB, Frontal Assessment Battery; MMSE, Mini-Mental State Examination; MMSE-edu, education-adjusted MMSE; MMSE-FAB, FAB-supplemented MMSE; MMSE-FAB-edu, education-adjusted MMSE-FAB; AD, Alzheimer's disease; NAD, Non-Alzheimer's disease dementia; Pr (case), probability of a case.
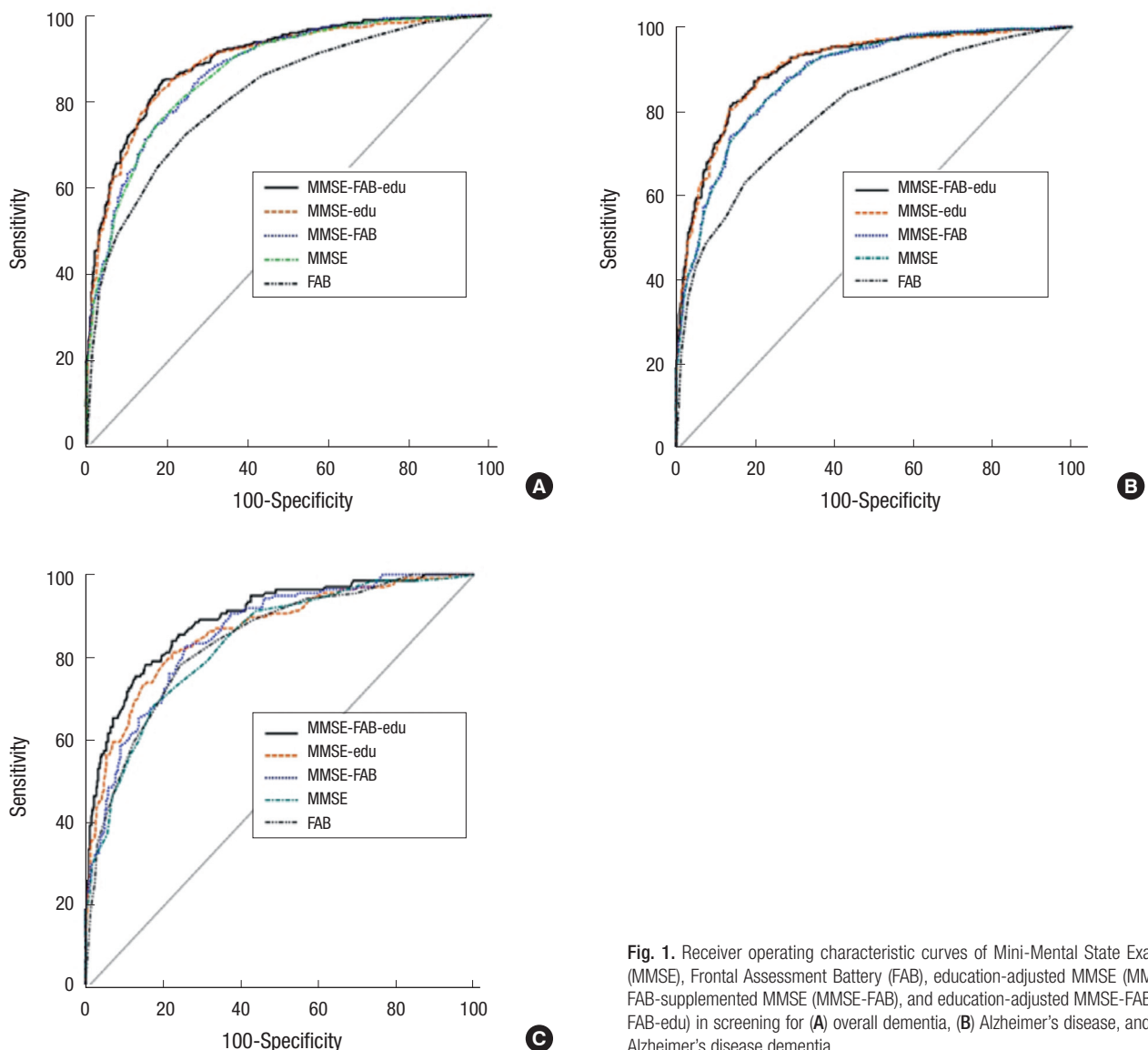
Fig. 1. Receiver operating characteristic curves of Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB), education-adjusted MMSE (MMSE-edu), FAB-supplemented MMSE (MMSE-FAB), and education-adjusted MMSE-FAB (MMSE-FAB-edu) in screening for (**A**) overall dementia, (**B**) Alzheimer's disease, and (**C**) non-Alzheimer's disease dementia.

