patients. The FIM-C profile of patients with dementia may mostly reflect global cognitive function, while the FIM-C *Social interaction* subscore of VaD patients may be more influenced by BPSD, especially *Aggressiveness*. The unique characteristics of the FIM-C seem to be useful to access cognitive disabilities inherent in dementia. A further functional neuroimaging study is necessary to provide more information on neurological background of the FIM-C profile among patients with dementia.

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Regular Article

Apathy is more severe in vascular than amnestic mild cognitive impairment in a community: The Kurihara Project

Kei Nakamura, MD, PhD, Mari Kasai, PhD, Yoshitaka Ouchi, PhD, Masahiro Nakatsuka, MD, PhD, Naofumi Tanaka, MD, PhD, Yuriko Kato, BA, Megumi Nakai, BA and Kenichi Meguro, MD, PhD*

Department of Geriatric Behavioral Neurology, Tohoku University Graduate School of Medicine, Sendai, Japan

Aim: The aim of this study was to estimate the prevalence of apathy, and to compare vascular mild cognitive impairment (vMCI), amnestic MCI (amMCI), and other type using Clinical Assessment for Spontaneity (CAS).

Methods: Agreement to take part in the study was obtained from 590 community dwellers, aged ≥75 years living in Kurihara, Japan. Of the 590 subjects, 221 had a clinical dementia rating (CDR) of 0 (normal); 295 had CDR 0.5 (mild cognitive impairment; MCI); and 74 had CDR 1+ (dementia). The CDR 0.5 subjects were divided into three groups: 55 with vMCI (Erkinjuntti *et al.* criteria), 91 with amMCI and 149 with other type. To evaluate the various aspects of apathy, we used the three CAS subscales: clinical interview (CAS1), self-evaluation (CAS2), and caregiver assessment (CAS3). Three analyses were then performed to determine: (i) the validity of CAS; (ii) the prevalence rate of apathy in CDR 0 versus CDR 0.5 versus CDR 1+; and (iii) the prevalence rate of apathy in normal versus vMCI versus amMCI versus other type.

Results: CAS was validated with the Apathy Evaluation Scale. There were significant differences among the three CDR groups in CAS1, CAS2 and CAS3 ($P < 0.001$). The prevalence rate of apathy in each CAS in the CDR 1+ group was higher than the CDR 0.5 group, which was higher than the CDR 0 group. There was a significant difference in CAS3 score between the four groups (the normal and the three subgroups; $P < 0.001$). Apathy in vMCI was more severe than in the other three groups ($P < 0.05$) on CAS3 score.

Conclusions: vMCI subjects have more severe apathy compared with amMCI subjects on caregiver assessment.

Key words: apathy, clinical dementia rating, dementia, mild cognitive impairment, subcortical vascular dementia.

APATHY, WHICH IS derived from the Greek pathos, or passions, is defined in broader terms conventionally as absence or lack of interest or concern.[1,2] Apathy is a common symptom in dementia, although the mechanisms of this apathy have not been studied.[1] According to cause of dementing disease, prevalence of apathy with Alzheimer's disease (AD) is 41.6% and that with subcortical vascular dementia (SVD) is 47.2%.[3] The qualitative difference of apathy between AD and SVD, however, is not clear.

Mild cognitive impairment (MCI) or clinical dementia rating (CDR) 0.5 is a transitional state between normal and dementia.[4–7] MCI with apathy is a risk factor of dementia.[8] There were some reports of prevalence of apathy in MCI subjects; the previous prevalence rate was 36.2% in the 75–95-year-old age group using Comprehensive Psychopathological Rating Scale by interviewer,[9] 18.5% in the 70–89-

*Correspondence: Kenichi Meguro, MD, PhD, Department of Geriatric Behavioral Neurology, Tohoku University Graduate School of Medicine, 2-1, Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan.
Email: k-meg@umin.ac.jp
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year-old age group using Neuropsychiatric Inventory (NPI) by caregiver,[10] and 15.0% in the ≥65-year-old age group using NPI by caregiver.[11] The prevalence of apathy may vary with age or testing method.

