Table 2. Demographic and clinical valuables in five dementia groups and the NE subjects group

	DLB (n = 55)	AD (n = 191)	FTLD (n = 16)	VAD (n = 18)	O/U DEMENTIA (n = 37)	NE SUBJECTS (n = 32)	P-VALUE
Age (in yrs.)	79.4 ± 5.4	75.4 ± 8.6	64.6 ± 9.6	77.7 ± 7.6	78.0 ± 7.9	74.7 ± 7.5	<0.001[a]
Male	32 (58.1%)	82 (41.9%)	10 (62.5%)	12 (66.7%)	15 (40.5%)	14 (43.8%)	0.107[b]
Duration (in yrs.)	3.6 ± 2.3	3.3 ± 2.1	4.1 ± 3.0	4.4 ± 4.6	3.5 ± 2.4	n.a.	0.287[a]
MMSE score	17.6 ± 6.3	18.3 ± 5.7	18.9 ± 6.3	18.6 ± 4.5	18.4 ± 6.2	27.9 ± 1.8	<0.001[a]
Medication							
Cholinesterase inhibitors	19 (34.5%)	50 (26.2%)	8 (50.0%)	3 (16.7%)	4 (10.8%)	n.a.	0.017[b]
Benzodiazepine anxiolytics	16 (29.1%)	28 (14.7%)	3 (18.8%)	3 (16.7%)	6 (16.2%)	n.a.	0.195[b]
Antipsychotics	6 (10.9%)	5 (2.6%)	2 (12.5%)	1 (5.6%)	6 (16.2%)	n.a.	0.004[b]
Antidepressants	7 (12.7%)	19 (9.9%)	2 (12.5%)	1 (5.5%)	2 (5.4%)	n.a.	0.798[b]
Bedroom sharing with patients	29 (52.7%)	110 (57.6%)	12 (75.0%)	4 (22.2%)	16 (43.2%)	n.a.	0.011[b]

Notes: Values are n (%), or mean ± SD.
DLB: dementia with Lewy bodies; AD: Alzheimer's disease; FTLD: frontotemporal lobar degeneration; VaD: vascular dementia; O/U dementia: other/unspecified dementia; NE subjects: normal elderly subjects; MMSE: Mini-Mental State Examination; n.a.: not applicable.
Analysis by [a]one-way ANOVA or [b]Fisher's exact probability test.

Table 3. Frequency of sleep talking, loud sleep talking, frequent sleep talking, long-term sleep talking, and SNBD in five dementia groups and the NE subjects group

SLEEP FEATURES	DLB (n = 55)	AD (n = 191)	FTLD (n = 16)	VAD (n = 18)	O/U DEMENTIA (n = 37)	NE SUBJECTS (n = 32)	p-VALUE
Sleep talking	34 (61.8%)	36 (18.8%)	2 (12.5%)	6 (33.3%)	10 (27.0%)	2 (6.3%)	<0.001*
Loud sleep talking	22 (40.0%)	6 (3.1%)	0 (0%)	1 (5.6%)	4 (10.8%)	1 (3.1%)	<0.001†
Frequent sleep talking	20 (36.4%)	16 (8.4%)	1 (6.3%)	3 (16.7%)	6 (16.2%)	2 (6.3%)	<0.001‡
Long-term sleep talking	14 (25.5%)	13 (6.8%)	1 (6.3%)	4 (22.2%)	4 (10.8%)	1 (3.1%)	0.002§
SNBD	27 (49.1%)	35 (18.3%)	5 (31.3%)	8 (44.4%)	12 (32.4%)	n.a.	<0.001§

Notes: Values are n (%).
DLB: dementia with Lewy bodies; AD: Alzheimer's disease; FTLD: frontotemporal lobar degeneration; VaD: vascular dementia; O/U dementia: other/unspecified dementia; NE subjects: normal elderly subjects; SNBD: sleep and night-time behavior disorder; n.a.: not applicable.
Analysis by Fisher's exact probability test and Bonferroni Z-test.
*DLB significantly higher than AD, FTLD, O/U dementia, and NE subjects.
†DLB significantly higher than AD, O/U dementia, and NE subjects (FTLD was not compared with other groups).
‡DLB significantly higher than AD and NE subjects.
§DLB significantly higher than AD.

Results

Table 2 presents the demographic and clinical indices of the subjects. Five dementia and NE subject groups were involved in the present study. There were significant differences in age, MMSE, and the ratio of bedroom sharing in six groups. As for medication, there was a significant difference in the frequency of cholinesterase inhibitors and antipsychotics prescription, but no significant differences were observed in the frequency of other drug usage in five dementia groups. Memantine or melatonin was not prescribed to any patient in this study.

Table 3 shows the prevalence of sleep talking, three features of sleep talking, and SNBD in all the

Table 4. Results of multiple logistic regression analysis associated with sleep talking

FACTORS	WALD	EXP (B)	95% CONFIDENCE INTERVAL	P-VALUE
Diagnosis (DLB or not)	32.323	6.967	3.568–13.603	<0.001
Age	0.359	1.011	0.976–1.046	0.549
Duration	0.004	0.996	0.889–1.116	0.947
MMSE score	0.017	0.997	0.950–1.046	0.897
Bedroom sharing	0.576	0.784	0.419–1.469	0.448
Cholinesterase inhibitors	0.767	0.758	0.407–1.410	0.381
Benzodiazepine	0.276	1.212	0.591–2.485	0.599
Antipsychotic	0.165	0.795	0.262–2.413	0.685
Antidepressant	0.130	0.840	0.327–2.160	0.718

Note: DLB: dementia with Lewy bodies; MMSE: Mini-Mental State Examination.

Table 5. Sensitivity and specificity of sleep talking, three features of sleep talking, and SNBD for the differentiation of DLB from AD or all other dementias

	DIFFERENTIATION OF DLB FROM AD		DIFFERENTIATION OF DLB FROM ALL OTHER DEMENTIAS	
	SENSITIVITY (%)	SPECIFICITY (%)	SENSITIVITY (%)	SPECIFICITY (%)
Sleep talking	61.8	81.2	61.8	79.4
Loud sleep talking	40.0	96.9	40.0	95.8
Frequent sleep talking	36.4	91.6	36.4	90.1
Long-term sleep talking	25.5	93.2	25.5	91.6
SNBD	49.1	81.7	49.1	77.1

Note: DLB: dementia with Lewy bodies; AD: Alzheimer's disease; SNBD: sleep and nighttime behavior disorder.

six groups. Sleep talking occurred most frequently in the DLB group, followed by the VaD group. It is noteworthy that only 6.3% of the NE subjects presented with sleep talking. There was a significant difference in the prevalence of sleep talking in these six groups. The prevalence of sleep talking in the DLB group was significantly higher than in other groups, except for the VaD group. Of the 34 DLB patients who had sleep talking, 22 patients (64.7%) showed loud sleep talking and the prevalence of loud sleep talking in the DLB group was significantly higher than that in the AD, O/U dementia, and NE subject groups. SNDB occurred most frequently in the DLB group and the prevalence of SNDB was significantly higher in the DLB group than in the AD group.

Multiple logistic regression analysis showed that a diagnosis of DLB was significantly associated with the presence of sleep talking (Table 4). There was no association between age, sex, duration of disease, MMSE score, bedroom sharing, or psychotropic drug usage and the presence of sleep talking.

Table 5 shows the sensitivity and specificity of sleep talking, three features of sleep talking, and SNBD for the differential diagnosis of DLB from AD and that of DLB from all other types of dementia. The sleep talking yielded high specificity (81.2%) and some sensitivity (61.8%) for the differential diagnosis of DLB from AD. The loud sleep talking could improve the specificity (96.9%), but the sensitivity would decrease (40.0%). Even with the differentiation of DLB from all other dementias, the specificity of sleep talking and loud sleep talking did not change (79.4% and 95.8% respectively).