Table 3. Area under the curves (AUC) and cutoff scores of MMSE, FAB, MMSE-edu, MMSE-FAB, and MMSE-FAB-edu in non-demented comparison (NC), dementia (D), Alzheimer's disease (AD), and non-Alzheimer's disease dementia (NAD) groups (n = 1,015)

Instruments	NC vs D (n = 1,015)	NC vs AD (n = 861)	NC vs NAD (n = 680)
MMSE			
AUC	**0.871**	**0.885**	**0.835**
SE	0.0109	0.0113	0.0189
95% CI	0.849 to 0.891	0.862 to 0.906	0.805 to 0.862
Cut off	20/21	21/22	20/21
Sen/Spe	74.9/82.6	83.7/76.3	68.3/82.6
FAB			
AUC	**0.818**	**0.805**	**0.838**
SE	0.0132	0.0156	0.0187
95% CI	0.792 to 0.841	0.777 to 0.831	0.808 to 0.865
Cut off	11/12	10/11	11/12
Sen/Spe	72.6/75.6	63.4/82.6	78.4/75.6
MMSE-FAB			
AUC	**0.874**	**0.885**	**0.857***
SE	0.0106	0.0113	0.0171
95% CI	0.852 to 0.894	0.862 to 0.906	0.828 to 0.882
Pr (case)	≥ 0.4	≥ 0.4	≥ 0.2
Sen/Spe	80.2/76.5	75.0/84.7	74.1/78.6
MMSE-edu			
AUC	**0.893*,‡**	**0.906*,‡**	**0.862***
SE	0.0101	0.0106	0.0185
95% CI	0.872 to 0.911	0.885 to 0.925	0.834 to 0.887
Pr (case)	≥ 0.4	≥ 0.4	≥ 0.2
Sen/Spe	85.2/79.3	80.6/86.5	77.0/81.1
MMSE-FAB-edu			
AUC	**0.900*,†,‡**	**0.908*,†,‡**	**0.892*,†,‡**
SE	0.00955	0.0104	0.0157
95% CI	0.880 to 0.918	0.886 to 0.926	0.866 to 0.914
Pr (case)	≥ 0.4	≥ 0.4	≥ 0.2
Sen/Spe	85.2/80.6	80.6/86.5	78.4/84.4

*Significantly greater than that of MMSE; †significantly greater than that of MMSE-edu; ‡significantly greater than that of MMSE-FAB. MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery; MMSE-FAB, FAB-supplemented MMSE; MMSE-edu, education-adjusted MMSE; MMSE-FAB-edu, education-adjusted MMSE-FAB; SE, standard error; CI, Confidence Interval; Sen/Spe, sensitivity/specificity; Pr (case), probability of a case.

NAD Screening

Both MMSE-edu and MMSE-FAB showed significantly superior NAD screening accuracy to MMSE (z = 2.341, P = 0.019 for MMSE-edu; z = 2.613, P = 0.009 for MMSE-FAB). NAD screening accuracy of MMSE-FAB-edu was significantly better than those of MMSE (z = 3.959, P < 0.001), MMSE-edu (z = 3.004, P = 0.003), and MMSE-FAB (z = 2.914, P = 0.004) (Table 3).

DISCUSSION

In this study, we found that education-adjustment improved the screening ability of MMSE for overall dementia and its subtypes including AD and NAD. In contrast, FAB supplementation effect for MMSE was found only for NAD screening, but not for overall dementia or AD screening. Additional supplementation of FAB to MMSE-edu further increased the ability for overall dementia or NAD screening, but not for AD screening.

Further education adjustment of MMSE-FAB also improved its ability for overall dementia, AD, and NAD screening.

In regard of the relative influences of education, age, and sex on MMSE performance, our result from stepwise linear regression is in line with previous reports indicating stronger effect of education compared to other variables (10, 26). Based on the result, we selected education as a demographic variable for MMSE adjustment. While we found that MMSE-edu score had superior dementia screening ability to MMSE raw score, Kraemer et al. (11) reported that education-adjusted MMSE scores had not shown an advantage compared to unadjusted ones. The conflicting results between studies may be attributed to the very different distribution of educational levels of study subjects. The subjects of Kraemer et al.'s study (11) had homogeneous educational levels (74.56% were higher-educated [more than 8 yr] and 25.44% less-educated). On the other hand, the subjects of ours had a very wide distribution of educational levels from without any formal education (12.20%) to higher than 12 yr (21.80%), and had relatively heterogeneous educational levels (51.82% were higher-educated and 48.18% less-educated). This implies that education-adjustment of MMSE is more important to improve dementia screening accuracy in a population with a wide range of educational levels.

