

**Table 2** Comparison of cognitive functions among the three groups

	LO-SD ( <i>n</i> = 10)	EO-SD ( <i>n</i> = 15)	LO-AD ( <i>n</i> = 47)	<i>P</i> -value	LO-SD vs EO-SD	<i>P</i> -value (post-hoc test)	
	(range)	(range)	(range)			LO-SD vs LO-AD	EO-SD vs LO-AD
MMSE total score (max. 30)	16.6 ± 8.2 (0–28)	19.5 ± 9.2 (0–28)	18.1 ± 6.0 (2–28)	0.335	NS	NS	NS
Orientation in time	3.00 ± 1.83	3.80 ± 1.74	2.85 ± 1.61	0.075	NS	NS	NS
Orientation in place	2.90 ± 1.66	2.80 ± 1.90	2.96 ± 1.35	0.997	NS	NS	NS
Registration	2.50 ± 0.97	2.53 ± 0.92	2.89 ± 0.37	0.081	NS	NS	NS
Serial-7 s	2.00 ± 2.00	2.87 ± 2.00	1.85 ± 1.85	0.200	NS	NS	NS
Repetition	0.80 ± 0.42	0.80 ± 0.41	0.96 ± 0.20	0.103	NS	NS	NS
Three-stage command	1.80 ± 0.92	2.27 ± 1.16	2.40 ± 0.97	0.072	NS	NS	NS
Reading	0.60 ± 0.52	0.73 ± 0.46	0.89 ± 0.31	0.059	NS	NS	NS
Recall	0.30 ± 0.48	0.73 ± 0.88	0.34 ± 0.76	0.145	NS	NS	NS
Naming	1.60 ± 0.70	1.33 ± 0.72	1.98 ± 0.15	<0.001*	0.545	0.005**	<0.001**
Writing	0.80 ± 0.42	0.73 ± 0.46	0.81 ± 0.40	0.823	NS	NS	NS
Construction (cube-copying)	0.30 ± 0.48	0.87 ± 0.35	0.21 ± 0.41	<0.001*	0.012**	0.818	<0.001**
RCPM score (max.36)	23.8 ± 7.2 (10–32)	31.9 ± 5.1 (17–36)	19.6 ± 7.9 (0–31)	<0.001*	0.006**	0.249	<0.001**
SMQ score (max.46)	26.8 ± 6.6 (13–35)	29.0 ± 7.3 <sup>†</sup> (19–40)	19.6 ± 8.8 (4–37)	<0.001*	0.453	0.034**	<0.001**

\*Significant difference was found by the Kruskal–Wallis test ( $P < 0.05$ ). \*\*Significant difference was found by the post-hoc Steel–Dwass test for multiple comparison ( $P < 0.05$ ). <sup>†</sup> $n = 14$ . Mean ± standard deviation. EO-SD, early-onset semantic dementia; LO-AD, late-onset Alzheimer's disease; LO-SD, late-onset semantic dementia; MMSE, Mini-Mental State Examination; NS, not significant; RCPM, Raven's Coloured Progressive Matrices; SMQ, Short-Memory Questionnaire.

**Table 3** Comparison of neuropsychiatric symptoms among the three groups

	LO-SD ( <i>n</i> = 10)	EO-SD ( <i>n</i> = 15)	LO-AD ( <i>n</i> = 47)	<i>P</i> -value	LO-SD vs EO-SD	<i>P</i> -value (post-hoc test)	
	(range)	(range)	(range)			LO-SD vs LO-AD	EO-SD vs LO-AD
NPI total score (max. 120)	17.2 ± 17.7 (0–46)	15.1 ± 14.1 (0–40)	14.0 ± 11.2 (0–44)	0.679	NS	NS	NS
Delusion	0.20 ± 0.63	0.00 ± 0.00	2.72 ± 3.59	<0.001*	0.425	0.047**	0.003**
Hallucination	0.00 ± 0.00	0.00 ± 0.00	0.40 ± 1.81	0.245	NS	NS	NS
Agitation	2.70 ± 3.37	2.80 ± 4.13	1.62 ± 2.52	0.587	NS	NS	NS
Dysphoria	0.20 ± 0.42	1.27 ± 2.58	1.40 ± 2.53	0.116	NS	NS	NS
Anxiety	0.90 ± 2.51	0.87 ± 1.88	1.23 ± 2.60	0.573	NS	NS	NS
Euphoria	1.70 ± 3.33	1.07 ± 1.62	0.13 ± 0.61	0.014*	0.932	0.022**	0.028**
Apathy	2.40 ± 2.63	4.00 ± 4.21	3.55 ± 3.40	0.634	NS	NS	NS
Disinhibition	2.40 ± 3.86	1.53 ± 2.77	0.19 ± 0.82	0.014*	0.937	0.044**	0.019**
Irritability	2.10 ± 4.28	1.00 ± 2.24	0.83 ± 1.51	0.615	NS	NS	NS
Aberrant motor behavior	4.00 ± 5.33	2.53 ± 3.98	1.77 ± 3.29	0.515	NS	NS	NS

\*Significant difference was found by the Kruskal–Wallis test ( $P < 0.05$ ). \*\*Significant difference was found by the post-hoc Steel–Dwass test for multiple comparison ( $P < 0.05$ ). Mean ± standard deviation. EO-SD, early-onset semantic dementia; LO-AD, late-onset Alzheimer's disease; LO-SD, late-onset semantic dementia; NPI, Neuropsychiatric Inventory; NS, not significant.

**Table 4** Comparison of stereotypic behaviors among the three groups

	LO-SD (n = 7) (range)	EO-SD (n = 14) (range)	LO-AD (n = 47) (range)	P-value	LO-SD vs EO-SD	P-value (post-hoc test) LO-SD vs LO-AD	EO-SD vs LO-AD
SRI total score (max. 60)	9.57 ± 6.32 (0–18)	18.1 ± 16.7 (0–51)	1.04 ± 2.58 (0–14)	<0.001*	0.920	<0.001**	<0.001**
Eating and cooking behaviors	2.71 ± 2.50	4.64 ± 3.89	0.55 ± 1.75	<0.001*	0.798	<0.001**	<0.001**
Roaming	1.00 ± 1.53	3.50 ± 3.59	0.06 ± 0.32	<0.001*	0.501	0.002**	<0.001**
Speaking	2.86 ± 3.24	3.57 ± 4.24	0.38 ± 1.36	0.004*	0.885	0.004**	0.036**
Movements	0.86 ± 1.57	2.93 ± 3.97	0.00 ± 0.00	<0.001*	0.955	<0.001**	<0.001**
Daily rhythm	2.14 ± 2.34	3.50 ± 3.41	0.00 ± 0.00	<0.001*	0.632	<0.001**	<0.001**