Discussion

Sleep talking is not necessarily a pathological symptom, and it often occurs in normal healthy people. Bjorvatn *et al.* (2010) reported that sleep talking occurs at least once a week in 6.3% of adults in the general population. In the present study, 6.3% of NE subjects showed sleep talking, which is very similar to Bjorvatn *et al.*'s data. These findings indicate that the high prevalence of sleep talking in patients with dementia may be associated with some underlying pathological changes.

In this study, the prevalence of sleep talking differed according to the diagnostic group. In

the DLB group, more than 60% of patients exhibited sleep talking, and the prevalence was significantly higher than in any other dementia types. Although the pathophysiology of sleep talking is not well understood, sleep talking is reported to be seen with high frequency in patients with RBD (Li *et al.*, 2010). Boeve (2010) summarized demographics and clinical phenomenology of RBD, and demonstrated that abnormal vocalization is considered to characterize RBD, which is considered to be frequently associated with an underlying synucleinopathy, such as DLB (Boeve *et al.*, 2003a), and rarely with other neurodegenerative disorders. Ferman *et al.* (2011) reported that a history of RBD was present in 76% of autopsy-confirmed DLB patients. Therefore, RBD may be responsible for sleep talking in people with DLB.

We observed a high specificity of sleep talking (81.2%) for the differentiation of DLB from AD. In particular, the presence of loud sleep talking showed extremely high specificity (96.9%). Even in the differentiation of DLB from all other dementias, the specificity of loud sleep talking was kept high (95.8%). These findings suggest the usefulness of sleep talking to discriminate patients with DLB from those with other types of dementia. Although the utilization of SPECT and 123I-MIBG myocardial scintigraphy are limited to well-equipped hospitals, screening questions concerning sleep talking are easy to ask in clinical practice. Thus, patients suspected of having DLB should be questioned about the presence of sleep talking, in particular, the volume of sleep talking.

There was no significant difference between the DLB and VaD groups in the prevalence of sleep talking. This result may reflect low statistical power due to small sample size in the VaD group. However, the prevalence of sleep talking in the VaD group (33.3%) was higher than in NE subjects (6.3%), which did not reach statistical significance. To our knowledge, there have been no reports that investigated the prevalence of RBD in patients with VaD. Although RBD is frequently seen in patients with neurodegenerative diseases, RBD in patients with a pure pontine infarction has also been reported (Xi and Luning, 2009). Some vascular damage around the pons may cause RBD in patients with VaD, and this might explain a certain prevalence of sleep talking in the VaD group.

Sleep disturbance occurs in many forms of dementia. Guarnieri *et al.* (2012) reported that over 60% of persons with cognitive decline had one or more sleep disturbances. In this study, we also investigated the prevalence of sleep and nighttime behavior disorder. In the VaD and FTLD groups, the prevalence of SNBD was higher than that of sleep talking. On the other hand, in the DLB group, the prevalence of SNBD was lower than that of sleep talking. Severe daytime sleepiness predicts VaD (Guarnieri *et al.*, 2012), and sleep-disordered breathing was frequent in VaD patients (Elwood *et al.*, 2011). Anderson *et al.* (2009) have demonstrated sleep–wake disturbance in patients with FTD, who showed increased nocturnal activity and decreased morning activity. These findings suggest that each form of dementia may have a disease-specific sleep disturbance. Ferman and Boeve (2007) reported that sleep disturbance is helpful in differentiating DLB from AD early in the disease course. However, it may be more efficient to focus on sleep talking than to assess overall sleep disturbances for the differentiation of DLB from other dementias.

A recent review of RBD has described that the commonly used medications may induce or unmask latent RBD, and antidepressants are most commonly implicated in altering muscle control during REM and causing RBD (Trotti, 2010). On the other hand, based on a large case series and clinical experience, benzodiazepine clonazepam is considered the first-line treatment for RBD (Chenck and Mahowald, 1990). In the present study, no significant differences were observed in the frequency of benzodiazepine anxiolytics and antidepressant usage between the dementia groups. However, there were significant differences in the frequency of cholinesterase inhibitors and antipsychotic prescriptions. To our knowledge, there are no reports that indicate an association between antipsychotics and RBD. As for cholinesterase inhibitors, Boeve *et al.* (2003c) reported that among 50 patients with DLB and RBD who were treated with donepezil, none experienced significant benefit. Furthermore, multiple logistic regression analysis did not reveal any significant association between the use of these psychotropic drugs and the presence of sleep talking. Therefore, the difference in the frequency of sleep talking between different dementia types cannot be attributed to the effect of psychotropic drugs.

Several methodological issues limit the interpretation of results of this study. First, the diagnosis relied solely on clinical basis without histopathologic confirmation, with inevitably some uncertainty about the rate of misclassification. Although clinical studies are in fact influenced by the quality of clinical diagnosis, clinical studies with prospective clinical data collection can assess patients' sleep disturbances more accurately than can autopsy studies with retrospective data review. Moreover, we supplemented clinical diagnosis with neuroimaging studies. Second, we obtained

information about sleep talking from patients' caregivers. However, nearly half of the caregivers did not share their bedroom with the patients. This condition may make it more difficult for the caregivers to note patients' sleep talking and would increase the false-negative rate of sleep talking. In our study, approximately 60% of the patients with DLB had sleep talking, but this rate might be lower than the true rate. Third, although we considered that RBD was primarily responsible for sleep talking in the dementia patients, no patient with sleep talking was confirmed by PSG whether they had RBD or not. Therefore, the relationship between sleep talking and RBD can only be hypothesized. However, our main aim was to find an alternative to PSG, which can discriminate DLB from AD or all other dementias easily. In the future study, sleep talking in people with dementia need to be evaluated by PSG.

Despite these limitations, we believe that our findings are quite reliable because they are based on a prospective study design and on a consecutive patient series whose diagnosis was carefully made using widely accepted clinical criteria.

Conclusion

The questionnaire about sleep talking, especially the volume of sleep talking, may be useful in the clinical discrimination of DLB from not only AD but also from all other types of dementia.

Conflict of interest

None.

Description of authors' role

Kazuki Honda designed this study, worked on data analysis, and wrote the paper. Yusuke Yatabe, Keiichiro Kaneda, Seiji Yuki, Yusuke Ogawa, Shiho Matuzaki, Atsuko Tsuyuguchi, Hibiki Tanaka, Hiroko Kashiwagi, Noriko Hasegawa, and Tomohisa Ishikawa helped in collecting the data. Mamoru Hashimoto supervised this study. Manabu Ikeda was responsible for the statistical design of the study.

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RESEARCH ARTICLE

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Association of cerebral small vessel disease with delusions in patients with Alzheimer's disease

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Background: Cerebral small vessel disease (SVD) is frequently observed in patients with Alzheimer's disease (AD). However, the association between SVD and clinical symptoms exhibited by patients with AD remains unclear. This study examined the association of SVD as observed on magnetic resonance imaging (MRI) with behavioural and psychological symptoms of dementia and cognitive function of patients with probable AD.

Methods: A total of 163 consecutive patients (55 men, 108 women) with probable AD were included in this cross-sectional study of a prospective cohort. Patients were divided into two groups based on the presence or absence of cerebral SVD [white matter hyperintensities (WMH) grade 0/1 (Fazekas scale) and no lacunes: SVD absent, WMH grade 2/3 (Fazekas scale) or the number of lacunes ≥1: SVD present]. Cognitive functions were assessed using the Mini mental state examination, word recall and recognition subtests in the Alzheimer's Disease Assessment Scale—Cognitive Subscale, as well as the letter fluency task and the category fluency task. Psychiatric symptoms were rated according to Neuropsychiatric Inventory.

Results: Patients with probable AD with cerebral SVD had significantly more delusions and depression than those without SVD. No significant differences were observed in other neuropsychiatric symptoms, MMSE or word recall and recognition tests between both groups.