In addition to education adjustment, supplementation with other instruments has been proposed to improve dementia screening ability of MMSE (27-29). Mackinnon and Mulligan (27) demonstrated that the combining MMSE with informant report-based dementia questionnaires had a superior dementia screening accuracy than either test used alone. However, the usefulness of informant report-based questionnaires is somewhat controversial. In contrast to the report of Mackinnon and Mulligan, Knafelc et al. (28) reported that MMSE supplemented with an informant report-based questionnaire did not show any advantage over MMSE alone in dementia screening. Furthermore, such questionnaires cannot even be applied if a reliable collateral informant is not available. Alternatively, other brief cognitive tests that specifically cover frontal executive dysfunction, to which MMSE is relatively less sensitive, could be considered. We chose FAB because it selectively and reliably assesses frontal dysfunction within a brief time (15). Supplementing MMSE with FAB has a couple of important cost-effect perspectives related with its little burden of clinicians and its application to specialized clinical settings. First, it could be widely used for the assessment of both AD and NAD with little burden of clinicians. Second, it could be greater applied in some specialized clinical settings (e.g., stroke clinic) rather than community settings due to its superior NAD screening accuracy.

In terms of the screening ability of MMSE for dementia subtypes, we found FAB supplementation effect only for NAD screening, but not for AD screening. This is probably associated with the fact that frontal executive function is relatively more impair-

ed in NAD, especially FTD (30, 31) and VD (14), compared to AD. In our subjects, as shown in Table 1, the mean FAB score of NAD group was slightly lower than that of AD (mean ± SD: 8.5 ± 3.8 for NAD vs 8.7 ± 4.2 for AD), although the mean MMSE score of NAD was significantly higher than that of AD (16.9 ± 6.2 for NAD vs 15.6 ± 5.8 for AD). Despite there being no significant difference of the mean FAB score between AD and NAD, FAB supplementation effect only for NAD screening may be explained by the greater weighted-value of FAB score relative to MMSE score in NAD, rather than the difference of mean FAB score between the two. In regard of overall dementia screening, however, FAB supplementation did not increase the accuracy of MMSE raw score. Greater proportion of AD patients, compared to NAD patients, among overall dementia subjects seems to be associated with the finding. However, FAB supplementation effect was significant for MMSE-edu even in overall dementia, as well as in NAD.

Our study has a couple of strong points. Our study population was quite large and had diverse educational background. It also included a lot of dementia patients with various subtypes, defined by thorough clinical evaluation and strict diagnostic criteria. All these may probably increase the stability and generalizability of our results. In addition, to our knowledge, this is the first study that demonstrated the effect of both education-adjustment and frontal assessment-supplementation on the dementia or its subtype screening ability of MMSE.

In conclusion, our results strongly support the usefulness of education-adjustment and supplementation of frontal function assessment to improve the screening performance of MMSE for dementia and its subtypes, NAD in particular. Our findings additionally imply that the effects of education-adjustment and frontal assessment-supplementation could be synergistically added to increase the dementia screening ability of MMSE.

DISCLOSURE

The authors have no conflicts of interest to disclose.

REFERENCES

1. Folstein MF, Folstein SE, McHugh PR. *"Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res* 1975; 12: 189-98.

2. Lee DY, Lee KU, Lee JH, Kim KW, Jhoo JH, Kim SY, Yoon JC, Woo SI, Ha J, Woo JI. *A normative study of the CERAD neuropsychological assessment battery in the Korean elderly. J Int Neuropsychol Soc* 2004; 10: 72-81.

3. Anthony JC, LeResche L, Niaz U, von Korff MR, Folstein MF. *Limits of the 'Mini-Mental State' as a screening test for dementia and delirium among hospital patients. Psychol Med* 1982; 12: 397-408.

4. Jones RN, Gallo JJ. *Education and sex differences in the mini-mental state examination: effects of differential item functioning. J Gerontol B Psychol Sci Soc Sci* 2002; 57: P548-58.

5. O'Connor DW, Pollitt PA, Treasure FP, Brook CP, Reiss BB. *The influence of education, social class and sex on Mini-Mental State scores. Psychol Med* 1989; 19: 771-6.

6. Kim JL, Park JH, Kim BJ, Kim MD, Kim SK, Chi YK, Kim TH, Moon SW, Park MH, Bae JN, et al. *Interactive influences of demographics on the Mini-Mental State Examination (MMSE) and the demographics-adjusted norms for MMSE in elderly Koreans. Int Psychogeriatr* 2012; 24: 642-50.

7. Han C, Jo SA, Jo I, Kim E, Park MH, Kang Y. *An adaptation of the Korean mini-mental state examination (K-MMSE) in elderly Koreans: demographic influence and population-based norms (the AGE study). Arch Gerontol Geriatr* 2008; 47: 302-10.

8. Lee DY, Lee KU, Lee JH, Kim KW, Jhoo JH, Youn JC, Kim SY, Woo SI, Woo JI. *A normative study of the Mini-Mental State examination in the Korean elderly. J Korean Neuropsychiatr Assoc* 2002; 41: 508-25.

