Article

Arq Neuropsiquiatr 2010;68(2):179-184

Impaired abstract thinking may discriminate between normal aging and vascular mild cognitive impairment

Felipe Kenji Sudo[1], Gilberto Sousa Alves[1], Carlos Eduardo de Oliveira Alves[1], Maria Elisa Lanna[2], Letice Ericeira-Valente[1], Denise Madeira Moreira[3], Eliasz Engelhardt[2], Jerson Laks[1,4]

ABSTRACT

Objective: Cerebrovascular disease (CVD) is associated with cognitive deficits. This cross-sectional study examines differences among healthy elderly controls and patients with vascular mild cognitive impairment (VaMCI) and vascular dementia (VaD) in performances on CAMCOG subscales. **Method:** Elderly individuals (n=61) were divided into 3 groups, according to cognitive and neuroimaging status: 16 controls, 20 VaMCI and 25 VaD. VaMCI and VaD individuals scored over 4 points on the Hachinski Ischemic Scale. **Results:** Significant differences in total CAMCOG scores were observed across the three groups ($p<0.001$). VaD subjects performed worse than those with VaMCI in most CAMCOG subscales ($p<0.001$). All subscales showed differences between controls and VaD ($p<0.001$). Performance on abstract thinking showed difference between VaMCI and controls ($p<0.001$). **Conclusion:** CAMCOG discriminated controls from VaMCI and VaD. Assessment of abstract thinking may be useful as a screening item for diagnosis of VaMCI.

Key words: CAMCOG, elderly, mild cognitive impairment, vascular dementia, cerebrovascular disease, abstract thinking.

O pensamento abstrato comprometido pode diferenciar o envelhecimento normal do comprometimento cognitivo leve vascular

RESUMO

Objetivo: A doença cerebrovascular (DCV) associa-se a déficits cognitivos. Este estudo transversal objetiva examinar diferenças entre controles saudáveis idosos e pacientes com comprometimento cognitivo leve vascular (CCLV) e demência vascular (DV) nas subescalas do CAMCOG. **Método:** Indivíduos idosos (n=61) foram divididos em 3 grupos, de acordo com o perfil cognitivo e com a neuroimagem: 16 controles, 20 CCLV e 25 DV. Pacientes com CCLV e DV pontuaram acima de 4 pontos no Escore Isquêmico de Hachinski. **Resultados:** Diferenças significativas foram observadas entre os três grupos no resultado final do CAMCOG. Pacientes com DV obtiveram escores inferiores àqueles dos indivíduos com CCLV em quase todas as subescalas. Todas as subescalas mostraram diferenças entre DV e controles. O desempenho no item pensamento abstrato mostrou diferenças entre CCLV e controles. **Conclusão.** O CAMCOG diferenciou controles de pacientes com CCLV e DV. A avaliação do pensamento abstrato pode ser útil para discriminar CCLV de controles.

Palavras-chave: CAMCOG, idosos, comprometimento cognitivo leve, demência vascular, doença cerebrovascular, pensamento abstrato.

Correspondence
Felipe Kenji Sudo
Rua Ministro Alfredo Valadão 35/206
22031-050 Rio de Janeiro RJ - Brasil
E-mail: fksudo@yahoo.com

Received 14 September 2009
Received in final form 12 November 2009
Accepted 22 November 2009

[1]Psychiatry Institute,Federal University Rio de Janeiro, Rio de Janeiro RJ, Brazil; [2]Neurology Institute Deolindo Couto, Federal University Rio de Janeiro, Rio de Janeiro RJ, Brazil; [3]Pró-Cardíaco Hospital, Radiology Department, Rio de Janeiro RJ, Brazil; [4]State University Rio de Janeiro, Rio de Janeiro RJ, Brazil.