Conclusions: Our results suggest that cerebral SVD observed on MRI of patients with AD is associated with delusions and depression. Copyright © 2012 John Wiley & Sons, Ltd.

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Introduction

Cerebral small vessel disease (SVD), including subcortical lacunar infarcts (lacunes) and white matter hyperintensities (WMH), is commonly observed on brain magnetic resonance imaging (MRI) of older people with and without dementia. Numerous post-mortem studies have shown that WMH correspond to several heterogeneous pathological substrates with a varying extent of demyelination, arteriolosclerosis and gliosis representing not only incomplete infarctions but also tissue degeneration (Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study, 2001; Fernando and Ince, 2004). Lacunes are small cavities located in the white matter or subcoritical gray matter. They have been considered small ischemic infarcts; however, several pathogenetic mechanisms have been proposed (Wardlaw *et al.*, 2003). Incidence of SVD increases with age and vascular risk factors (Pantoni and Garcia, 1995).

In older people, Alzheimer's disease (AD) is considered the most common cause of dementia, characterised by gradual progressive cognitive impairment (McKhann *et al.*, 1984). In addition to cognitive

impairment, behavioural and psychological symptoms of dementia (BPSD) are important manifestations of AD. These symptoms have been shown to be associated with a reduced quality of life (Shin *et al.*, 2005), a higher cost of care (Beeri *et al.*, 2002), institutionalisation (Steele *et al.*, 1990) and increased caregiver burden (Robert *et al.*, 2005). Vascular risk factors including hypertension (Skoog *et al.*, 1996; Kivipelto *et al.*, 2001), diabetes (Luchsinger *et al.*, 2001), hypercholesterolemia (Kivipelto *et al.*, 2001) and tobacco smoking (Ott *et al.*, 1998) are also associated with increased AD risk and their treatment reduces AD risk (Li *et al.*, 2011). Furthermore, examination of several patients with AD at autopsy has shown a high prevalence of undiagnosed vascular lesions (Lim *et al.*, 1999; Fernando and Ince, 2004).

MRI has revealed that SVD is more prevalent in patients with AD than in older people without dementia (Scheltens *et al.*, 1992; Jellinger and Mitter-Ferstl, 2003). SVD may play a role, at least to some extent, in the clinical symptoms of AD. WMH are known to affect frontal lobe function, resulting in executive dysfunction in patients with AD (Pantel *et al.*, 2004; Tullberg *et al.*, 2004). However, it is still unclear whether SVD is associated with other symptoms such as BPSD in AD. Reports about the roles of SVD and BPSD in AD have been conflicting. Associations among the following conditions have been reported: WMH and depression (O'Brien *et al.*, 2000); apathy (Scheltens *et al.*, 1992); suicidal ideation (Lopez *et al.*, 1997); delusional misidentification (Lee *et al.*, 2006); aberrant motor behaviour (Hirono *et al.*, 2000); and anxiety, aberrant motor behaviour and night-time disturbance (Berlow *et al.*, 2010). However, these studies had relatively small sample sizes, and only few of them could confirm the results of previous studies. Moreover, some studies failed to find any association between WMH and BPSD (Harrell *et al.*, 1991; Lopez *et al.*, 1992; Staekenborg *et al.*, 2008).

In this study, we assessed the relationship of SVD observed on MRI with BPSD and cognitive functions in a relatively large sample of patients with AD attending a memory clinic.

Methods

Subjects

All procedures followed the Clinical Study Guidelines of the Ethics Committee of Kumamoto University Hospital and were approved by the internal review board. A complete description of all procedures was provided to the patients, and written informed consent was obtained from them or their caregivers.

In this cross-sectional study of a prospective cohort, a total of 163 patients with probable AD were selected from a consecutive series of 1253 patients who underwent a medical examination at the Dementia Clinic of the Department of Neuropsychiatry, Kumamoto University Hospital, from April 2007 to May 2011. All patients were examined comprehensively by two senior neuropsychiatrists (M. I. and M. H.), having sufficient experience in examining patients with dementia. Routine laboratory and standardised neuropsychological tests, such as the Mini mental state examination (MMSE) (Folstein *et al.*, 1975) and Alzheimer's Disease Assessment Scale—Cognitive Subscale Japanese version (ADAS-J cog; Honma *et al.*, 1992) were also conducted. Brain MRI, brain MR angiography and single photon emission computed tomography for cerebral perfusion were also performed. Information on patient demographics including prescribed medications collected from caregivers and investigative data were entered prospectively into the Kumamoto University Dementia Follow-up Registry in a standardised manner. Patients had to meet the criteria of the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (McKhann *et al.*, 1984) for probable AD to be included in this study. Patients under 60 years of age; those who had any evidence suggestive of vascular dementia (VaD), such as focal neurological signs, abrupt deterioration or stepwise progression of cognitive deficits; those with focal vascular lesions except SVD, such as hematomas; significant neurologic antecedents, such as brain trauma, brain tumour, epilepsy or inflammatory disease; those with serious psychiatric diseases, substance abuse or developmental abnormalities; those who had severe behavioural or communication problems that would make clinical or MRI examination difficult or those without a reliable informant were excluded from the study.

The subjects consisted of 108 women and 55 men with a mean age of 76.3 ± 7.2 years and a mean educational attainment of 10.5 ± 2.7 years. The mean duration of symptoms determined through interviews with caregivers was 2.5 ± 1.8 years. Forty-one patients (25.2%) were prescribed cholinesterase inhibitors at examination. The Clinical Dementia Rating scale (CDR; Hughes *et al.*, 1982) revealed a functional severity of very mild in 75 patients, mild in 71, moderate in 16 and severe in 1.

Subjects were divided into two groups based on the presence or absence of SVD, and cognitive functions and BPSD were compared between the two groups.

Assessment of cognitive functions

All patients underwent neuropsychological tests to assess their general cognitive functioning as well as memory and executive functions. General cognitive functioning was assessed using MMSE. Memory function was assessed using ADAS-J cog word recall and recognition subtests. ADAS-J cog word recall subtest is equivalent to a verbal learning test in which the retention of a list of 10 written words was measured using free immediate recall after each of the three learning trials. The score is the mean number of correct responses in three repeated trials. In the ADAS word recognition subtest, the subject was asked to read aloud 12 written high-imagery words and then to select the target words among 24 words randomly mixed with 12 irrelevant words. The score is the mean number of correct responses in three repeated trials. Executive function was assessed using the letter fluency task and the category fluency task. In the letter fluency task, subjects were instructed to say as many words as possible that begin with the letter 'Ka' for 1 min. The score was the number of different words listed. In the category fluency task, the subjects were asked to list as many animals as possible within 1 min. The score was the number of different animals listed.

Assessment of behavioural and psychological symptoms of dementia

We evaluated the comprehensive BPSD semiquantitatively through interviews with their caregivers using the Japanese version of the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994; Hirono *et al.*, 1997). In NPI, the following 10 BPSD were rated on the basis of the patients' condition in the month before interviews: delusions, hallucinations, agitation, depression (dysphoria), anxiety, euphoria, apathy, disinhibition, irritability and lability and aberrant motor behaviour. According to the criteria-based rating scheme, severity of each manifestation was classified into four grades (from 1 to 3; 0 if absent), whereas frequency was classified into five (from 1 to 4; 0 if absent). The NPI score (severity × frequency) was calculated for each manifestation (range of possible scores, 0–12). Thus, the maximum total score for the 10 manifestations is 120.