In order to evaluate the various aspects of apathy, Clinical Assessment for Spontaneity (CAS) was developed by the Japan Society for Higher Brain Dysfunction.[12,13] This scale has demonstrated substantial inter-rater and test–retest reliabilities,[12] and consists of CAS1 (clinical interview by physicians), CAS2 (self-evaluation), and CAS3 (caregiver assessment). Thus, CAS can evaluate apathy from three viewpoints: the physician, the person himself/herself, and a caregiver; and it may also reflect the disease characteristics. There has been no report, however, of a community-based study using CAS for MCI subjects.

Chiu *et al.* reported that the prevalence rate of apathy in outpatients with vascular cognitive impairment no dementia (VCIND; $n = 41$) was 24% using the NPI.[14] That, however, was not a community-based study, and they did not compare results with regard to the presence or absence of vascular lesions in CDR 0.5 subjects.

The Chiu *et al.* subjects with SVD had a very mild state (CDR 0.5) and then progressed to a mild state (CDR 1) due to poor control of vascular risk factors.[15] Individuals with very mild SVD, defined as vascular MCI (vMCI) are treatable, although most of them are hidden within the community.[15]

Thus, there is no consistent view of the prevalence of apathy on MCI subjects, and there has been no report of vMCI subjects using CAS in Japan.

The purpose of the present study was therefore to estimate the prevalence rate of apathy in each CDR group, and to compare the apathy prevalence rate and the apathy scale score among vMCI, amnestic MCI (amMCI), and other type of dementia using CAS.

METHODS

Subjects

From October 2009 to December 2010, 590 of the 1252 people aged ≥75 years living in the model area of Kurihara, Northern Japan agreed to take part in the study (47.1%).[16,17] Figure 1 shows the recruitment protocol for selecting the subjects: 221 had CDR 0, which means they were healthy elderly; 295 had CDR 0.5, which means they had MCI; and 74 had CDR 1+, which means they had dementia. We obtained written informed consent from all subjects. We utilized CDR, clinical examination, blood tests, neuropsychological tests and magnetic resonance imaging (MRI). The subjects with CDR 0.5 were divided into three subtype groups: 55 had vMCI; 91 had amMCI; and 149 had other type of dementia. The procedures for CDR assessment, MRI, and diagnostic criteria for dementia and CDR 0.5 subtypes (vMCI, amMCI and other type) are described in the following sections.

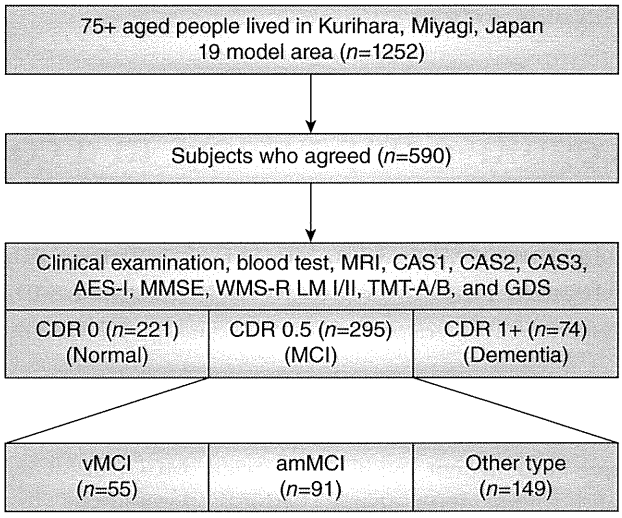

Figure 1. Study protocol. AES-I, Apathy Evaluation Scale–Informant version; amMCI, amnestic mild cognitive impairment; CAS, Clinical Assessment for Spontaneity; CDR, clinical dementia rating; GDS, Geriatric Depression Scale; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; TMT-A/B, Trail Making Test-A and B; vMCI, vascular mild cognitive impairment; WMS-R LM I/II, Wechsler Memory Scale–Revised Logical Memory I/II.