\*Significant difference was found by the Kruskal–Wallis test ( $P < 0.05$ ), \*\*Significant difference was found by the post-hoc Steel–Dwass test for multiple comparison ( $P < 0.05$ ), Mean ± standard deviation. EO-SD, early-onset semantic dementia; LO-AD, late-onset Alzheimer's disease; LO-SD, late-onset semantic dementia; NS, not significant; SRI, Stereotypy Rating Inventory.

showed significantly lower values than the EO-SD patients in the 'construction' (cube-copying) score of the MMSE and the RCPM score. In general, the RCPM and the Rey–Osterrieth Complex Figure Test (ROCF) scores tend to be lower in even healthy older people,<sup>9</sup> because visuospatial cognition is more likely to be affected by ageing than verbal cognition.<sup>19</sup> In contrast, 'getting lost behaviour' in dementia has been reported as a problem of spatial memory or visuospatial processes.<sup>20</sup> In the present study, none of the 10 primary caregivers of the LO-SD patients noticed 'getting lost behaviour' in daily life, whereas 13 out of 47 primary caregivers of the LO-AD patients noticed 'getting lost behaviour' in daily life. Therefore, the visuospatial deficits of the LO-SD patients might be mild compared to the LO-AD patients, and be causally related to ageing. Additionally, the RCPM requires not only visuospatial processing, but also executive function for reasoning. Executive function deficits might occur with lesions of the dorsolateral prefrontal circuit, which is connected with subcortical white matter (frontal-subcortical circuits).<sup>21</sup> There is also a possibility that the LO-SD patients presented with executive function deficits, because some of them showed a mild degree of subcortical vascular disease on structured imaging.

The impairment of semantic memory in the verbal domain results in a loss of word-meaning. Both naming and comprehension deficits for infrequent single words are the most prominent features of SD.<sup>22</sup> Therefore, both SD groups in the present study scored significantly lower than the LO-AD patients in 'naming' of the MMSE.

Although severe memory impairment is characteristic of AD, no significant differences were found in 'recall' of the MMSE among the three groups. However, the SMQ result showed that both SD groups were far less impaired than the LO-AD patients in recent episodic memory. As for the reasons for that, there is a possibility that it was difficult to carry out accurate assessment of memory in both SD groups, because 'recall' of the MMSE is a verbal memory test.

According to the previous reports about neuropsychiatric symptoms, it has been reported that approximately half of AD patients present with 'delusion',<sup>23</sup> and 'delusion' is significantly more common in AD patients than in SD patients.<sup>24,25</sup> Meanwhile, 'euphoria' and 'disinhibition' are significantly more common in SD patients than in AD patients.<sup>26</sup> In the present

study, the results of the NPI corresponded with these previous reports. Both SD groups were distinct in the BPSD profiles from the LO-AD patients.

No significant differences were found in the duration of disease, sex ratio, the CDR score, MMSE total score and NPI total score among the three groups. Although the education level was significantly lower in the LO-SD patients and the LO-AD patients than in the EO-SD patients, this difference seems to be influenced by a change in the Japanese education system between before and after the Second World War.

In the present study, there are a few methodological issues. First, age at onset was ascertained by interviews with the primary caregivers and then patients were classified into the LO-SD patients, the EO-SD patients and the LO-AD patients. However, in some cases, caregivers' memories might have been inaccurate,<sup>27</sup> making it difficult to obtain an accurate medical history. Although we should exclude patients aged between 65 and 70 years at the first assessment to reduce the likelihood of having patients older than 65 years with a disorder that had its onset before that age,<sup>28</sup> we could not exclude these patients, because the number of both SD groups was small. Second, although there was no significant difference in the CDR score among the three groups, the CDR was designed to assess the severity of dementia mainly in AD patients. Therefore, the severity of dementia in SD patients could not be assessed accurately in the present study. Third, the sample size of SD patients in the present study was not large. Therefore, there is a possibility that the negative results in test scores other than the RCPM and 'construction' subtest of the MMSE were a type II error.

In conclusion, our findings suggest that LO-SD patients might present with mild visuospatial and constructive deficits in some neuropsychological tasks, whereas other cognitive and behavioural profiles of LO-SD patients are quite similar to EO-SD patients. Age-associated changes in the brain should be considered when we diagnose SD among the elderly population. Pathologically, most SD patients have ubiquitin-positive, tau-negative inclusion pathology and non-AD pathology. However, recently, it has been reported that an autopsy case of LO-SD showed AD pathology.<sup>29</sup> We await comprehensive study results in the future as to whether some atypical cognitive profiles in LO-SD patients stem from different pathological backgrounds from EO-SD patients.

## ACKNOWLEDGEMENTS

We thank the late Professor H. Tanabe for his encouragement and helpful suggestions on our research. The present study was undertaken with the support of grants provided by the Ministry of Education, Culture, Sports, Science and Technology (Grant no. 20591414) for M.I. (Grant no. 21500260) for K.K. and the Ministry of Health, Labor and Welfare (Research on dementia) for M.I. and R.F.