Assessment of small vessel disease

Scans were made on a 3.0-T MR scanner. Fluid-attenuated inversion recovery (FLAIR), T2-weighted, diffusion-weighted, magnetization-prepared rapid acquisition of gradient echo imaging and susceptibility-weighted imaging were performed. The presence of lacunes and the extent of WMH were determined by a neuroradiologist who was blinded to the clinical data, including cognitive test results and NPI scores. The extent of WMH severity was rated visually on axial FLAIR images using the Fazekas scale as grade 1 (punctate), grade 2 (early confluent) or grade 3 (confluent) (Fazekas *et al.*, 1987). In this study, WMH were considered present if the Fazekas grade was 2 or 3 (Pompili *et al.*, 2008; Staekenborg *et al.*, 2008). Changes in the basal ganglia were rated in the same way and considered as white matter lesions even if they were located in the gray matter nuclei. Lacunes were defined as lesions with diameters of more than 2 mm with hyperintensity on T2-weighted images with central hypointensity on FLAIR images. Seventy-nine patients (48.0%) showed WMH, whereas 54 patients (33.1%) showed with lacunes. Both WMH and lacunes were observed in 40 patients (24.5%). Patients were divided into two groups based on the presence or absence of SVD (WMH grade 0/1 and no lacunes: SVD absent, WMH grade 2/3 or the number of lacunes ≥ 1: SVD present).

Statistical analysis

Group differences were analysed using two-tailed Student t test, two-tailed Mann–Whitney U test or χ^2 test. $p < 0.05$ was considered to be statistically significant. No correction for multiple comparisons was performed because of the exploratory nature of the study. In the present study, patients with SVD were significantly older than those without SVD. Therefore, we also analysed group differences in the neuropsychological tests and NPI scores using analysis of covariance (ANCOVA) with age as the covariate. Furthermore, we performed ANCOVA, with age, sex, years of education, disease duration, cholinesterase inhibitor usage and CDR as covariates, as these variables might affect cognition and BPSD. Statistical analysis was performed with SPSS for Windows, version 17.0 (IBM Corporation, Armonk, NY, USA).

Results

Demographic variables of the two groups (patients with SVD and patients without SVD) are shown in Table 1. Patients with SVD were significantly older than those without SVD ($p = 0.005$); however, no significant differences were observed for the male to female ratio, mean level of education, duration of

Table 1 Patient demographics

	Total ($n = 163$)	SVD present ($n = 93$)	SVD absent ($n = 70$)	p
Age (years)	76.3 ± 7.2	77.8 ± 6.1	74.4 ± 8.1	0.005[a,**]
Sex (male/female)	55/108	33/60	22/48	0.588[b]
Education (years)	10.5 ± 2.7	10.3 ± 2.8	10.8 ± 2.5	0.208[a]
Duration of history (years)	2.5 ± 1.8	2.4 ± 1.9	2.6 ± 1.7	0.596[a]
Cholinesterase inhibitor use	41 (25.2)	20 (21.5)	21 (30)	0.216[b]
CDR	0.88 ± 0.47	0.94 ± 0.53	0.80 ± 0.38	0.116[c]
WMH present (Fazekas score ≥2)	79 (48.5)	79	0	
Lacunes present	55 (33.7)	55	0	

Values are presented as mean ± SD, n (%) or n.
SVD, small vessel disease; CDR, Clinical Dementia Rating; WMH, White Matter Hyperintensities
[a]t test; [b]χ^2 test; [c]Mann–Whitney U test; **$p < 0.01$.

symptoms and percentage of patients who were prescribed cholinesterase inhibitors between both groups.

Results of neuropsychological tests are shown in Table 2. No significant differences were observed for MMSE and ADAS-J cog word recall and recognition subtests between both groups. In contrast, patients with SVD were significantly more impaired than those without SVD on the letter fluency task ($p = 0.013$). This difference remained significant after adjustment for age ($p = 0.021$, ANCOVA), but the significance disappeared after adjustment for age, sex, years of education, disease duration, cholinesterase inhibitor usage and CDR ($p = 0.065$, ANCOVA).

Results of NPI are given in Table 3. In the total cohort of 163 patients, prevalence of any BPSD was 90.8%, with a median NPI score of 7 (range, 0–63). Furthermore, apathy was found to be the most common symptom, whereas euphoria was the rarest (affecting 67% and 1% of the patients, respectively). Delusions were present in 39 patients (23.9%). The total NPI score was significantly higher in patients with SVD than in those without SVD after adjustment for age, sex, years of education, disease duration, cholinesterase inhibitor usage and CDR ($p = 0.042$, ANCOVA). Patients with SVD had significantly higher scores than those without SVD in the delusion domain ($p = 0.013$), and the difference remained significant even after adjustment for age ($p = 0.036$, ANCOVA), and age, sex, years of education, disease duration, cholinesterase inhibitor usage and CDR ($p = 0.049$, ANCOVA). In addition, patients with SVD had significantly higher scores than those without SVD in the depression domain after adjustment for age, sex, years of education, disease duration, cholinesterase inhibitor usage and CDR ($p = 0.044$, ANCOVA).

Discussion

The most remarkable finding of this study was that patients with AD and SVD had significantly more delusions than those without SVD. In the present

Table 2 Neuropsychological performances of subjects

	SVD present ($n = 93$)	SVD absent ($n = 70$)	p	Adjusted $p1$	Adjusted $p2$
MMSE scores	19.7 ± 4.5	20.2 ± 4.1	0.425[a]	0.232	0.633
ADAS-J cog					
Word recall (correct response)	4.1 ± 1.6	3.9 ± 1.4	0.415[a]	0.456	0.166
Word recognition (correct response)	7.7 ± 3.0	8.2 ± 2.8	0.285[a]	0.522	0.888
LFT scores ('Ka')	5.3 ± 3.0	6.5 ± 3.1	0.013[a,*]	0.021*	0.065†
CFT scores (animals)	9.0 ± 4.0	9.8 ± 3.3	0.210[a]	0.317	0.571

Values are presented as mean ± SD.
SVD, small vessel disease; MMSE, Mini mental state examination; ADAS-J cog, Alzheimer's Disease Assessment Scale—Cognitive subscale (Japanese version); LFT, letter fluency task; CFT, category fluency task.
[a]t test; age adjustment was performed using analysis of covariance and is represented as adjusted $p1$. Adjustment of age, sex, years of education, disease duration, cholinesterase inhibitor usage and Clinical Dementia Rating scale using analysis of covariance is represented as adjusted $p2$.
*$p < 0.05$; †$p < 0.10$.

Table 3 Prevalence of behavioural and psychological symptoms of dementia and mean composite scores (frequency × severity) of individual Neuropsychiatric Inventory symptoms in patients

	SVD present ($n = 93$)	SVD absent ($n = 70$)	p	Adjusted $p1$	Adjusted $p2$
NPI total scores ≥1	84 (90.3)	64 (91.4)	0.809[b]		
NPI scores					
Total score	11.7 ± 11.4	8.3 ± 9.2	0.036[a*]	0.053[†]	0.042*
Delusion	1.5 ± 3.0	0.5 ± 1.6	0.013[a*]	0.036*	0.049*
Hallucination	0.3 ± 1.0	0.1 ± 0.6	0.288[a]	0.421	0.839
Agitation/aggression	0.9 ± 1.9	0.9 ± 2.1	0.912[a]	0.938	0.860
Depression/dysphoria	1.5 ± 2.8	0.9 ± 1.6	0.075[a†]	0.062[†]	0.044*
Anxiety/indifference	0.9 ± 2.6	0.8 ± 2.0	0.726[a]	0.749	0.828
Euphoria	0.0 ± 0.0	0.1 ± 0.5	0.321[a]	0.471	0.358
Apathy	3.9 ± 4.0	3.2 ± 3.2	0.202[a]	0.248	0.332
Disinhibition	0.6 ± 2.0	0.3 ± 1.6	0.373[a]	0.528	0.354
Irritability/lability	1.0 ± 1.8	0.8 ± 1.9	0.521[a]	0.536	0.304
Aberrant motor behaviour	1.2 ± 2.8	0.7 ± 1.9	0.222[a]	0.210	0.478

Values are presented as mean ± SD or n (%).
SVD, small vessel disease; NPI, Neuropsychiatric Inventory.
[a]t test; [b]χ^2 test; age adjustment was performed using analysis of covariance and is represented as adjusted $p1$. Adjustment of age, sex, years of education, disease duration, cholinesterase inhibitor usage and Clinical Dementia Rating scale using analysis of covariance is represented as adjusted $p2$.
*$p < 0.05$; [†]$p < 0.10$.

study, patients with SVD were significantly older than those without SVD. Both WMH and lacunes have been shown to be associated with aging (Fazekas *et al.*, 1988; Longstreth *et al.*, 1998). Some studies have found a significant association between psychosis in AD and age (Levy *et al.*, 1996; Bassiony *et al.*, 2000) and age at onset of AD (Hwang *et al.*, 1996; Gormley and Rizwan, 1998). However, delusions in patients with AD and SVD were significantly more severe than in those without SVD after adjustment for age in this study. Therefore, the present results cannot be explained by the differences of age between the two groups.