CDR assessment

A clinical team consisting of skilled physicians (neurologists and a psychiatrist) and skilled public health nurses determined CDR for each participant,[6,7] and were blinded to the cognitive test results. They used a Japanese version of the questionnaire of the CDR scoring sheet.[18] Before the physician interview, the public health nurses visited the subjects' homes to evaluate their daily activities. Observations by family members regarding the subjects' lives were described in a semistructured questionnaire. Subjects who lived alone were visited frequently by public health nurses to evaluate their daily lives. The physicians interviewed the subjects to assess episodic memory, ori-

entation, and judgment. Finally, with reference to the information provided by the family members, the CDR for each of the subjects was determined at a joint meeting of the physicians and public health nurses. One author (KM) was certified as a CDR rater at the Washington University School of Medicine Alzheimer's Disease Research Center Memory and Aging Project. We used CDR scores and CDR-sum of boxes (CDR-SOB) scores.

Diagnostic criteria for dementia and CDR 0.5 subtypes

Dementia was diagnosed according to DSM-IV criteria.[19] In this study, CDR 0.5 subtypes were divided into the three groups: vMCI, amMCI, and other type.

vMCI

According to the criteria of Erkinjuntti *et al.*, the subjects who met the following criteria were diagnosed with SVD:[20] memory item of CDR score ≥0.5; presence of executive dysfunction (we used mean performance time +1 SD of Trail Making Test [TMT] A or B by age and educational levels[21]); ≥5 lacunar infarctions along with white matter lesions (Erkinjuntti *et al.* criteria[20]); presence of neurologic signs, and absence of cortical infarction (≥8 mm) on MRI. The subjects with SVD who scored CDR 0.5 were defined as 'vMCI' in this study.[15]

AmMCI

CDR score 0.5; memory item of CDR score ≥0.5; absence of neurologic signs, the absence of infarction on MRI; and possible AD based on NINCDS-ADRDA criteria.[22]

Other type

By definition, this group consisted of subjects excluded from vMCI and amMCI, therefore heterogeneity was high. Other type included very mild stage of mixed type dementia, front temporal dementia, dementia with Lewy bodies, vascular dementia other than SVD, or unknown etiology, and so on. A few subjects who were not able to undergo MRI due to metal in their body, such as a cardiac pacemaker, were also included in this group.

MRI

We used the 1.5-T MRI (Achiva 1.5T or Intera 1.5T; Philips Electronics Japan, Tokyo, Japan). The combined axial T1-weighted, T2-weighted and fluid attenuated inversion recovery (FLAIR) images were used to evaluate cerebrovascular disease (CVD). Lesions were considered to be CVD when they had low intensity on T1-weighted or FLAIR MRI and high intensity on T2-weighted MRI at the same location. We operationally considered those changes with diameter ≥4 mm as CVD (cerebral infarction presence). The images were visually evaluated by two teams, which consisted of two neurologists and a psychiatrist, and a senior neurologist.[23]

Apathy assessment

We used CAS to evaluate apathy.[12,13] CAS was developed by the Japan Society for Higher Brain Dysfunction, and demonstrated substantial inter-rater and test–retest reliabilities.[12] We used CAS1 (clinical interview), CAS2 (self-evaluation), and CAS3 (caregiver assessment). We did not use CAS4 (observation of daily life) and CAS5 (clinical overview) because they were difficult to use in a community-based study.

CAS1 is a clinical interview by a skilled physician and consists of 15 items (e.g. expression, eye contact, grooming and appearance etc.), which are then summed to give a total score (range 0–60). Each item is scored on a 5-point scale from 0 (no problem) to 4 (severe apathy). In this study, the physician performed the evaluation by observation at a medical examination. The cut-off score of CAS1 was 2 (without apathy)/3 (with apathy) for the 70s age group.[13]

CAS2 is a self-evaluation consisting of 33 items (e.g. loss of interest or concern and energy loss). Each item is scored on a 4-point scale from 0 (frequent) to 3 (nothing) (accumulative range 0–99). The cut-off score of CAS2 was 32 (without apathy)/33 (with apathy) for the 70s age group.[13]