## REFERENCES

- 1 Neary D. Overview of frontotemporal dementias and the consensus applied. *Dement Geriatr Cogn Disord* 1999; **10** (Suppl 1): 6–9.
- 2 Graham A, Davies R, Xuereb J *et al.* Pathologically proven frontotemporal dementia presenting with severe amnesia. *Brain* 2005; **128**: 597–605.
- 3 Shinagawa S, Ikeda M, Fukuhara R, Tanabe H. Initial symptoms in frontotemporal dementia and semantic dementia compared with Alzheimer's disease. *Dement Geriatr Cogn Disord* 2006; **21**: 74–80.
- 4 Hodges JR, Patterson K. Semantic dementia: a unique clinicopathological syndrome. *Lancet Neurol* 2007; **6**: 1004–1014.
- 5 Bozeat S, Gregory CA, Lambon Ralph MA, Hodges JR. Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *J Neurol Neurosurg Psychiatry* 2000; **69**: 178–186.
- 6 Rosen HJ, Gorno-Tempini ML, Goldman WP *et al.* Patterns of brain atrophy in frontotemporal dementia and semantic dementia. *Neurology* 2002; **58**: 198–208.
- 7 Fujimori M, Imamura T, Yamashita H *et al.* Age at onset and visuocognitive disturbances in Alzheimer disease. *Alzheimer Dis Assoc Disord* 1998; **12**: 163–166.
- 8 Shinagawa S, Toyota Y, Ishikawa T *et al.* Cognitive function and psychiatric symptoms in early- and late-onset frontotemporal dementia. *Dement Geriatr Cogn Disord* 2008; **25**: 439–444.
- 9 Spreen O, Strauss E. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary*, 2nd edn. New York: Oxford University Press, 1998.
- 10 Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry* 1982; **140**: 566–572.
- 11 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.
- 12 Raven JC, Court JH, Raven J. *Manual for Raven's Coloured Progressive Matrices*. Oxford: Oxford Psychologists Press, 1990.
- 13 Koss E, Patterson MB, Ownby R, Stuckey JC, Whitehouse PJ. Memory evaluation in Alzheimer's disease: caregivers' appraisals and objective testing. *Arch Neurol* 1993; **50**: 92–97.
- 14 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.
- 15 Shigenobu K, Ikeda M, Fukuhara R *et al.* The stereotypy rating inventory for frontotemporal lobar degeneration. *Psychiatry Res* 2002; **110**: 175–187.

- 16 Neary D, Snowden JS, Gustafson L *et al*. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology* 1998; **51**: 1546–1554.
- 17 Ikeda M, Ishikawa T, Tanabe H. Epidemiology of frontotemporal lobar degeneration. *Dement Geriatr Cogn Disord* 2004; **17**: 265–268.
- 18 McKhann G, Drachman D, Folstein M. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology* 1984; **34**: 939–944.
- 19 Jenkins L, Myerson J, Joerding JA, Hale S. Converging evidence that visuospatial cognition is more age-sensitive than verbal cognition. *Psychol Aging* 2000; **15**: 157–175.
- 20 Chiu YC, Algase D, Liang J, Liu HC, Lin KN. Conceptualization and measurement of getting lost behavior in persons with early dementia. *Int J Geriatr Psychiatry* 2005; **20**: 760–768.
- 21 Cummings JL. Frontal-subcortical circuits and human behavior. *Arch Neurol* 1993; **50**: 873–880.
- 22 Snowden JS, Goulding PJ, Neary D. Semantic dementia: a form of circumscribed cerebral atrophy. *Behav Neurol* 1989; **2**: 167–182.
- 23 Ikeda M, Shigenobu K, Fukuhara R *et al*. Delusions of Japanese patients with Alzheimer's disease. *Int J Geriatr Psychiatry* 2003; **18**: 527–532.
- 24 Levy ML, Miller BL, Cummings JL, Fairbanks LA, Craig A. Alzheimer disease and frontotemporal dementias: behavioral distinctions. *Arch Neurol* 1996; **53**: 687–690.
- 25 Hokoishi K, Ikeda M, Maki N *et al*. Frontotemporal lobar degeneration: a study in Japan. *Dement Geriatr Cogn Disord* 2001; **12**: 393–399.
- 26 Ikeda M, Fukuhara R, Shigenobu K *et al*. Dementia associated mental and behavioural disturbances in elderly people in the community: findings from the first Nakayama study. *J Neurol Neurosurg Psychiatry* 2004; **75**: 146–148.
- 27 Oppenheim G. The earliest signs of Alzheimer's disease. *J Geriatr Psychiatry Neurol* 1994; **7**: 116–120.
- 28 Suribhatla S, Baillon S, Dennis M *et al*. Neuropsychological performance in early and late onset Alzheimer's disease: comparisons in a memory clinic population. *Int J Geriatr Psychiatry* 2004; **19**: 1140–1147.
- 29 Hodges JR, Mitchell J, Dawson K *et al*. Semantic dementia: demography, familial factors and survival in a consecutive series of 100 cases. *Brain* 2010; **133**: 300–306.

ORIGINAL ARTICLE

## Differentiation between amnesic-mild cognitive impairment and early-stage Alzheimer's disease using the Frontal Assessment Battery test

Ayumi YAMAO,<sup>1</sup> Tomoyuki NAGATA,<sup>1,2</sup> Shunichiro SHINAGAWA,<sup>2</sup> Kazutaka NUKARIYA,<sup>1</sup>  
Yusuke OCHIAI,<sup>1</sup> Hiroo KASAHARA<sup>1</sup> and Kazuhiko NAKAYAMA<sup>2</sup>

<sup>1</sup>Department of Psychiatry, Jikei University School of Medicine, Kashiwa Hospital, Chiba and <sup>2</sup>Department of Psychiatry, Jikei University School of Medicine, Tokyo, Japan

*Correspondence:* Dr Ayumi Yamao MD, Department of Psychiatry, Jikei University School of Medicine, Kashiwa Hospital, 163-1 Kashiwashita, Kashiwa, Chiba 277-8567, Japan. Email: a-yamao@jikei.ac.jp

*Received 18 March 2011; revision received 18 May 2011; accepted 10 July 2011.*

**Key words:** *Alzheimer's disease, amnesic-mild cognitive impairment (A-MCI), executive function, Frontal Assessment Battery (FAB), non-memory.*

### INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that is mainly characterized by memory disorder (episodic and recent memory), visuospatial and attentional impairment, and executive

### Abstract

**Background:** Previous research has described the executive dysfunction that occurs in patients with amnesic-mild cognitive impairments (A-MCI) and early-stage Alzheimer's disease (EAD), which are comparatively similar stages of dementia. The aim of the present cross-sectional study is to evaluate executive dysfunction using the Frontal Assessment Battery (FAB) screening test in two groups and to investigate the interaction with other cognitive impairments.

**Methods:** Among 170 consecutive patients with Alzheimer's disease or A-MCI, we recruited 48 subjects who were under 75 years of age and had been diagnosed as having either A-MCI or EAD. We then compared the total and the subtest scores of the mini-mental state examination (MMSE) and the FAB between the two groups. Moreover, we investigated the statistical interactive associations of the FAB subtest scores with the influential MMSE subtest scores or the diagnosis (A-MCI or EAD).

**Results:** No significant differences in the age, sex ratio, duration of illness, and education years were observed between the two groups. However, significant differences in the FAB total and subtest scores (conflicting instructions and go/no-go) were found between the two groups. Furthermore, significant differences in the MMSE total and subtest scores (orientation, memory delayed recall, and attention and calculation) were also noted between the two groups. In a generalized linear model analysis, only two FAB subtest scores (conflicting instructions and go/no-go) were significantly influenced by the diagnosis (A-MCI or EAD) in a manner that was independent of the interaction with the orientation or memory delayed recall.