Previous studies have reported relationships between delusions and severity of white matter changes observed on MRI (Lee *et al.*, 2006) and between delusions and lacunar infarcts of white matter observed on computed tomography (Binetti *et al.*, 1995) in patients with AD. Furthermore, one study reported that a history of hypertension increased the risk of delusions in patients with AD (Treiber *et al.*, 2008), and another showed an association between delusions and the use of antihypertensives in patients with AD (Bassiony *et al.*, 2000). Thus, it can be suggested that SVD is a risk factor of delusions in patients with AD.

Mechanisms underlying delusions in patients with AD remain unclear. However, some neuroimaging studies have suggested an association between psychotic symptoms in AD and frontal lobe dysfunction (Sultzer *et al.*, 1995; Mega *et al.*, 2000; Sultzer *et al.*, 2003). Mentis *et al.* (1995) suggested that delusional misidentification in patients with AD are caused because of the abnormal integration of perceptual information from multimodal association cortices with affective information from paralimbic–limbic structures. White matter changes may result in a disruption of the functional connections between the frontal cortex and other related cortices or paralimbic–limbic structures, thus resulting in delusions. Furthermore, white matter changes in basal ganglia may alter connections between the frontal cortex and subcortical regions, resulting in development of delusions (Mentis *et al.*, 1995; McMurtray *et al.*, 2008). Further studies are needed to localise areas on MRI and single-photon emission computed tomography and support this hypothesis.

In this study, there was a trend for patients with SVD to be more impaired on the letter fluency task (for evaluating executive dysfunction) compared with those without SVD. No significant differences were observed in MMSE (for evaluating general cognitive functioning) and ADAS-J cog word recall and recognition subtests (for evaluating memory function) between both groups. In older people, appearance of SVD and incident lacunes on MRI have been reported to be associated with decreases in executive function and processing speed but not in memory or global cognition (Prins *et al.*, 2005; Jokinen *et al.*, 2011). In patients with AD, white matter lesions observed on MRI have been reported to be associated with impaired frontal lobe function, regardless of their

location (Tullberg *et al.*, 2004). These findings were consistent with our results, which suggest that SVD was associated with the impairment of executive function but not to impairments of global cognitive and memory functions. In a study examining the association between cognitive function and BPSD assessed by NPI, the letter fluency task and the category fluency task scores were significantly associated with changes in the psychosis subdomain but not in other subdomains (Tsai *et al.*, 2010). In addition, Swanberg *et al.* (2004) reported that symptoms of psychosis were more frequent in patients with AD with executive dysfunction than in those without. The lesions of the dorsolateral prefrontal circuit mainly involved in executive function are associated with performances of verbal fluency (Duffy and Campbell, 1994; Tekin and Cummings, 2002). In addition, lesions in the dorsolateral prefrontal circuit are associated with psychosis in patients with AD (Sultzer *et al.*, 1995). These previous neuroimaging and cognitive findings and the present result suggest that executive dysfunction due to SVD may be associated with delusions in patients with AD.

In the present study, patients with AD with SVD had significantly more depression than those without SVD after adjustment estimated covariates. Previous study suggests that white matter lesions confer an increased risk for depression in AD (O'Brien *et al.*, 2000). In this study, we did not find evidence to support the previously reported association of WMH with apathy (Scheltens *et al.*, 1992), aberrant motor behaviour (Hirono *et al.*, 2000) as well as anxiety and aberrant motor behaviour (Berlow *et al.*, 2010) in patients with AD. Unlike our study, previous studies failed to find any association between WMH and BPSD (Harrell *et al.*, 1991; Lopez *et al.*, 1992; Staekenborg *et al.*, 2008). Results obtained in our and previous studies may have differed because of the small sample sizes of the previous studies. An advantage of our study is the relatively large study cohort.

This study had some limitations. First, despite the exclusion of patients with any evidence suggestive of VaD, probably a few patients with VaD was included. However, patients with AD have been reported to have more delusions than patients with VaD (Lyketsos *et al.*, 2000; Ikeda *et al.*, 2004), suggesting that a combination of AD pathology and SVD may contribute to delusions. Second, WMH and lacunes are collectively treated as SVD. In this study, 40 patients (43.0% of patients with SVD) had both WMH and lacunes. Because our main aim was to investigate the effect of SVD on clinical symptoms in patients with AD, we analysed the two major representations of SVD together. In the future, WMH and lacunes need to be evaluated separately in order to investigate their independent effect on BPSD of patients with AD in a larger population. Third, in order to measure the extent of WMH, we used a visual rating scale, which may not be as accurate as the MRI volumetric method. However, the Fazekas rating scale, which was used in the present study, is widely accepted and has been shown to provide good global assessments of WMH. In an overview of 26 rating scales used to evaluate WMH on MRI, it was suggested that the simplicity of the Fazekas scale might make it robust, even for images of poorer quality (Scheltens *et al.*, 1998). In addition, simple rating scales, such as the Fazekas scale, have been shown to be comparable with complex measures of WMH in terms of associations with clinical outcome measures (Gouw *et al.*, 2006). Importantly, histopathological analyses have been used to validate this rating scale (Fazekas *et al.*, 1991; Fazekas *et al.*, 1993). Fourth, the study results might be able to be biased because all patients were recruited in only one dementia clinic.

Conclusion

Our results suggest that cerebral SVD observed on MRI is associated with symptoms of delusions and depression in patients with AD.

Key points

- Cerebral SVD in patients with AD is associated with symptoms of delusions and depression.
- No significant differences were observed in other neuropsychiatric symptoms, memory or global cognition between patients with AD with SVD and those without SVD.

Conflict of interest

None declared.

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特集 認知症臨床のトピックスを吟味する

2．認知症治療の現状と課題

4）認知症に関わる医療連携

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はじめに

わが国における認知症高齢者に対する医療の問題は，認知症高齢者の増加とともに社会全体の重大な関心事の1つである．2012年8月，厚生労働省は『認知症高齢者数について』を公表し，それによると介護保険における「認知症高齢者の日常生活自立度Ⅱ以上」の高齢者数は2012年時点で305万人と推計されている[1]．あくまでも介護保険申請者からの推計であるので，すべてが認知症高齢者というわけではないが，従来考えられていた認知症高齢者の増加ペースをはるかにしのぐ急速な増加である．これだけの人数の認知症高齢者医療を，一部の専門医・専門医療機関などだけで対応することはおよそ現実的ではない．おのずから，認知症専門医・専門医療機関以外の各科医師を含む医療関係者や，多くの介護関係者，行政担当者などが，それぞれの専門領域を生かしながら分担して，認知症高齢者に対応することになる．すなわち，「医療連携」「多職種連携」がキーワードになる．最近では，一般市民への啓発活動も進み，増加する認知症高齢者に対する医療介護の在り方について，認知症高齢者を地域で支えるシステムづくりが各地域で様々に展開されている．われわれは，熊本県内一円で，認知症高齢者を地域で支えるシステムづくりを目指して，認知症疾患医療センターを中心に据えた，通称「熊本モデル」と称する認知症地域医療連携モデルをシステム化した[2,3]．