CAS3 is a caregiver assessment about daily activities consisting of 16 items (e.g. preparing a meal, toilet activities, brushing of teeth etc). Items are scored on a 5-point scale from 0 (always spontaneously) to 4 (no spontaneity at all) with regard to how they are performed (range 0–100%). The cut-off score of CAS3 was 0 (without apathy)/1 (with apathy) for the 70s age group.[13]

To clarify the validity of CAS, we used the Apathy Evaluation Scale–Informant version (AES-I) as the standard apathy scale. The AES-I was given as a paper and pencil test to the caregiver or family member of each subject. The cut-off score of AES-I

Table 1. Demographic data

	CDR 0 (Normal)	CDR 0.5 (MCI)	CDR 1+ (Dementia)
n (M/F)[†]	221 (92/129)	295 (108/187)	74 (25/49)
Age (years)	79.0 ± 3.6[b]	80.4 ± 4.3[a]	82.3 ± 4.4[ab]
Educational level	9.3 ± 2.1[b]	8.5 ± 1.7[a]	7.8 ± 1.5[ab]
MMSE	25.4 ± 2.6[b]	22.8 ± 3.4[a]	16.2 ± 5.4[ab]
GDS	3.9 ± 2.6[b]	4.8 ± 3.1[a]	6.1 ± 3.2[ab]

Statistical analysis: one-way ANOVA (post-hoc test; Bonferroni test). [†]χ^2 test, $P < 0.05$. [a]Significant difference with CDR 0 ($P < 0.05$); [b]significant difference with CDR 0.5 ($P < 0.05$). CDR, clinical dementia rating; GDS, Geriatric Depression Scale; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

was 40 (without apathy)/41 (with apathy) for all age groups.[2]

Neuropsychological tests

We used Mini Mental State Examination (MMSE)[24] for assessing global intellectual function; Wechsler Memory Scale–Revised (WMS-R) Logical Memory (LM) I/II[25] for assessing memory (I, encoding; II, delayed memory); TMT A/B for assessing executive function (A, divided attention; B, cognitive flexibility);[26] and Geriatric Depression Scale (GDS) short version[27] for assessing depression.

Demographics

Table 1 lists subject demographic data for each CDR group. There was no significant difference in sex among the three groups. The CDR 1+ group was oldest with the lowest education level and MMSE score, and highest GDS score. The CDR 0.5 group was older with lower education level and MMSE score, and higher GDS score than the CDR 0 group.

Table 2 lists demographics and CAS scores for normal, vMCI, amMCI, and other types. There was no significant difference in sex, age, educational level, and GDS score. MMSE score for vMCI was lowest in

Table 2. Demographics and CAS scores vs MCI type (mean ± SD)

	CDR 0	CDR 0.5		
	Normal	vMCI	amMCI	Other type
n (M/F)[†]	221 (92/129)	55 (23/32)	91 (24/67)	149 (61/88)
Age (years)[‡]	79.0 ± 3.6[b]	81.3 ± 4.6[a]	80.0 ± 4.1	80.3 ± 4.3[a]
Educational level[‡]	9.3 ± 2.1[b]	8.2 ± 1.6[a]	8.7 ± 1.8[a]	8.5 ± 1.7[a]
MMSE[‡]	25.4 ± 2.6[b]	21.5 ± 2.9[a]	23.1 ± 3.3[ab]	23.1 ± 3.5[ab]
CDR-SOB[§]	0.25 ± 0.36[bcd]	1.76 ± 0.97[ac]	1.34 ± 0.78[ab]	1.47 ± 0.90[a]
GDS[‡]	3.9 ± 2.6[b]	5.4 ± 3.3[a]	4.3 ± 2.9[a]	4.8 ± 3.1[a]
CAS1[§]	1.9 ± 2.9[bcd]	4.8 ± 6.1[a]	5.6 ± 5.4[a]	4.4 ± 4.9[a]
CAS2[§]	14.5 ± 9.8[bcd]	22.1 ± 15.0[a]	18.8 ± 10.6[a]	20.5 ± 13.6[a]
CAS3[§]	0.9 ± 2.3[bcd]	4.9 ± 5.1[acd]	2.7 ± 4.8[ab]	2.9 ± 4.9[ab]