**Conclusion:** The present findings suggest that the FAB total score and subtest scores reflecting interference performances (conflicting instructions and go/no-go) significantly declined in patients with EAD, independent of the disorientation and memory disorder. Such characteristics of neuropsychological screening test scores may be useful to clinicians for differentiating EAD and A-MCI at bedside.

dysfunction as its core symptoms.<sup>1,2</sup> Amnesic-mild cognitive impairment (A-MCI) is characterized by subjective forgetful complaints and a mild mnemonic reduction in neuropsychological tests; it has been considered as a prodromal state of AD.<sup>3</sup> Longitudinally,

about 30% of A-MCI patients progress or develop clinically diagnosable AD within three years, but about 60% of them do not and instead maintain the MCI stage as non-dementia.<sup>4,5</sup> Thus, it may be important to diagnose patients with A-MCI who are at risk of developing AD in order to prevent its conversion into dementia. However, A-MCI is difficult to discriminate clinically from early-stage AD (EAD), which has a similar symptomatic spectrum and represents a similar stage of dementia both cross-sectionally and temporarily.<sup>1,2</sup>

In previous studies investigating executive dysfunction in AD or A-MCI, a significant decline in motor programming and inhibition control among some executive functions was reported in AD patients, compared with patients with A-MCI.<sup>1,6-8</sup> Thus, an evaluation of executive dysfunction among non-memory impairments between A-MCI and AD may be important for effectively diagnosing these disease groups. From neurocognitive aspects, some studies have examined the pathogenesis of executive dysfunction and have investigated the association with other cognitive impairments, although a crucial conclusion has not yet been reached.<sup>1,9</sup>

The Frontal Assessment Battery (FAB), consisting of six main components, is an easily administered screening test that can be completed at bedside within 10 minutes and can be used to measure executive function without tools or instruments.<sup>10</sup> Kugo *et al.* and Nakaaki *et al.* confirmed the validity and reliability of the Japanese version of the FAB for patients with dementia and reported a strongly significant correlation between the FAB and the Wisconsin Card Sorting Test, which is the representative neuropsychological test reflecting executive function.<sup>11,12</sup> Hanyu *et al.* reported significant differences in the FAB total and subtest scores between A-MCI and AD patients in two groups and demonstrated the utility of the FAB for diagnosis of some screening tests.<sup>6</sup>

In the present study, we compared the FAB total and subtest scores between patients with A-MCI and those with EAD so as to differentiate these two groups, which have similar stages of dementia, using a screening test that reflects executive function. Moreover, we investigated the interaction with the mini-mental state examination (MMSE) subtest scores, a representative neuropsychological screening test that reflects disorientation, memory impairment, or attention deficits, and assessed the influence

of other cognitive functions on executive function in patients with A-MCI or EAD.

## METHODS

### Participants

One hundred seventy consecutive patients with AD and A-MCI who had been referred to the Jikei University Kashiwa Hospital (Chiba, Japan) outpatient clinic were enrolled in this study. After an examination of the patients' past medical history, an evaluation of their physical or neurological examination results, routine blood tests, and MRI findings by a geriatric psychiatrist, all the patients were diagnosed as having probable AD or A-MCI according to the National Institute of Neurology and Communicative Disorder and Stroke/Alzheimer Disease and Related Disorder Association criteria or the diagnostic criteria for A-MCI.<sup>3,13</sup> The exclusion criteria were a history of alcohol or other substance abuse, brain injury, major depressive or psychotic disorder, epilepsy, delirium, metabolic disorder, or treatment with acetylcholine esterase inhibitor. Our A-MCI group included both A-MCI-single domain and A-MCI-multiple domain types.<sup>3</sup> Among them, we recruited 48 patients (24 men, 24 women; 48-74 years) with A-MCI ( $n = 26$ ; A-MCI-single domain,  $n = 18$ ; A-MCI-multiple domain,  $n = 8$ ) or EAD ( $n = 22$ ). To evaluate general cognitive function, the MMSE and Wechsler Memory Scale-Revised (WMS-R) or the Japanese version of the Neurobehavioural Cognitive Status Examination (J-COGNISTAT) were used as a standardized test battery.<sup>14</sup> In the present study, A-MCI was defined as the presence of subjective forgetfulness, a global clinical dementia rating score of 0.5, an MMSE score  $\geq 24$  points,<sup>15</sup> and either a WMS-R general memory score  $\leq 85$  or a J-COGNISTAT memory score  $\leq 7$  (moderate impairment). Moreover, we selected EAD patients whose global clinical dementia rating scores were 0.5 or 1.0 and whose MMSE scores were  $\geq 18$  points.<sup>1</sup> These neuropsychological tests were administered by two clinical psychologists. Finally, four geriatric psychiatrists discussed the results of all the patients' diagnoses once a month to exclude other forms of dementia, such as vascular dementia, frontotemporal lobar degeneration, Lewy body disease, or idiopathic normal pressure hydrocephalus. The present study was approved by the Ethics Committee of the Jikei University School of Medicine.

### FAB and its subtests

The Japanese version of FAB consists of six subtests: (i) similarities (conceptualization); (ii) lexical fluency (mental flexibility); (iii) motor series (programming); (iv) conflicting instructions (sensitivity to interference); (v) go/no-go (inhibition control); and (vi) prehension behaviour (environmental autonomy). Each subtest is rated from 3 to 0, with the total score therefore ranging from 18 to 0.<sup>10</sup>

### Statistical analysis

SPSS 19.0J for Windows (SPSS Japan Inc, Tokyo, Japan) was used for all the statistical analyses. Age, years of education, duration of illness, MMSE total and representative five subtest scores reflecting memory impairment or attention deficit ((i) orientation (time and place), (ii) memory registration, (iii) memory delayed recall, (iv) attention and calculation and (v) three-stage commands score), and FAB total and subtest scores were compared using a one-way ANOVA with Tukey's post-hoc test between the two groups: A-MCI and EAD. The sex ratio was assessed using a  $\chi^2$  test. Furthermore, a generalized linear model analysis was performed to examine the contribution or interactions between the MMSE subtest

scores and the diagnosis (EAD or A-MCI) as independent variables of the FAB subtest scores. A  $P$ -value < 0.05 was considered statically significant.