本稿では，認知症疾患医療センターを中心に構築してきた「熊本モデル」の取り組みを紹介しながら，認知症診療に関わる地域医療連携づくりの過程でみえてきた現状と課題について，考察する．

「熊本モデル」の概要[2,3]

われわれは，前任地である愛媛大学時代から，認知症医療の地域拠点となるような医療機関を，県内二次医療圏もしくは地域行政区域ごとにおおむね1カ所設置し，かかりつけ医や介護施設にとって認知症診療のバックアップ病院として位置づける，という構想を模索していた．同時に，これらの地域拠点病院では，緊急時には入院に対応したり，診断が困難な場合や，ごく初期の認知症で，脳機能画像などの検査が必要なケースなどは，地域拠点病院から大学病院へ紹介したりする2層構造をとっていた．これが，いわゆる「熊本モデル」の原型である．

当時はまだ，試行錯誤であったため十分な検証を行っていないが，このような原型になった背景には，愛媛県は東西方向に長く，一部は南北方向にも広がる県域をもち，愛媛県東端や南端から愛媛大学のある中予地域まで通院することが困難であるという事情がある．また愛媛県の地形の特徴として，各集落が峠で隔てられているために集落間での人口流入・流出が少ない．そのため各地域内でのかかりつけ医と住民との信頼関係が十分にとれており，地域住民同士のつながりが密であるという風土が関係していたものと推察している．

そして，これらの試行錯誤の中から，

・地域から認知症専門医療機関への要望で特に期待が高いのは，認知症の周辺症状（いわゆるbehavioral

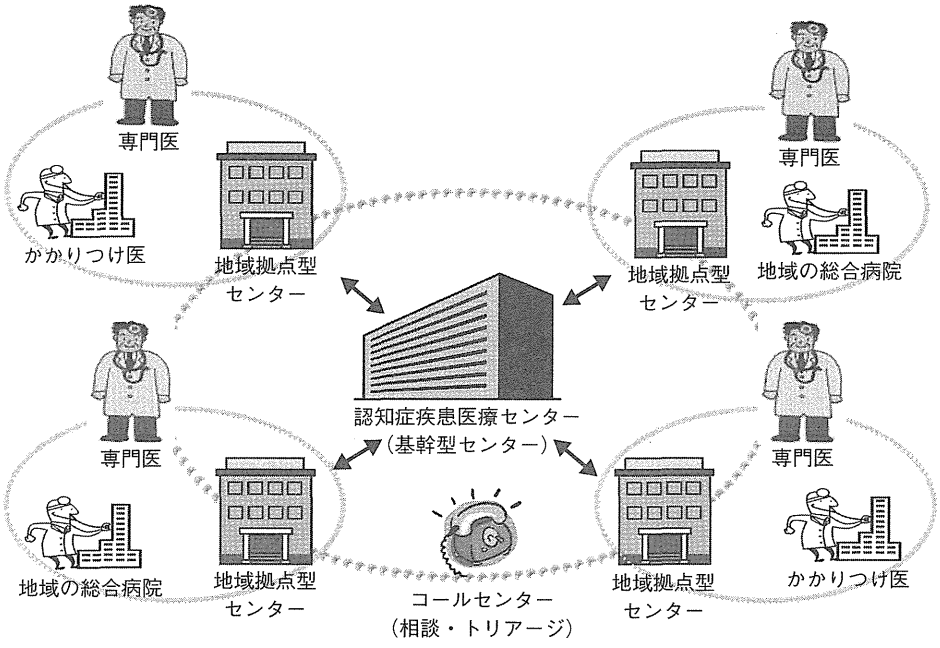

図1　熊本モデルにおける医療連携の2層構造

and psychological symptoms of dementia：BPSD)の治療であること．

・BPSDによる緊急時の入院対応が可能で，数カ月後に治療がうまくいった場合には，再度在宅介護が可能になること．

・在宅だけでなく施設介護にも余裕が生まれ，施設スタッフ，介護スタッフの技量アップにつながること．

・二次医療圏内であれば，地域のかかりつけ医と「顔の見える連携」が可能であること．

・身体疾患合併例であっても，認知症診療の拠点病院の支援によって，一般総合病院などで認知症高齢者の受け入れが可能になること．

などの手ごたえを感じ取っていた．

そのような中，2008年厚生労働省(以下，厚労省)は，認知症疾患医療センター設置の事業を開始した．「認知症疾患医療センター」とは，認知症患者とその家族が住み慣れた地域で安心して生活ができるようにするための，支援の切り札的存在の1つとして提案され，各都道府県や政令指定都市が指定する病院に設置するものである．認知症疾患における鑑別診断，地域における医療機関などの紹介，BPSDへの対応についての相談受付などを行う専門医療機関とされた．ちょうど時期を前後して，われわれは熊本県へ赴任することとなり，熊本県でも認知症疾患医療センター設置に向けた事前協議があり，県側から大学へ協力要請があった．協議を重ねていく中で，既にこれまで構築された大学病院神経精神科と各地域の精神科病院とのネットワークを基盤に，認知症対策を組み入れることとし，愛媛大学での経験を踏まえて，1カ所の基幹型センター(熊本大学医学部附属病院)と7カ所の地域拠点型センターという形で，認知症疾患医療センター事業を開始した．これが「熊本モデル」構築の概要である．

もちろん，県行政，熊本県医師会，熊本県精神科病院協会などとの協議を十分に重ねた上で，各方面の関係者の深いご理解と多大なご協力があってこその開始であることを，強調しておきたい．

「熊本モデル」における基幹型センターと地域拠点型センターの役割[2,3]

2012年に，地域拠点型の認知症疾患医療センターが2カ所追加指定され，現在の熊本モデルは，認知症疾患医療センターを1カ所の基幹型センターと9カ所の地域拠点型センターの計10カ所で運営を行っている(図1)．

基幹型センターの主な役割は，9カ所すべての認知症疾患医療センターを統括するとともに，各地域拠点型センターにおけるスタッフの人材育成と啓発活動を担っている．また，認知症疾患医療センターと県行政，県医師会などの外部機関との交渉チャネルとしての機能を有する．特に，各地域拠点型センターの担当医師や連携担当者，数名のスタッフには2カ月に一度の事

例検討会への参加を義務づけ，困難事例の情報交換・事例検討と，基本的な認知症についての研修を継続している．実際に顔を合わせて事例検討を行うことで，各地域拠点型センターの担当者間で顔の見える関係をつくるとともに，地域ごとの特色や地域の現状の情報交換ができるほか，各センターの診断・技術の均質化とレベルアップを図っている．

地域拠点型センターの主な役割は，認知症の早期発見・早期治療，鑑別診断，BPSDへの対応・治療，治療計画・ケアプランの策定およびアドバイス，合併症治療への対応・アドバイス，地域医療・地域介護との連携調整など，地域における認知症治療の実務的拠点としての役割である．ここでは，一般住民からの認知症相談や介護相談，一般かかりつけ医からの相談，介護職員および地域包括支援センター職員などからの相談，各方面からの情報提供などを受け付け，専門医療が必要かどうかなどの判断を行っている．その上で，鑑別の困難なケースや治療の難しいケースは，大学病院などの高度先進医療機関へ紹介するなどしている．

また，熊本モデルにおいては，認知症コールセンターの存在も大きい．県からの発案で「公益社団法人認知症の人と家族の会熊本県支部」内に，熊本県認知症コールセンター(愛称，認知症ほっとコール)の業務が委託され，熊本市中心部のオフィスで休日も電話対応などを行っている．これは，地域拠点型センターへ相談が集中するのを未然に防ぐ意味合いもある．相談内容に応じて，介護相談については傾聴し，案件によっては地域包括支援センターへ情報提供したり，専門医療機関への受診を勧めたりなど，相談内容のトリアージを行っている．さらに，コールセンターでは電話相談だけでなく，実際に家族などがセンターへ来所して相談することも可能である．