[†]χ^2 test, $P < 0.05$; [‡]one-way ANOVA (post-hoc test; Bonferroni test); [§]Kruskal–Wallis test (post-hoc test; Mann–Whitney test). [a]Significant difference with the normal group ($P < 0.01$); [b]significant difference with the vMCI group ($P < 0.01$); [c]significant difference with the amMCI group ($P < 0.01$); [d]significant difference with the other type group ($P < 0.01$). amMCI, amnestic MCI; CAS, Clinical Assessment for Spontaneity; CDR, clinical dementia rating; CDR-SOB, clinical dementia rating–sum of box; GDS, Geriatric Depression Scale; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; vMCI, vascular MCI.

the three groups. CDR-SOB for amMCI was lower than for vMCI.

Analyses

Validity of CAS

We evaluated convergent and discriminate validity coefficients (Pearson's r) between CAS1, CAS2 and CAS3 and AES-I, WMS-R LM I/II and TMT-A/B for all participants.

Using the cut-off score of the AES-I, we calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) as well as likelihood ratios of CAS3 (standard and new cut-off scores) with standard formulas for all participants.

Prevalence of apathy vs CDR score

We calculated the prevalence rate of apathy among the three CDR groups using CAS1, CAS2 and CAS3 (new cut-off score, 7/8). We used the chi-squared test in statistical analysis ($P < 0.05$, post-hoc test; chi-squared test, $P < 0.05/3$).

Prevalence and severity of apathy vs MCI type

Prevalence of apathy vs MCI type

We calculated the prevalence of apathy for each of the three CDR 0.5 subgroups and the normal group using CAS1, CAS2, and CAS3 (new cut-off score; 7/8). We used the chi-squared test ($P < 0.05$, post-hoc test; chi-squared test, $P < 0.05/4$) in statistical analysis. Cut-off score of CAS1 was 2/3 (apathy absence/presence), CAS2 was 32/33, and CAS3 was 0/1%, according to the previous study.[11]

Severity of apathy vs MCI type

We compared the normal, vMCI, amMCI and other type on CAS1, CAS2, and CAS3 scores. We used Kruskal–Wallis test ($P < 0.05$; post hoc tests, Mann-Whitney test, $P < 0.05/4$) in statistical analysis.

Additional analysis

We carried out ANCOVA with covariates (age, education, SOB, and MMSE) for CAS1, CAS2 and CAS3 among the three CDR 0.5 subgroups.

Ethics

Written informed consent was obtained from each of the participants with CDR 0 and 0.5, and also from the family of those with CDR 0.5 and those with dementia. The study was approved by the ethics committees of the Kurihara city government and Tohoku University Graduate School of Medicine.

RESULTS

Validity of CAS

Convergent and discriminate validity coefficients for apathy, depression, memory, executive function were all significant ($P < 0.001$). For apathy, the convergent validity coefficients were between 0.37 and 0.78. The convergent validity coefficient between the CAS3 and AES-I as caregiver-rated was higher than the intercorrelations among CAS1, CAS2, and CAS3. CAS1 had moderately higher correlations with TMT-B and WMS-R LM I. CAS2 had a moderately higher correlation with GDS. CAS3 and AES-I had moderately higher correlations with TMT-B (Table 3).

The cut-off scores of the CAS3 and AES-I were 7/8 (new cut-off score) and 40/41, or 0/1 (standard cut-off score) and 40/41, sensitivity was 91.8 and 98.0%, and specificity 90.2 and 58.7%, respectively; the PPV were 47.9 and 18.9%, and the NPV 99.1 and 99.7%, respectively. The positive likelihood ratios were 9.37 and 2.37, and the negative likelihood ratios 11.00 and 29.35, respectively.

Prevalence of apathy vs CDR score

Figure 2 shows the apathy prevalence rate for each CDR group using CAS1, CAS2, and CAS3.