## RESULTS

### Patient characteristics

Forty-eight subjects were enrolled in the present study, and Table 1 shows the demographics of this sample and statistical comparisons between the A-MCI and EAD groups. No significant differences in age, sex ratios, duration of illness (months), or education (years) were observed between the two groups. However, the FAB scores ( $P < 0.01$ ) and the MMSE scores ( $P < 0.001$ ) were significantly different between the two groups (Table 1).

### The comparison of FAB and MMSE subtest scores

In the FAB subtest, the conflicting instructions ( $P < 0.01$ ) and go/no-go ( $P < 0.01$ ) scores were significantly lower among the patients with EAD than among those with A-MCI (Table 2). Among the four MMSE subtests representatively reflecting memory impairment or attention deficit, three subtest scores, orientation ( $P < 0.001$ ), memory delayed recall

**Table 1** Subject characteristics (mean  $\pm$  SD)

Group	A-MCI ( $n = 26$ ) (Mean $\pm$ SD)	EAD ( $n = 22$ ) (Mean $\pm$ SD)	$\chi^2$ or $F$ score	$P$ -value
Sex (male/female)	15 / 11	9/ 13	0.1343 <sup>†</sup>	0.247
Age	68.7 $\pm$ 5.7	69.5 $\pm$ 4.9	0.269	0.606
Education (years)	12.9 $\pm$ 2.0	12.0 $\pm$ 2.5	2.228	0.142
Duration of illness (months)	21.5 $\pm$ 20.1	26.4 $\pm$ 16.9	0.821	0.37
MMSE score	26.9 $\pm$ 2.1	21.5 $\pm$ 2.9	56.732	<0.001 <sup>***</sup>
FAB score	14.7 $\pm$ 2.2	12.3 $\pm$ 3.1	10.159	0.003 <sup>**</sup>

\*\* $P < 0.01$ , \*\*\* $P < 0.001$  (one-way ANOVA with post-hoc test). <sup>†</sup> $\chi^2$  score. Sex ratio was analyzed by  $\chi^2$  test. A-MCI, amnesic-mild cognitive impairment; EAD, early-stage Alzheimer's disease; FAB, Frontal Assessment Battery; MMSE, mini-mental state examination.

**Table 2** FAB subtest scores (mean  $\pm$  SD)

Subtest	A-MCI ( $n = 26$ ) (Mean $\pm$ SD)	EAD ( $n = 22$ ) (Mean $\pm$ SD)	$F$ score	$P$ -value
Similarities	2.08 $\pm$ 1.09	1.68 $\pm$ 1.17	1.46	0.233
Lexical fluency	2.23 $\pm$ 0.71	1.77 $\pm$ 0.87	4.038	0.05
Motor series	2.50 $\pm$ 0.91	2.32 $\pm$ 0.95	0.461	0.5
Conflicting instructions	2.96 $\pm$ 0.20	2.55 $\pm$ 0.74	7.643	0.008 <sup>**</sup>
Go/no-go	2.19 $\pm$ 0.80	1.27 $\pm$ 1.08	11.473	0.001 <sup>**</sup>
Prehension behaviour	2.73 $\pm$ 0.67	2.73 $\pm$ 0.63	0	0.985

\*\* $P < 0.01$  (one-way ANOVA with post-hoc tests). A-MCI, amnesic-mild cognitive impairment; EAD, early-stage Alzheimer's disease; FAB, Frontal Assessment Battery.

**Table 3** The MMSE subtest scores (mean  $\pm$  SD)

Subtest	A-MCI (n = 26) (Mean $\pm$ SD)	EAD (n = 22) (Mean $\pm$ SD)	F score	P-value
Orientation (time, place)	9.00 $\pm$ 1.23	6.71 $\pm$ 1.95	2.3898	<0.001***
Memory registration	2.92 $\pm$ 0.27	3.00 $\pm$ 0	1.676	0.202
Memory delayed recall	2.38 $\pm$ 0.80	1.14 $\pm$ 1.21	18.272	<0.001***
Attention and calculation	3.77 $\pm$ 1.11	2.57 $\pm$ 1.69	8.547	0.005**
Three-stage commands	3.00 $\pm$ 0.00	2.90 $\pm$ 0.3	2.62	0.112

\*\* $P < 0.01$ , \*\*\* $P < 0.001$  (one-way ANOVA with post hoc-tests). A-MCI, amnesic-mild cognitive impairment; EAD, early-stage Alzheimer's disease; MMSE, mini-mental state examination.

**Table 4** Association of (a) conflicting construction and (b) go/no-go with memory delayed recall and diagnosis

Statistical comparison	d.f.	Mean-squares	F score	P-value
(a) Memory delayed recall	3	0.295	1.095	0.362
Diagnosis (A-MCI or EAD)	1	1.294	4.813	0.034*
Memory delayed recall $\times$ diagnosis	3	0.454	1.69	0.185
(b) Memory delayed recall	3	0.964	1.03	0.39
Diagnosis (A-MCI or EAD)	1	6.94	7.417	0.01†
Memory delayed recall $\times$ diagnosis	3	0.151	0.161	0.922

\* $P < 0.05$ ,  $R^2 = 0.257$ . Generalized linear models were used to investigate whether memory delayed recall and diagnosis (A-MCI or EAD) were associated with the conflicting construction scores. † $P < 0.05$ ,  $R^2 = 0.259$ . Generalized linear models were used to investigate whether memory delayed recall and diagnosis (A-MCI or EAD) were associated with the go/no-go scores. A-MCI, amnesic-mild cognitive impairment; EAD, early-stage Alzheimer's disease.

( $P < 0.001$ ), and attention and calculation ( $P < 0.01$ ), were significantly lower among the patients with EAD than among the patient with A-MCI (Table 3).

#### Interactive associations of the conflicting instructions and go/no go scores with the MMSE subtest scores or diagnosis (EAD or A-MCI)

To examine whether the MMSE subtest scores and diagnoses were associated with either the conflicting instructions or the go/no-go score as a dependent variable, we defined each MMSE subtest score (orientation, memory delayed recall, and attention and calculation) and diagnosis (A-MCI or EAD) as independent variables and performed a generalized linear analysis (one variable). As a result, we found that both the conflicting instructions and the go/no-go scores were significantly associated with only the diagnosis (conflicting instructions:  $F = 4.813$ , d.f. = 1,  $P = 0.034$ ; go/no-go:  $F = 7.417$ , d.f. = 1,  $P = 0.01$ ), but not with the memory delayed recall score (range: 0–3; conflicting instructions:  $F = 1.095$ , d.f. = 3,  $P = 0.362$ ; go/no-go:  $F = 1.03$ ; d.f. = 3;  $P = 0.39$ ) (Table 4). Moreover, the interaction between the delayed recall and diagnosis significantly influenced neither the conflicting instructions nor the go/no-go scores (conflicting instructions:  $F = 1.69$ , d.f. = 3,  $P = 0.185$ ; go/no-go:  $F = 0.167$ , d.f.