Vascular mild cognitive impairment (VaMCI) can be defined as a cognitive impairment of vascular etiology that does not fulfill criteria for dementia[1]. It has been proposed that vascular-related cognitive impairment exists throughout a continuum comprising VaMCI, vascular cognitive impairment no-dementia (Va-CIND) and vascular dementia (VaD)[2]. In a sample of cerebrovascular disease (CVD) patients with cognitive difficulties, Wentzel et al.[3] reported a 50% rate of conversion to dementia over a five-year period. The early detection of VaMCI may allow therapeutic intervention designed to halt or delay the progression of vascular lesions so as to prevent the conversion to dementia[4,5]. Presently, the diagnosis of mild cognitive impairment (MCI) requires improvement in the sensitivity of conventional screening tests for dementia, since the rate of false-negative results is usually high for those individuals[6,7]. Studies attempting to increase such sensitivity have shown that a combination of different screening tests provides higher diagnostic accuracy compared to each test individually[8,9]. Diniz et al.[7] analyzed Mini-Mental State Examination (MMSE) subtests in a sample of MCI subjects and managed to identify distinct profiles of cognitive deficits among the MCI subtypes. A higher rate of patients with MCI could be identified when the item scores were analyzed, which was not possible when only MMSE final scores were considered. ROC curve analyses were performed to determinate cutoff scores in the Cambridge Cognitive Examination (CAMCOG) for MCI patients, but discrimination between MCI subjects and controls with this method showed low accuracy[10].

It was suggested that some cognitive domains might be specifically impaired in MCI subjects and these aspects could serve as differential markers to distinguish this condition from normal aging. Rodríguez et al. found that individuals diagnosed as MCI performed significantly worse than controls in CAMCOG subtests assessing various areas, with higher significance levels corresponding to the variables memory, abstract thinking and executive function[11]. In a previous study, Erkinjuntii et al. observed impairment in memory, conceptual functions and arithmetical skills in a sample of individuals presenting age-related cognitive changes[12]. Recently, one other study showed that memory, constructive ability and abstract thinking were particularly impaired in MCI individuals compared to controls[13].

The purpose of this study is to evaluate the performance of VaMCI patients in comparison to cognitively unimpaired controls and VaD individuals on the CAMCOG tasks. We hypothesized that characterization of cognitive deficits using CAMCOG subtests may provide an increase in sensitivity in the screening for VaMCI, in addition to total test score. Furthermore, we intended to verify if cognitive domains specially impaired in MCI individuals, such as memory, abstract thinking and executive function, could also serve as cognitive markers to diagnosis of VaMCI.

METHOD

Participants

Sixty-one elderly outpatients (mean age: 73.49±7.24 years; 68.85% female; mean education level: 6.86±4.57 years) were consecutively assessed at the Centre for Alzheimer Disease and Related Disorders (CDA), Federal University of Rio de Janeiro (UFRJ), Brazil, between July 2006 and October 2008. The sample comprised both subjects who spontaneously demanded medical assistance due to cognitive complaints and those referred from other clinics. Cognitive unimpaired controls were volunteers recruited from several sources who accepted invitation to participate in the study. Informed consent was obtained from participants or from a family member responsible prior to enrolment. This study is a branch of a larger project on vascular cognitive disorder, approved by the Ethics Committee of IPUB-UFRJ.

Clinical and neuropsychological assessment

Patients and controls were examined by a multidisciplinary team, comprising psychiatrists, neurologists, one radiologist and one neuropsychologist. An interview with patient and caregiver was performed and those who had history of alcohol or drug abuse, psychiatric disorders (e.g. schizophrenia, bipolar mood disorder or lifetime depressive disorder), non-corrected visual or auditory disorders, exposure to neurotoxic substances and cranioencephalic traumatism were excluded from the study. The cognitive assessment included the Cambridge Cognitive Examination (CAMCOG)[14], Mini-Mental State Examination (MMSE)[15], semantic verbal fluency (category animals)[16,17], Trail Making Tests (TMT) A and B[18] and the 12-item-Boston Naming Test[19]. Behavioral evaluation was assessed by the Neuropsychiatric Inventory (NPI)[20,21]. Depressive symptoms were measured with Cornell Depression Scale[22,23]. Pfeffer's Functional Activities Questionnaire (FAQ)[24] was administered to informants (a close relative or a caregiver) in order to identify evidence of functional decline. Risk factors for CVD were scored using Hachinski Ischemic Score (HIS)[25]. Individuals were rated according to severity of cognitive deficits on the Clinical Dementia Rating scale (CDR)[26,27]. Laboratory tests were carried out to rule out reversible causes of cognitive decline, such as nutritional deficiencies, syphilis or diseases of the thyroid. All subjects underwent MRI scan of the brain.