In CAS1, the prevalence of apathy for CDR 0, CDR 0.5, and CDR 1+ was 27.2%, 51.6%, and 87.5%, respectively. There were significant differences among the three CDR groups on CAS1 ($\chi^2 = 83.2$, d.f. = 2, $P < 0.001$). The prevalence of apathy in the CDR 1+ group was higher than in the CDR 0.5 group, which was higher than in the CDR 0 group ($P < 0.01$).

In CAS2, the prevalence of apathy for CDR 0, CDR 0.5, and CDR 1+ was 5.1%, 17.4%, and 52.4%, respectively. There were significant differences between the three CDR groups on CAS2 ($\chi^2 = 72.9$, d.f. = 2, $P < 0.001$). The prevalence of apathy in the CDR 1+ group was higher than in the CDR 0.5 group, which was higher than in the CDR 0 group ($P < 0.01$).

On CAS3, using the new cut-off score (7/8), the prevalence of apathy for CDR 0, CDR 0.5, and CDR 1+ was 2.3%, 14.2%, and 71.6%, respectively. There were significant differences between the three CDR

Table 3. Convergent and discriminant validity of CAS in all participants

	Apathy			
	CAS1 (clinician)	CAS2 (self)	CAS3 (caregiver)	AES-I (caregiver)
Apathy				
CAS1 (clinician)				
CAS2 (self)	0.50*			
CAS3 (caregiver)	0.46*	0.37*		
AES-I (caregiver)	0.46*	0.45*	0.78*	
Depression				
GDS (self)	0.27*	0.49*	0.19*	0.25*
Memory				
WMS-R LM I	−0.42*	−0.25*	−0.31*	−0.31*
WMS-R LM II	−0.35*	−0.25*	−0.28*	−0.30*
Executive function				
TMT-A	0.28*	0.22*	0.25*	0.19*
TMT-B	0.47*	0.19*	0.51*	0.52*

*$P < 0.001$. Intercorrelations are shown for clinician-, self-, and caregiver-rated measures of apathy and depression (Pearson's r). AES-I, Apathy Evaluation Scale–Informant version; CAS, Clinical Assessment for Spontaneity; GDS, Geriatric Depression Scale; TMT, Trail-Making Test; WMS-R LM, Wechsler Memory Scale–Revised Logical memory.

groups on CAS3 ($\chi^2 = 192.5$, d.f. = 2, $P < 0.001$). The prevalence of apathy in the CDR 1+ group was higher than in the CDR 0.5 group, which was higher than in the CDR 0 group ($P < 0.01$). In contrast, using a standard cut-off score (0/1) for CAS3, the prevalence of apathy for CDR 0, CDR 0.5, and CDR 1+ was 23.5%, 50.8%, and 95.9%, respectively. There were significant differences among the three CDR groups on CAS3 ($\chi^2 = 39.5$, d.f. = 2, $P < 0.001$). The prevalence of apathy in the CDR 1+ group was higher than in the CDR 0.5 group, which was higher than in the CDR 0 group ($P < 0.01$).

Using a cut-off score of 40/41 on the AES-I[2], the apathy prevalence was 1.0% in CDR 0, 3.2% in CDR 0.5, and 56.5% in CDR 1+ participants. There were significant differences among the three CDR groups on AES-I ($\chi^2 = 220.6$, d.f. = 2, $P < 0.001$). The prevalence of apathy in the CDR 1+ group was higher than in the CDR 0.5 group, which was higher than in the CDR 0 group ($P < 0.05$).