= 3,  $P = 0.922$ ) (Table 4). Additionally, we divided the subjects into the following three graded groups according to their orientation scores: 0–4 points, severe impairment; 5–7 points, moderate impairment; or 8–10 points, mild impairment. The subjects were also divided according to their attention and calculation scores: 0–1 points, severe impairment; 2–3 points, moderate impairment; or 4–5 points, mild impairment. These scores were regarded as independent variables. The groups were then used in a generalized linear analysis to investigate the association with conflicting instructions and go/no-go scores. The conflicting instructions and the go/no-go scores were significantly associated with only the diagnosis (conflicting instructions:  $F = 8.092$ , d.f. = 1,  $P = 0.007$ ; go/no-go:  $F = 11.128$ , d.f. = 1,  $P = 0.002$ ), but not with the orientation score (conflicting instructions:  $F = 1.892$ , d.f. = 2,  $P = 0.163$ ; go/no-go:  $F = 1.218$ ; d.f. = 2;  $P = 0.306$ ) (Table 5). The interaction between the orientation and the diagnosis did not significantly influence either the conflicting instructions or the go/no-go scores (conflicting instructions:  $F = 0.154$ , d.f. = 1,  $P = 0.697$ ; go/no-go:  $F = 0.149$ , d.f. = 1,  $P = 0.702$ ) (Table 5). Neither the conflicting instruments nor the go/no-go scores were significantly associated with attention and calculation (conflicting instructions:

**Table 5** Association of (a) conflicting construction and (b) go/no-go with diagnosis and orientation

Statistical comparison	d.f.	Mean-squares	F score	P-value
(a) Orientation severity (mild, moderate, severe)	2	0.5	1.892	0.163
Diagnosis (A-MCI or AD)	1	2.137	8.092	<b>0.007**</b>
Orientation × diagnosis	1	0.041	0.154	0.697
(b) Orientation severity (mild, moderate, severe)	2	1.075	1.218	0.306
Diagnosis (A-MCI or AD)	1	9.826	11.128	<b>0.002††</b>
Orientation × diagnosis	1	0.131	0.149	0.702

\*\* $P < 0.01$   $R^2 = 0.216$ . Generalized linear models were used to investigate whether the orientation severity and diagnosis (A-MCI or AD) were associated with the conflicting construction scores. †† $P < 0.01$ ,  $R^2 = 0.248$ . Generalized linear models were used to investigate whether the orientation severity and diagnosis (A-MCI or AD) were associated with the go/no-go scores. Orientation severity: mild, raw score of 8–10; moderate, raw score of 5–7; severe, raw score of 0–4. A-MCI, amnesic-mild cognitive impairment; AD, Alzheimer's disease.

**Table 6** Association of (a) conflicting construction and (b) go/no-go with the diagnosis and attention and calculation

Statistical comparison	d.f.	Mean-squares	F score	P-value
(a) Attention and calculation severity (mild, moderate, severe)	2	0.709	2.775	0.074
Diagnosis (A-MCI or EAD)	1	0.521	2.04	0.16
Attention and calculation × diagnosis	1	0.086	0.335	0.566
(b) Attention and calculation severity (mild, moderate, severe)	2	1.894	2.286	0.114
Diagnosis (A-MCI or EAD)	1	3.329	4.017	0.051
Attention and calculation × diagnosis	1	1.259	1.52	0.224

(a) Generalized linear models were used to investigate whether attention and calculation severity and diagnosis (A-MCI or EAD) were associated with the conflicting construction scores. Attention and calculation severity: mild (raw score: 4 or 5), moderate (raw score: 2 or 3), severe (raw score: 0 or 1).  $R^2 = 0.242$ . (b) Generalized linear models were used to investigate whether attention and calculation severity and diagnosis (A-MCI or EAD) were associated with the go/no-go scores. Attention and calculation severity: mild (raw score: 4 or 5), moderate (raw score: 2 or 3), severe (raw score: 0 or 1).  $R^2 = 0.294$ . A-MCI, amnesic-mild cognitive impairment; EAD, early-stage Alzheimer's disease.

$F = 2.775$ , d.f. = 2,  $P = 0.074$ ; go/no-go:  $F = 2.286$ , d.f. = 2,  $P = 0.114$ ) (Table 6). Furthermore, an interaction between the diagnosis and attention and calculation did not influence the conflicting instructions and go/no-go scores (conflicting instructions:  $F = 0.335$ , d.f. = 1,  $P = 0.566$ ; go/no-go:  $F = 1.52$ , d.f. = 1,  $P = 0.224$ ) (Table 4).

## DISCUSSION

In the present cross-sectional study, we found a significant difference in the total FAB and subtest scores (conflicting instructions and go/no-go scores) between the A-MCI and EAD groups. Significant differences in the MMSE total and subtest scores reflecting attention and memory function were also observed between the two groups. Moreover, the two FAB subtest scores (conflicting instructions and go/no-go) were significantly influenced only by the diagnosis (A-MCI or EAD) and not by the interaction with memory impairment or disorientation. These results support the a previous study's finding that, among the FAB subtest scores, the go/no-go score was significantly different between patients with

A-MCI and those with AD, while executive dysfunction in EAD was not influenced by other cognitive impairments.<sup>6,9</sup> On the other hand, some studies have suggested that deficits in responses to the interference or inhibitory tasks might result from psychomotor speed decrements or selective attention deficits.<sup>11,16–19</sup> Therefore, if simple scales or tests measuring attentional function had been administered, significant differences might have been observed. However, the present results may show the usefulness of the go/no-go and conflicting instructions scores among the FAB tests as a screening evaluation for differentiating A-MCI and EAD, without confounding interactions from memory impairment or attention deficit.