The inclusion of VaD patients was based on the Diagnostic and Statistical Manual of Mental Disorders –

Fourth Edition (DSM-IV)[28] and the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences (NINDS-AIREN)[29] criteria for probable VaD.

The diagnosis of MCI was made according to Petersen's criteria[30]. MCI individuals scored below 4 points on Pfeffer's FAQ and this cutoff value was adopted to show functional activities largely preserved. Furthermore, VaMCI patients were identified as those who obtained above 4 points on the HIS, showing high risk-factors for CVD, which were correlated with vascular subcortical lesions and absence of significant cortical atrophy in MRI images.

The control group was submitted to the same procedures described above. Subjects in this group did not present evidence of cognitive and functional impairment and had no or not significant neuroimaging abnormalities, such as vascular subcortical lesions or cortical atrophy not correspondent to the expected for normal aging. Also, they had no history of major psychiatric disorders or substance-abuse.

Statistical analyses

Statistical analyses were made using SPSS for Windows version 11.5. Univariate Analysis of Variance (ANOVA) was carried out to assess significant mean differences for "Age" and "Educational Level", followed by post-hoc Bonferroni analysis. Pearson's Chi-square analysis was performed to evaluate differences in the distribution of gender among the three groups. Analysis of covariance (ANCOVA) was performed to control for the potential confounding effects of schooling on cognitive variables.

RESULTS

Table 1 illustrates the sociodemographic data of individuals among the three groups. Proportion of male and female subjects did not differ significantly among the groups. The control group showed a higher educational level when compared to VaD patients. This is depicted in Figure.

Results of the cognitive and behavioral evaluations are displayed in Table 2. Multiple comparison tests showed that VaD patients had worse performances in HIS, Cornell Depression Scale, changes in TMT A and TMT B (both time and errors) and Boston Naming Test as compared to controls. In comparison to controls and VaMCI, VaD individuals had worse scores in NPI, FAQ, TMT A and Verbal Fluency.

Multivariate analyses indicated that the three groups differed significantly in CAMCOG final scores. Analyses of scores in the CAMCOG subtests demonstrated that abstract thinking was the only item that showed differences among the three groups. Mean scores in orientation, language, memory, attention and praxis indicated significant differences between VaMCI persons and those with VaD, and also between controls and VaD individuals. Visual and spatial perception, as well as calculation showed significant differences only between controls and VaD subjects. These data are shown in Table 3.

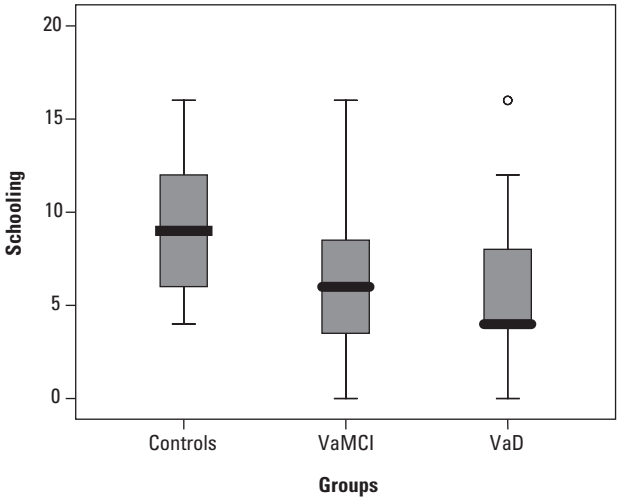

Figure. Schooling (years) according to diagnostic groups.

Table 1. Demographic variables and MMSE according to diagnostic groups.

	Controls	VaMCI	VaD	p-value	Post Hoc
Gender					
Male	N=4 (75%)	N=4 (80%)	N=11 (56%)	0.186*	–
Female	N=12 (25%)	N=16 (20%)	N=14 (44%)		
Schooling (years)	9.44±3.88	6.55±4.60	5.48±4.43	0.022**	C=VaMCI VaMCI=VaDV C≠VaD
Age (years)	73.00±7.83	72.95±6.78	74.24±7.44	0.803**	C=VaMCI=VaD
MMSE (m±sd)	27.94±1.43	25.90±2.59	17.50±6.00	<0.001**	C=MCI MCI≠DV C≠DV

m: mean; sd: standard deviation; *Pearson's Chi-Square; **ANOVA; MMSE: Mini Mental State Examination.