Prevalence and severity of apathy vs MCI type

Prevalence of apathy vs MCI type

On CAS1, there was a significant difference among the three CDR 0.5 subgroups and the normal group

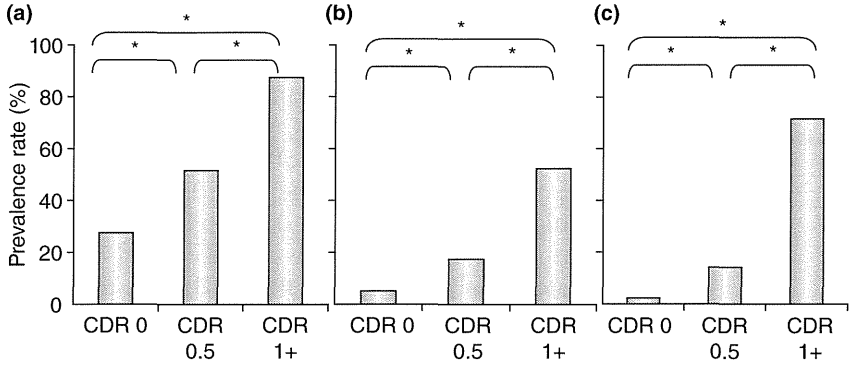

Figure 2. Prevalence of apathy vs clinical dementia rating (CDR) score. (a) Clinical Assessment for Spontaneity (CAS)1, (b) CAS2, and (c) CAS3 (cut-off, 7/8). Statistical analysis: chi-squared test, $P < 0.05$ (post-hoc test; chi-squared test, $P < 0.05/3$), *$P < 0.001$.

in prevalence of apathy (normal, vMCI, amMCI and other type: 27.2%, 47.3%, 55.1% and 51.0%, respectively; $\chi^2 = 30.8$, d.f. = 3, $P < 0.001$). On post-hoc test, the normal group had a significantly lower prevalence of apathy than vMCI, amMCI and other type on CAS1 ($P < 0.01$).

On CAS2, there was a significant difference among the three CDR 0.5 subgroups and the normal group in prevalence of apathy (normal, vMCI, amMCI and other type: 5.1%, 33.3%, 7.8% and 17.2%, respectively; $\chi^2 = 38.1$, d.f. = 3, $P < 0.001$). On post-hoc test, the normal group had a significantly lower prevalence of apathy than vMCI and other type on CAS2 ($P < 0.01$). The vMCI group had a significantly higher prevalence of apathy than the amMCI group ($P < 0.01$).

Using the new cut-off score on CAS3 (7/8), there was a significant difference among the three CDR 0.5 subgroups and the normal group in prevalence of apathy (normal, vMCI, amMCI and other type: 2.3%, 25.5%, 11.0% and 12.1%, respectively; $\chi^2 = 32.2$, d.f. = 3, $P < 0.001$). On post-hoc test, the normal group had a significantly lower prevalence of apathy than vMCI, amMCI and other type on CAS3 ($P < 0.01$).

Using the standard cut-off score for CAS3 (0/1), there was a significant difference among the three CDR 0.5 subgroups and the normal group in prevalence of apathy (normal, vMCI, amMCI and other type: 23.5%, 67.3%, 46.2% and 47.7%, respectively; $\chi^2 = 47.3$, d.f. = 3, $P < 0.001$). On post-hoc test, the normal group had a significantly lower prevalence of apathy than vMCI, amMCI and other type on CAS3 ($P < 0.01$).

Severity of apathy vs MCI type

Table 2 lists the demographics and CAS scores for normal, vMCI, amMCI and other type.

On CAS1, there was a significant difference among the four groups (three CDR 0.5 subgroups and the normal group; H = 54.3, d.f. = 3, $P < 0.001$). Each CDR 0.5 subgroup had significantly more severe apathy than the normal group ($P < 0.01$).

On CAS2, there was a significant difference among the four groups (H = 27.1, d.f. = 3, $P < 0.001$). Each CDR 0.5 subgroup had significantly more severe apathy than the normal group ($P < 0.01$).

In CAS3, there was significant difference among the four groups (H = 57.3, d.f. = 3, $P < 0.001$). Each CDR 0.5 subgroup had significantly more severe apathy than the normal group ($P < 0.01$). vMCI subjects had significantly severer apathy than normal, amMCI, and other type subjects ($P < 0.01$).