Some previous neuropsychological studies have confirmed the reliability and validity of FAB by measuring the executive function in various patients with dementia and comparing them with healthy controls.<sup>11,12</sup> FAB is one of the easiest tests to administer and can be completed at bedside without requiring any tools or instruments; it consists of six main cognitive components that are reportedly associated with different anatomical frontal regions.<sup>10</sup> In several

neuroimaging studies using single-photon emission CT and comparing patients with dementia and healthy controls, the FAB scores were significantly correlated with regional cerebral blood flow in the left lateral frontal lobe, right medial frontal lobe, and bilateral callosomarginal area.<sup>20,21</sup> In a cortical volumetric study, we reported that parahippocampal gyrus and entorhinal cortex atrophy in patients with EAD or A-MCI was associated with the go/no-go score among the FAB subtest scores.<sup>22</sup> Collette *et al.* also implied that a disconnection syndrome may exist in EAD patients, based on the results of neuroimaging studies showing an association between inhibitory dysfunction as executive dysfunction and the cerebral regions, except for the frontal lobe.<sup>18,23</sup> While the association between memory impairment in AD patients and hippocampal atrophy has been confirmed in previous studies, the association with executive function continues to be discussed, and a conclusion has not yet been reached.<sup>24–28</sup> Therefore, these pathways of pathogenesis should be elucidated in future studies.

The present study has some limitations. Firstly, among 170 consecutive outpatients, we restrictively selected 48 subjects so as to compare only the neuropsychological test scores between the two groups without any additional statistically confounding factors, such as age, sex, duration of illness, and years of education. Thus, the sample size was comparatively small, and a significant difference in the illness duration (months) between the two groups might not have been apparent. Second, only subjects under the age of 75 years were enrolled. One reason for this limitation was that we used either the J-COGNISTAT ( $n = 12$ ) or the WMS-R ( $n = 14$ ) evaluation test to support the diagnosis of A-MCI ( $n = 26$ ). The WMS-R test is designed for use in subjects between the ages of 16 and 74 years. Moreover, we hoped to recruit comparatively younger homogeneous subjects in two groups and to exclude various physical problems or disadvantageous factors arising from aging because of the explosive increase in the prevalence dementia after the age of 75 years.<sup>29</sup> Thirdly, to support the diagnosis, only one test, either the J-COGNISTAT or the WMS-R, was used, according to the wishes of the patients (who did not desire to spend the time necessary to complete further tests at bedside). Thus, we could not statistically compare any scores other than the FAB and MMSE scores between

the two groups. Therefore, we should have used only one neuropsychological test in all the subjects. Finally, the present study has a cross-sectional design, and longitudinal observations of the subjects were not performed. Thus, the use of FAB scores as a risk factor for the conversion of A-MCI to AD should be examined longitudinally in the future.

In conclusion, these results support the findings of previous studies, which cross-sectionally showed significant differences in the FAB total and subtest scores between patients with AD and those with A-MCI. Moreover, among the FAB subtests, the conflicting instructions and go/no go scores were useful for differentiating between EAD and A-MCI, independent of attentional and memory functions. Therefore, in daily examinations, the observation of executive dysfunction as non-memory impairments using the FAB test as a screening tool may be important and helpful for clinicians diagnosing A-MCI and EAD at bedside.

## REFERENCES

- 1 Baudic S, Barba GD, Thibaudet MC, Smaggha A, Remy P, Traykov L. Executive function deficits in early Alzheimer's disease and their relations with episodic memory. *Arch Clin Neuropsychol* 2006; **21**: 15–21.
- 2 Perry RJ, Watson P, Hodges JR. The nature and staging of attention dysfunction in early (minimal and mild) Alzheimer's disease: relationship to episodic and semantic memory impairment. *Neuropsychologia* 2000; **38**: 252–271.
- 3 Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol* 1999; **56**: 303–308.
- 4 Maruyama M, Matsui T, Tanji H *et al.* Cerebrospinal fluid tau protein and periventricular white matter lesions in patients with mild cognitive impairment: implications for 2 major pathways. *Arch Neurol* 2004; **61**: 716–720.
- 5 Zanetti M, Ballabio C, Abbate C, Cutaia C, Vergani C, Bergamaschini L. Mild cognitive impairment subtypes and vascular dementia in community-dwelling elderly people: a 3-year follow-up study. *J Am Geriatr Soc* 2006; **54**: 580–586.
- 6 Hanyu H, Sato T, Takasaki A, Akai T, Iwamoto T. Frontal lobe dysfunctions in subjects with mild cognitive impairment. *J Neurol* 2009; **256**: 1570–1571.
- 7 Ready RE, Ott BR, Grace J, Cahn-Weiner DA. Apathy and executive dysfunction in mild cognitive impairment and Alzheimer disease. *Am J Geriatr Psychiatry* 2003; **11**: 222–228.
- 8 Traykov L, Raoux N, Latour F *et al.* Executive functions deficit in mild cognitive impairment. *Cogn Behav Neurol* 2007; **20**: 219–224.
- 9 Binetti G, Magni E, Padovani A, Cappa SF, Bianchetti A, Trabucchi M. Executive dysfunction in early Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1996; **60**: 91–93.
- 10 Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: a Frontal Assessment Battery at bedside. *Neurology* 2000; **55**: 1621–1626.