Table 2. Cognitive tests and behavioral evaluation according to diagnostic groups.

Variables	Controls Mean±sd	VaMCI Mean±sd	VaD Mean±sd	p-value*	Post Hoc+
Hachinski	2.25±2.23	7.85±2.90	10.16±3.17	<0.001	C=VaMCI VaMCI=VaD C≠VaD
NPI	2.69±3.79	13.32±15.27	30.12±18.88	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
CORNELL	1.88±2.68	8.55±7.00	10.56±6.06	0.001	C=VaMCI VaMCI=VaD C≠VaD
Pfeffer	0.13±0.34	0.90±1.33	16.48±7.79	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
TMTA	63.44±22.89	120.85±51.91	273.80±198.72	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Errors TMTA	0.06±0.25	0.35±0.58	1.00±1.51	0.037	C=VaMCI VaMCI=VaD C≠VaD
TMTB	158.69±56.22	324.63±172.07	731.33±461.28	<0.001	C=VaMCI VaMCI=VaD C≠VaD
Errors TMTB	1.19±0.91	1.76±1.82	2.75±1.28	0.047	C=VaMCI VaMCI=VaD C≠VaD
Verbal fluency	15.94±3.37	12.60±3.97	7.46±3.98	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Boston	11.06±1.12	10.00±1.12	9.40±1.35	0.006	C=VaMCI VaMCI=VaD C≠VaD

*ANCOVA; +C: controls

DISCUSSION

The present study showed that VaMCI and controls had significantly different performances in regards to the CAMCOG total scores (p<0.001). Another interesting finding was that impairment in abstract thinking was present in VaMCI but not in controls. Other subtests, such as orientation, language, memory, attention and praxis showed accuracy in separating VaMCI subjects from VaD individuals (p<0.001), whereas tactile and visual perception and calculation could only identify VaD patients from controls (p<0.001). MMSE failed in discriminating controls from VaMCI. VaMCI subjects and controls had similar overall performances on cognitive and behavioral evaluation, as depicted in Table 2.

Nunes et al.[10] showed that CAMCOG presented a sensitivity of 64% and a specificity of 88%. One previous study, however, which explored psychometric properties (reliability, discriminative capacity and factorial structure) of the CAMCOG, found an excellent reliability of the individual subscales and high levels of sensitivity and specificity of the instrument in differentiating between demented and non-demented individuals[31].

This study shows some limitations that should be outlined and commented. Significant differences were found in scores on Cornell Depression Scale between VaD individuals and controls. Depression is a common condition observed in patients with CVD and it can be related to poorer performances in cognitive assessment, acting as a confounding factor to cognitive deficits primarily associated to dementia[32,33]. Therefore, our results in cognitive evaluation of VaD patients should be considered with care. On the other hand, no significant difference in assessment of depressive symptoms was found between VaMCI subjects and controls, indicating that comparison of cognitive performances among those groups did not suffer this confounding effect. Schooling was lower in VaD patients compared to controls, which may also lead to difficulties in distinguishing cognitive impairment from

Table 3. CAMCOG subtests according to diagnostic groups.

Variables	Controls Mean±sd	VaMCI Mean±sd	VaD Mean±sd	p-value*	Post Hoc+
Orientation	9.63±0.61	8.70±1.38	5.25±2.59	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Language	27.13±1.92	25.10±2.02	20.88±4.56	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Memory (total)	20.81±2.68	17.20±7.00	8.63±6.06	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Memory (spontaneous recall)	3.50±1.50	2.80±1.60	1.08±1.24	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Memory (cued recall)	5.06±0.85	5.15±1.26	3.13±1.45	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Attention	5.50±1.82	3.70±1.80	1.92±1.97	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Praxis	11.06±1.18	9.60±1.60	7.67±2.12	<0.001	C=VaMCI VaMCI≠VaD C≠VaD
Tactile perception	1.94±0.25	1.80±0.52	1.58±0.58	0.042	C=VaMCI VaMCI=VaD C≠VaD
Visual perception	5.69±1.07	4.60±1.09	3.54±1.79	0.001	C=VaMCI VaMCI=VaD C≠VaD
Calculation	2.38±1.50	1.85±0.36	1.17±0.63	0.003	C=VaMCI VaMCI=VaD C≠VaD
Abstract thinking	6.50±1.31	4.05±2.12	2.13±1.91	<0.001	C≠VaMCI VaMCI≠VaD C≠VaD
Total score	90.44±5.21	76.60±8.35	52.75±16.05	<0.001	C≠VaMCI VaMCI≠VaD C≠VaD