かかりつけ医との医療連携構築[4]

かかりつけ医は，地域，本人，家族にとって最も身近で信頼できる存在であるとともに，地域での認知症診療の重要な担い手として期待されている[5]．今後は，増加する認知症高齢者への対応のみならず，身体疾患管理，患者指導・家族指導，患者家族の心理的サポートや医療介護のマネジメントなどの役割も期待される．熊本県では，これらの視点を踏まえて，かかりつけ医への認知症対応力向上をさらに目指したプログラムを取り入れている．

厚労省は，認知症地域医療支援事業の一環として，2006年度から全国でかかりつけ医認知症対応力向上研修事業を開始した．これは，認知症専門医・専門医療機関が不足する中，かかりつけ医に認知症診療への協力を促すことで，地域で認知症患者を支える基盤を構築しようとするものである[6]．すなわち，認知症診療の1つの理想形として，かかりつけ医で認知症を早期発見し，確定診断や鑑別診断を認知症疾患医療センターで行い，診断確定後や病状が安定した患者は，高血圧などの他の身体疾患管理とともにかかりつけ医での診療を継続するというシステムづくりを提唱した．このシステムにあっては，かかりつけ医が認知症診療の一翼を担えるよう，一定の知識と技量を備えておくことが必要と考えられる．かかりつけ医認知症対応力向上研修は，この目的のために事業展開しているものであるが，研修会を一度受けただけでは不十分で，継続して研修を受けられる仕組みにすることが求められる．

熊本県では，2010年度から全国共通の研修会を「(基礎編)」と位置づけ，認知症対応力向上研修をさらに深めた内容で県独自の研修会を企画し，それを「(ステップアップ編)」と銘打って実施している(図2)[4]．ステップアップ編の研修受講要件は，全国版のかかりつけ医認知症対応向上研修(基礎編)の修了者で，認知症診療に関心の高いかかりつけ医である．ステップアップ編は熊本県および認知症疾患医療センター(基幹型)の共催で，講師は基幹型センターの認知症専門医が担当し，年2回実施している．内容は，認知症診断や薬物治療，BPSDへの対応など，より臨床現場に即した内容としている．各年度1回目の研修会の際に，次回取り上げて欲しい内容についてアンケートをとり，2回目は，そのアンケートをもとに，受講者からの質問や疑問に答える形の研修を実施している．年2回の研修会受講者には，県独自の修了証を県知事名で授与し，県ホームページなどで認知症診療に関わるかかりつけ医として積極的に県民に公表している．

認知症サポート医との連携構築[4]

厚労省は，認知症地域医療支援事業の一環として，2005年度から全国で認知症サポート医養成研修事業を開始した．認知症サポート医には，かかりつけ医を対象とした認知症対応力向上のための研修を企画運営することを第一の目的とし，日常診療におけるかかりつけ医からの認知症診療に関する事案に対して相談役・

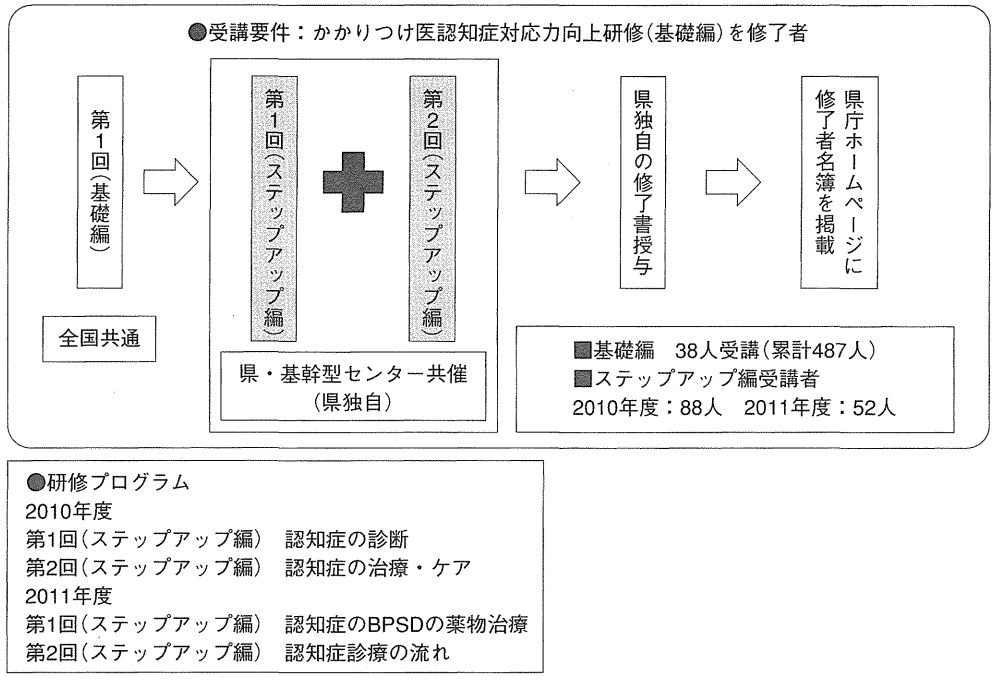

図2　熊本県かかりつけ医認知症対応力向上研修

(文献4より引用)

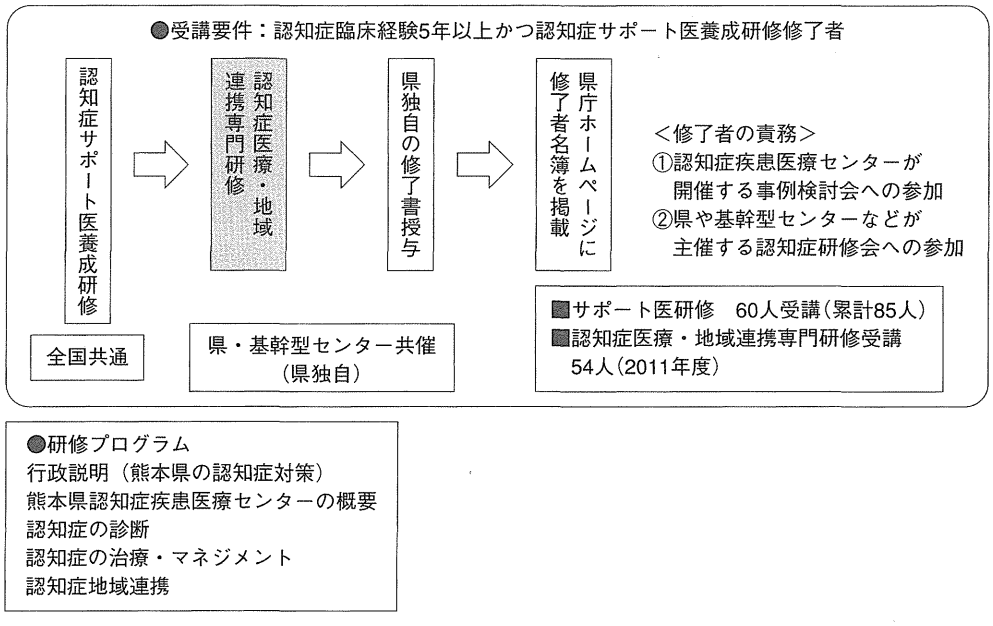

図3　熊本県認知症医療・地域連携専門研修

(文献4より引用)

アドバイザー的役割，他の認知症サポート医や各医師会，地域包括支援センターと協同しての，地域ネットワークづくりへ協力することなど，いわば地域における認知症診療のリーダー的役割となることを期待されている[5,6]．しかし，2006年度から2010年度にかけて，全国で3万人程度の研修修了者がいるとされるものの，必ずしも期待された役割を十分果たせていないことも指摘されている．