Additionally, we carried out ANCOVA with covariates (age, education, SOB, and MMSE) for CAS1, CAS2 and CAS3 among the three CDR 0.5 subgroups. There was no significant difference among the three groups on CAS1 ($F = 2.3$, $P = 0.103$) with significant SOB ($F = 7.1$, $P = 0.008$) and MMSE effects ($F = 5.0$, $P = 0.027$), but no age ($F = 0.6$, $P = 0.444$) or education effects ($F = 2.6$, $P = 0.105$). There was no significant difference among the three groups on CAS2 ($F = 0.5$, $P = 0.616$) with a significant SOB effect ($F = 7.1$, $P = 0.008$), but no age ($F = 2.1$, $P = 0.146$), education ($F = 0.3$, $P = 0.578$), or MMSE effects ($F = 0.3$, $P = 0.869$). There was no significant difference among the three groups on CAS3 ($F = 1.8$, $P = 0.173$) with a significant SOB effect ($F = 64.0$, $P < 0.001$), but no age ($F = 0.4$, $P = 0.505$), education ($F = 0.04$, $P = 0.833$), or MMSE effects ($F = 0.1$, $P = 0.756$).

DISCUSSION

In this study, we confirmed the validity of CAS using AES-I as the standard apathy scale. The prevalence of apathy in the CDR 1+ group was higher than in the CDR 0.5 group, which was higher than in the CDR 0 group on each CAS. The vMCI subjects had more severe apathy than the normal, the amMCI and the other type groups on CAS3 scores.

Given that the convergent validity coefficient between CAS3 and AES-I as caregiver-rated was comparatively high, it is suggested that CAS3 is a valid assessment of apathy. Using the cut-off score of the AES-I, we calculated sensitivity and specificity for a new cut-off score of CAS3. CAS3 (new cut-off score) was very close to the previous estimate of apathy prevalence rate.[11] We recommend use of the new cut-off score for CAS3 (7/8).

When the three CDR groups were compared, the prevalence of apathy was significantly higher in the order of CDR 0, CDR 0.5 and CDR 1+. In MCI subjects, CAS2 and CAS3 (new cut-off score) were close to previous estimates of apathy prevalence (18.5%,[10] 15.0%[11]), and lower than the Palmer *et al.* study (36.2%[9]). CAS1 produced a higher prevalence rate of apathy than other tests; in contrast, AES-I produced a lower prevalence rate of apathy than other tests in MCI participants. This may be due to the difference in apathy assessment method between the present study (CAS) and the previous studies (NPI).[10,11]

The present vMCI group had significantly more severe apathy than the normal, the amMCI, and the other type groups on CAS3. In the present study, we considered vMCI as CDR 0.5 with CVD, with neurological signs, and meeting the Erkinjuntti *et al.* SVD criteria, rather than amMCI +lacunes. vMCI subjects had a higher prevalence of apathy than amMCI on CAS2 and CAS3, and vMCI had severer apathy scores than amMCI. We consider that the reason for this is because very mild SVD involves damaged fronto-subcortical networks related to executive function, emotion, and motivation. Meguro *et al.* reported that the CDR 0.5 with CVD group, who need early medical intervention, had a higher mortality rate than the CDR 0.5 without CVD group.[15] We need to investigate the relationship between apathy and neurobiology, especially thalamic infarction in the future.

There were two limitations in the present study. First, apathy may exist in those people who did not agree to take part in the study. We need to increase the agreement rate for the survey, and to investigate the function of daily activities among non-agreeing people. Second, the CAS result for apathy in community-dwelling elderly people may be misinterpreted, because the cut-off for CAS was set up for head-injury patients and healthy people in a clinic-based study.[12]

Earlier therapeutic intervention would be needed for community-dwelling people with vMCI who have apathy. Because elderly people with vMCI and apathy do not tend to participate in community activities, it is necessary to urge the participation in activity. Moreover, it seems that it is necessary to treat the vascular risk factor positively because there is sometimes refusal of hospital consultation.

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班　長　　清原　裕
〒812－8582　福岡市東区馬出3-1-1
九州大学大学院医学研究院環境医学
TEL：092-642-6104　　FAX：092-642-6108

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