*ANCOVA; + C: controls; sd: standard deviation; CAMCOG: Cambridge Cognitive Examination.

low scores in cognitive assessment associated to educational level.

Moreover, our results do not agree with some studies wherein the cognitive tests of MCI patients showed a ceiling effect, thus not being able to accurately recognize patients from controls. A possible explanation for the absence of a ceiling-effect could be the small sample, and similar studies with a larger sample should be performed. A great heterogeneity of individuals classified as MCI following Petersen's criteria has been described in many studies[34], and our findings may have been influenced by this limitation. Characterization of MCI may vary according to the different neuropsychological instruments employed[35], which may also explain the variation of cognitive profiles of MCI among the studies. Differently from the studies mentioned previously, our sample is constituted by individuals with vascular-related cognitive deficits, instead of those associated to neurodegeneration, and this aspect may be related to the particularities of the results of this study. Furthermore, our sample was recruited at the Centre for Alzheimer Disease and Related Disorders (CDA-UFRJ), and population-based studies, as well as studies with a larger sample are needed in order to replicate the results.

The assessment of abstract thinking requires the ability of establishing similarities between objects. This capac-

ity has been related to frontal lobe functioning[35]. Impairment of abstract thinking has been considered one important cognitive marker in the discrimination between MCI and normal aging[11,13] and, since evaluation can be considered simple, it may be a helpful item for clinical assessment of aged individuals with suspect of VaMCI. In conclusion, we propose that the analyses of each CAMCOG subtest, with emphasis on abstract thinking task, could be important as a screening item for early diagnosis of cognitive deficits in patients with high risk for CVD.