9. Tombaugh TN, McIntyre NJ. *The mini-mental state examination: a comprehensive review. J Am Geriatr Soc* 1992; 40: 922-35.

10. Kittner SJ, White LR, Farmer ME, Wolz M, Kaplan E, Moes E, Brody JA, Feinleib M. *Methodological issues in screening for dementia: the problem of education adjustment. J Chronic Dis* 1986; 39: 163-70.

11. Kraemer HC, Moritz DJ, Yesavage J. *Adjusting Mini-Mental State Examination scores for age and educational level to screen for dementia: correcting bias or reducing validity? Int Psychogeriatr* 1998; 10: 43-51.

12. Royall DR, Mahurin R. *EXIT, QED, and DSM-IV: very early Alzheimer's disease. J Neuropsychiatry Clin Neurosci* 1994; 6: 62-5.

13. Gleichgerrcht E, Roca M, Manes F, Torralva T. *Comparing the clinical usefulness of the Institute of Cognitive Neurology (INECO) Frontal Screening (IFS) and the Frontal Assessment Battery (FAB) in frontotemporal dementia. J Clin Exp Neuropsychol* 2011; 33: 997-1004..

14. Oguro H, Yamaguchi S, Abe S, Ishida Y, Bokura H, Kobayashi S. *Differentiating Alzheimer's disease from subcortical vascular dementia with the FAB test. J Neurol* 2006; 253: 1490-4.

15. Dubois B, Slachevsky A, Litvan I, Pillon B. *The FAB: a Frontal Assessment Battery at bedside. Neurology* 2000; 55: 1621-6.

16. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC, American Psychiatric Association Press, 1994.*

17. 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: 939-44.

18. Román GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeu JC, Garcia JH, Amaducci L, Orgogozo JM, Brun A, Hofman A, et al. *Vascular dementia: diagnostic criteria for research studies: report of the NINDS-AIREN International Workshop. Neurology* 1993; 43: 250-60.

19. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H, Cummings J, Duda JE, Lippa C, Perry EK, et al. *Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology* 2005; 65: 1863-72.

20. Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, Freedman M, Kertesz A, Robert PH, Albert M, et al. *Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology* 1998; 51: 1546-54.

21. Morris JC, Heyman A, Mohs RC, Hughes JP, van Belle G, Fillenbaum G,

Mellits ED, Clark C. *The Consortium to Establish a Registry for Alzheimer's Disease (CERAD): part I. clinical and neuropsychological assessment of Alzheimer's disease. Neurology* 1989; 39: 1159-65.

22. Lee JH, Lee KU, Lee DY, Kim KW, Jhoo JH, Kim JH, Lee KH, Kim SY, Han SH, Woo JI. *Development of the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K): clinical and neuropsychological assessment batteries. J Gerontol B Psychol Sci Soc Sci* 2002; 57: P47-53.

23. Morris JC. *The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology* 1993; 43: 2412-4.

24. Kim TH, Huh Y, Choe JY, Jeong JW, Park JH, Lee SB, Lee JJ, Jhoo JH, Lee DY, Woo JI, et al. *Korean version of frontal assessment battery: psychometric properties and normative data. Dement Geriatr Cogn Disord* 2010; 29: 363-70.

25. Hanley JA, McNeil BJ. *A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology* 1983; 148: 839-43.

26. Narasimhalu K, Lee J, Auchus AP, Chen CP. *Improving detection of dementia in Asian patients with low education: combining the Mini-Mental State Examination and the Informant Questionnaire on Cognitive Decline in the Elderly. Dement Geriatr Cogn Disord* 2008; 25: 17-22.

27. Mackinnon A, Mulligan R. *Combining cognitive testing and informant report to increase accuracy in screening for dementia. Am J Psychiatry* 1998; 155: 1529-35.

28. Knafelc R, Lo Giudice D, Harrigan S, Cook R, Flicker L, Mackinnon A, Ames D. *The combination of cognitive testing and an informant questionnaire in screening for dementia. Age Ageing* 2003; 32: 541-7.

29. Pozueta A, Rodríguez-Rodríguez E, Vazquez-Higuera JL, Mateo I, Sánchez-Juan P, González-Perez S, Berciano J, Combarros O. *Detection of early Alzheimer's disease in MCI patients by the combination of MMSE and an episodic memory test. BMC Neurol* 2011; 11: 78.

30. Lipton AM, Ohman KA, Womack KB, Hynan LS, Ninman ET, Lacritz LH. *Subscores of the FAB differentiate frontotemporal lobar degeneration from AD. Neurology* 2005; 65: 726-31.

31. Slachevsky A, Villalpando JM, Sarazin M, Hahn-Barma V, Pillon B, Dubois B. *Frontal assessment battery and differential diagnosis of frontotemporal dementia and Alzheimer disease. Arch Neurol* 2004; 61: 1104-7.