熊本県では，このような実態を鑑み，2011年度より，認知症サポート医への研修を内容をさらに深めて，認知症サポート医を対象とした県独自の研修として，熊本県認知症医療・地域連携専門研修を実施している(**図3**)[4]．本研修の目的は，認知症医療ネットワーク体制の構築と，認知症専門医の育成である．認知症疾患

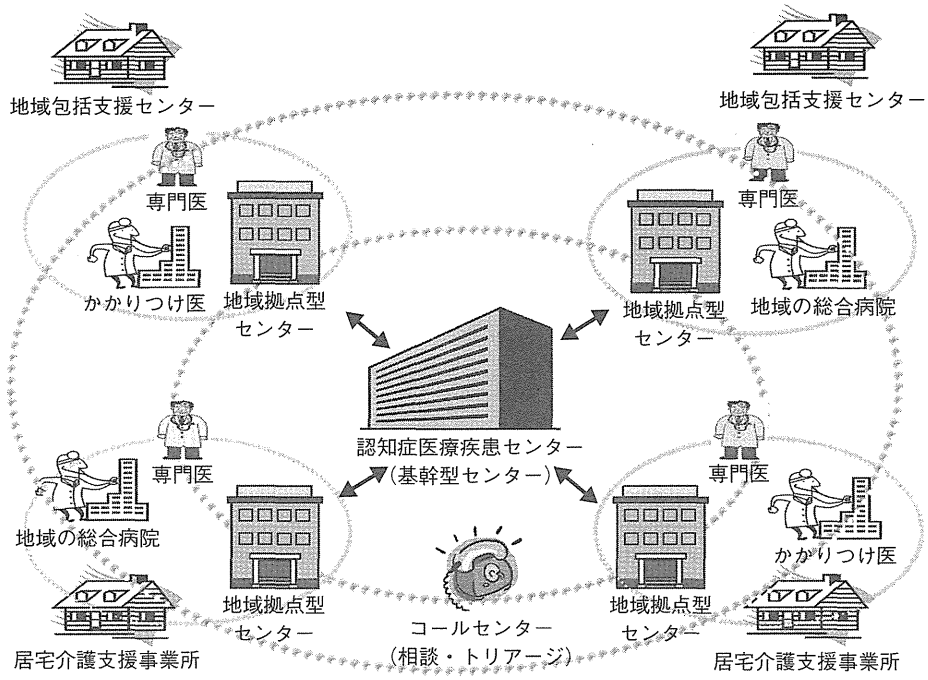

図4　熊本モデル－2層構造から3層構造へ

医療センター以外の医療機関であっても，認知症専門医として県内の認知症医療ネットワークに参画してもらうことをねらいとしている．そのため，受講要件として，認知症臨床経験5年以上かつ認知症サポート医研修修了者であることを取り決めている．企画運営は熊本県および基幹型センターの共催で，講師は基幹型センタースタッフおよび行政担当者，認知症専門医が担当している．内容としては，地域連携に直接携わってもらうことをねらいにしていることから，認知症施策についての行政説明や認知症疾患医療センターの活動内容，診療報酬や介護施設の役割や連携の実際など，診療以外に関わることも大幅に含めているため，約7時間の研修会設定としている．さらに，研修修了者の責務として，地域拠点型センターの主催する事例検討会へのコメンテーターとしての参加義務，基幹型センターなどの主催する研修会への参加など，地域の中核となるべく尽力いただいている．こちらも，研修修了者には，県知事名で修了証を授与し，地域の専門医として県やセンターのホームページで名簿公開するなど，情報公開を積極的に行っている．

医療連携づくりでみえてきた現状と課題

かかりつけ医認知症対応力向上研修や認知症サポート医養成研修など，厚労省の掲げるプランには，一定の評価がなされて良いものと考えるが，実際にはそれぞれの研修修了者が十分に機能しているとはいえない現状がある．熊本県の場合，それらの既存のシステムを発展的に展開することで，厚労省の提示する地域システムをより具現化することができつつある．そこには認知症疾患医療センターの役割が大きい．県と認知症疾患医療センターが主導的役割を果たすことにより，公的な性格を前面に出すことができ，各医療機関やかかりつけ医の積極的な参画を促すことにつながったと思われる．

課題としては，熊本県の場合，すべての認知症疾患医療センターが精神科病院に設置されていることから，重症肺炎や骨折などの身体疾患に対応する連携づくりが急がれる．現状でも，近隣の総合病院などと医療提携を事前に交渉することで対応しているが，今後身体疾患を合併した認知症高齢者が増えた場合に，どのような医療連携が図れるかについて，今後検討する必要がある．

おわりに

認知症診療における医療連携システムづくりの参考例として，「熊本モデル」を概観し，熊本県における認知症疾患医療センターを中心とした，かかりつけ医・認知症サポート医への研修体制を紹介した．

認知症高齢者を地域で支えていくためには，認知症専門医や専門医療機関だけではなく，かかりつけ医や認知症サポート医など，より多くの医療機関が参画したシステムづくりが必要である．熊本県では定期的な研修会を通じて，かかりつけ医や連携担当者同士がお互いになじみの関係をつくることで，地域においての多職種連携が円滑に進むよう，工夫をしている．

認知症疾患医療センターとかかりつけ医・サポート医との連携は徐々に構築されつつあるが，今後の展開として，各地域拠点型認知症疾患医療センターを中心としてそれらを取り巻く施設，すなわち，地域の介護福祉事業所や居宅介護支援事業所，介護サービス事業所などとの連携を図ることが課題である(**図4**)．これまでの2層構造から3層構造へ，そして，よりきめの細かい地域ネットワークへと展開していく構想を考えており，新たな展開への方策を模索中である．

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特集　認知症治療の最前線―包括的ケアを踏まえた新しい治療戦略―

Seminar

2．認知症の薬物療法
2）認知症の周辺症状に着目した治療薬の使用方法と注意点（使用基準が緩和された抗精神病薬も含めて）

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KEY WORD
●認知症
●BPSD
●抗精神病薬
●抗認知症薬

SUMMARY

■認知症の周辺症状に対する治療に関しては，まず非薬物療法の検討が必要である．しかし，実地臨床では，薬物療法を検討せざるを得ないほどの周辺症状にしばしば直面する．従来から鎮静目的で非定型抗精神病薬など適応外使用が行われてきたが，プラセボ群と比較して使用群の死亡率が高いという問題がある．本邦では，『認知症疾患治療ガイドライン 2010』が公表されたので，本稿はガイドラインに推奨される治療を中心に，認知症の周辺症状に対する薬物利用について症状別に概説した．

はじめに

認知症に伴う行動異常および精神症状を周辺症状と呼び，近年では認知症の行動・心理症状を behavioral and psychological symptoms of dementia（BPSD）と呼んでいる．認知症患者にBPSDが出現した場合，その発現に関連する要因を評価し，それらに応じた環境調整や身体的治療などの非薬物療法を優先する．しかし，BPSDが高度で患者や介護者の負担が著明な場合は，薬物療法を考慮しなければならないことも多い．BPSDの薬物療法には抗精神病薬が主に使用されてきたが，適応外使用，利点とリスク，用法用量などの問題がある．近年，わが国で使用可能となった抗認知症薬であるメマンチンのBPSDに対する肯定的な効果も報告されつつある．これらを踏まえ，本稿では，『認知症疾患治療ガイドライン 2010』[1]に推奨されるBPSDに対する薬物療法を中心に，症状別に推奨グレード（表1）を参照して概説する．

BPSDへの薬物治療の注意点と原則

高齢の認知症患者の薬物治療においては，過剰反応や有害事象を生じやすい．そのため，薬物は少量で開始し，若年成人投与量の1/2～1/4程度にし，肝機能・腎機能障害や体重を勘案して用量を少なめに設定する．また，薬効を短期間で評価し，服薬方法を簡易（服薬回数を減らす，一包化するなど）にすることは重要であり，

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