REFERENCES

1. Román G, Sachdev P, Royall D, et al. Vascular cognitive disorder: a new diagnostic category updating vascular cognitive impairment and vascular dementia. J Neurol Sci 2004;226:81-87.
2. Garrett KD, Browndyke JN, Whelihan W, et al. The neuropsychological profile of vascular cognitive impairment-no dementia: comparison to patients at risk for cerebrovascular disease and vascular dementia. Arch Clin Neuropsych 2004;19:745-757.
3. Wentzel C, Rockwood K, MacKnight C, et al. Progression of impairment in patients with vascular cognitive impairment without dementia. Neurology 2001;57:714-716.
4. Bowler JV, Hachinski V. Criteria for vascular dementia: replacing dogma with data. Arch Neurol 2000;57:170-171.
5. Engelhardt E, Laks J, Cavalcanti JL, Moreira DM, Madalen C. Demência vascular. Rev Bras Neurol 2004;40:5-25.
6. De Jager CA, Milwain E, Budge M. Early detection of isolated memory deficits in the elderly: the need for more sensitive tests. Psychol Med 2002;32:483-491.
7. Diniz BS, Yassuda MS, Nunes PV, Radanovic M, Forlenza OV. Mini-Mental State Examination performance in mild cognitive impairment subtypes. Int Psychoger 2007;19:647-656.
8. Lonie JA, Herrmann LL, Donaghey CL, Ebmeier KP. Clinical referral patterns and cognitive profile in mild cognitive impairment. Br J Psychiatry 2008;192: 59-64.
9. Heinik J, Shaikewitz D. The Clock Drawing Test-Modified and Integrated Approach (CDT-MIA) as an instrument for detecting mild cognitive impairment in a specialized outpatient setting. J Geriatr Psych Neurol 2009; [Epub ahead of print].
10. Nunes PV, Diniz BS, Radanovic M, et al. CAMCOG as a screening tool for diagnosis of mild cognitive impairment in a Brazilian clinical centre of moderate to high education. Int J Geriatr Psychiatry 2008;23:1127-1133.
11. Rodríguez NR, Juncos-Rabádan O, Mayo FD. Cognitive markers to discriminate between mild cognitive impairment and normal ageing. Rev Esp Geriatr Gerontol 2008;43:291-298.
12. Erkinjuntti T, Laaksonen R, Sulkava R, Syrjäläinen R, Palo J. Neuropsychological differentiation between normal aging, Alzheimer's disease and vascular dementia. Acta Neurol Scand 1986;74;393-403.
13. Matsuda O, Saito M. Multiple cognitive déficits in patients during the mild cognitive impairment stage of Alzheimer's disease: how are cognitive domains other than episodic memory impaired? Int Psychogeriatr 2009;21:970-976.
14. Roth M, Tym E, Mountjoy CO, et al. CAMDEX: a standardized instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. Br J Psychiatry 1986;149: 698-709.
15. 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;12:189-198.
16. Rosen WG. Verbal fluency in aging and dementia. J Clin Exp Neuropsychol 1980;2:135-146.
17. Brucki SMD, Malheiros SMF, Okamoto IH, Bertolucci PHF. Dados normativos para o teste de fluência verbal categoria animais em nosso meio. Arq Neuropsiquiatr 1997;55:56-61.
18. Reitan RM. Validity of the trail making test as an indicator of organic brain damage. Percept Mot Skills 1958; 8:271-276.
19. Kaplan, E, Goodglass H, Weintraub S. The Boston Naming Test. Philadelphia: Lea & Febiger 1983.
20. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44:2308-2314.
21. Camozzato AI, Kochhann R, Simeoni C, et al. Reliability of the Brazilian Portuguese version of the Neuropsychiatric Inventory (NPI) for patients with Alzheimer's disease and their caregivers. Internat Psychogeriatrics 2008;20:383-393.
22. Alexopoulos GS, Abrams RC, Young RC, Shamoiam CA. Cornell scale for depression in dementia. Biol Psychiatry 1988;23:271-284.
23. Carthery-Goulart MT, Areza-Fegyveres R, Schultz R, et al. Brazilian version of the Cornell depression scale in dementia. Arq Neuropsiquiatr 2007;65:912-915.
24. Pfeffer RI, Kurosaki TT, Harrah CH Jr, Chance JM, Filos S. Measurement of functional activities in older adults in the community. J Gerontol 1982;37:323-329.
25. Hachinski VC, Iliff LD, Zilhka E, et al. Cerebral blood flow in dementia. Arch Neurol 1975;32:632-637.
26. Chaves MI, Camozzato AI, Godinho C, et al. Validity of the Clinical Dementia Rating scale for the detection and staging of dementia in Brazilian patients. Alzheimer Dis Assoc Disord 2007; 21:210-217.
27. Hughes CP, Berg L, Danziger WL, et al. A new clinical scale for the staging of dementia. Br J Psychiatry 1982; 140: 566-572.
28. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th Ed. Washington, DC, 1994.
29. Román GC, Tatemichi TK, Erkinjuntti T, at al. Vascular dementia: diagnostic criteria for research studies: report of the NINDS-AIREN international workshop. Neurology 1993;4:250-260.
30. Petersen RC, Doody R, Kurz A et al. Current concepts in mild cognitive impairment. Arch Neurol 2001;58:1985-1992.
31. Huppert FA, Jorm AF, Brayne C, et al. Psychometric properties of the CAMCOG and its efficacy in the diagnosis of dementia. Aging Neuropsychol 1996;3:201-214.
32. Wright SL, Persad C. Distinguishing between depression and dementia in older persons: neuropsychological and neuropathological correlates. J Geriatr Psychiatry Neurol 2007;20:189-198.
33. Desmond DW. Vascular dementia: a construct in evolution. Cerebrovasc Brain Metab Rev 1996;8:296-325.
34. Norlund A, Rolstad S, Hellstrom P, Sjogren M, Hansen S, Wallin A. The Göteborg MCI study: mild cognitive impairment is a heterogeneous condition. J Neurol Neurosurg Psychiatry 2005;76:1485-1490.
35. Alladi S, Arnold R, Mitchell J, Nestor PJ, Hodges JR. Mild cognitive impairment: applicability of research criteria in a memory clinic and characterization of cognitive profile. Psychol Med 2006;36:507-515.