- 11 Kugo A, Terada S, Ata T *et al.* Japanese version of the Frontal Assessment Battery for dementia. *Psychiatry Res* 2007; **153**: 69–75.
- 12 Nakaaki S, Murata Y, Sato J *et al.* Reliability and validity of the Japanese version of the Frontal Assessment Battery in patients with the frontal variant of frontotemporal dementia. *Psychiatry Clin Neurosci* 2007; **61**: 78–83.
- 13 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; **34**: 939–944.
- 14 Matsuda O, Saito M. Multiple cognitive deficits 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.
- 15 Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry* 1982; **140**: 566–572.
- 16 Amieva H, Phillips LH, Della Sala S, Henry JD. Inhibitory functioning in Alzheimer's disease. *Brain* 2004; **127**: 949–964.
- 17 Amieva H, Lafont S, Rouch-Leroyer I *et al.* Evidencing inhibitory deficits in Alzheimer's disease through interference effects and shifting disabilities in the Stroop test. *Arch Clin Neuropsychol* 2004; **19**: 791–803.
- 18 Collette F, Van der Linden M, Delrue G, Salmon E. Frontal hypometabolism does not explain inhibitory dysfunction in Alzheimer disease. *Alzheimer Dis Assoc Disord* 2002; **16**: 228–238.
- 19 Langley LK, Overmier JB, Knopman DS, Prod'Homme MM. Inhibition and habituation: preserved mechanisms of attentional selection in aging and Alzheimer's disease. *Neuropsychology* 1998; **12**: 353–366.
- 20 Kume K, Hanyu H, Murakami M *et al.* Frontal Assessment Battery and brain perfusion images in amnesic mild cognitive impairment. *Geriatr Gerontol Int* 2010; **11**: 77–82.
- 21 Yoshida H, Terada S, Sato S *et al.* Frontal assessment battery and brain perfusion imaging in early dementia. *Dement Geriatr Cogn Disord* 2009; **27**: 133–138.
- 22 Nagata T, Shinagawa S, Ochiai Y *et al.* Association between executive dysfunction and hippocampal volume in Alzheimer's disease. *Int Psychogeriatr* 2011; **23**: 764–771.
- 23 Delbeuck X, Van der Linden M, Collette F. Alzheimer's disease as a disconnection syndrome? *Neuropsychol Rev* 2003; **13**: 79–92.
- 24 den Heijer T, van der Lijn F, Koudstaal PJ *et al.* A 10-year follow-up of hippocampal volume on magnetic resonance imaging in early dementia and cognitive decline. *Brain* 2010; **133**: 1163–1172.
- 25 Dickerson BC, Eichenbaum H. The episodic memory system: neurocircuitry and disorders. *Neuropsychopharmacology* 2010; **35**: 86–104.
- 26 Grundman M, Jack CR Jr, Petersen RC *et al.* Hippocampal volume is associated with memory but not nonmemory cognitive performance in patients with mild cognitive impairment. *J Mol Neurosci* 2003; **20**: 241–248.
- 27 Mungas D, Harvey D, Reed BR *et al.* Longitudinal volumetric MRI change and rate of cognitive decline. *Neurology* 2005; **65**: 565–571.
- 28 Tulving E, Markowitsch HJ. Episodic and declarative memory: role of the hippocampus. *Hippocampus* 1998; **8**: 198–204.
- 29 De Ronchi D, Berardi D, Menchetti M *et al.* Occurrence of cognitive impairment and dementia after the age of 60: a population-based study from Northern Italy. *Dement Geriatr Cogn Disord* 2005; **19**: 97–105.

REVIEW ARTICLE

## Exploring strategies to alleviate caregiver burden: Effects of the National Long-Term Care insurance scheme in Japan

Yumiko ARAI<sup>1</sup> and Steven H. ZARIT<sup>2</sup>

<sup>1</sup>Department of Gerontological Policy, National Institute for Longevity Sciences (NILS), National Center for Geriatrics and Gerontology (NCGG), Aichi, Japan and <sup>2</sup>Department of Human Development and Family Studies, Penn State University, University Park, Pennsylvania, USA

*Correspondence:* Dr Yumiko Arai MD, PhD, Departmental Head, Department of Gerontological Policy, National Institute for Longevity Sciences (NILS), National Center for Geriatrics and Gerontology (NCGG), 35 Gengo, Morioka-cho, Obu-shi, Aichi 474-8511, Japan. Email: yarai903@ncgg.go.jp

*Received 21 February 2011; accepted 17 March 2011.*

**Key words:** caregivers, carers, dementia, long-term care, long-term care policy.

### INTRODUCTION

Worldwide, the number of older people with disabilities is increasing; correspondingly, there have been marked increases in the number of family members providing assistance to these individuals. Care demands can become stressful and exhausting, especially in cases of dementia and other degenerative conditions, and, as a result, family caregivers may experience significant mental health problems, as well as a deterioration of their own health. Thus, 'alleviation' of caregiver burden has become a primary public health goal in many countries.

In the present article, we explore initiatives to 'prevent' the burden of caregiving among those who look after older disabled family members. Japan and

### Abstract

The ever-increasing population of older people with disabilities, including dementia, has been accompanied by a corresponding growth in the number of family caregivers, who are themselves at risk of developing mental and physical health problems. As a result, the need for practical and effective approaches for alleviating caregiver burden has become a major public health concern. One approach involves the development of public policy initiatives to allow the caregiver burden to be borne partly by society as a whole, rather than falling solely on individuals. In 2000, Japan introduced a National Long-Term Care (LTC) insurance scheme that requires adults over the age of 40 years to pay compulsory monthly premiums, with one aim of the program being to reduce caregiver burden. The present paper reviews the effects of this scheme on caregivers' and the general public's perception of caregiver burden and assesses what other measures are needed to further reduce and/or prevent burden. Drawing on recent studies, four questions are addressed: (i) have caregivers' attitudes towards caregiving changed since the implementation of the scheme; (ii) do services provided under the scheme alleviate caregiver burden; (iii) what are the general public's attitudes to and understanding of family caregiving; and (iv) what is the general public's level of understanding of dementia? Results from recent studies suggest that the LTC insurance scheme in Japan appears to be an effective measure for alleviating the burden of caregiving among current family caregivers, but larger studies are needed to determine overall effectiveness.

its long-term care system will be used as an example of one approach to reducing burden.

A review of the literature suggests that there are three common approaches that attempt to alleviate or reduce the burden of caregiving among those looking after older family members. The first approach is to treat the symptoms and problems of patients (care recipients) that are troublesome for caregivers. An example would be to use medication to reduce the occurrence of behavioral and psychological symptoms of dementia (BPSD), which, of course, is a major risk factor for caregiver burden. By targeting these problems in the patient, treatment should also reduce the burden on the caregiver.

The second approach is to intervene with family caregivers in a clinical or community setting to provide resources that may alleviate the impact of BPSD and other stressors. Examples of this approach would be providing respite care or counseling programs for caregivers. Some intervention studies, which have applied the first two approaches, have proven effective for certain study populations. Notable examples include Mittelman's work on a counseling intervention<sup>1-3</sup> and the studies of Zarit *et al.* on the impact of adult day care on caregiver burden.<sup>4-6</sup>

The third approach is at the societal level. In this approach new public policies would be established, or current ones modified, so that a portion of caregiving burden is borne by society as a whole. In contrast to intervening with caregivers and care recipients on an individual level, this approach makes information and resources more readily available for the whole population, as well as for targeted groups of vulnerable care recipients and their family caregivers. This may remove the isolation that caregivers feel and the stigma associated with using services. This population-wide approach is exemplified by Japan's National Long-Term Care (LTC) insurance scheme.

Japan has the world's fastest aging population. It also has a relatively high (but rapidly decreasing) proportion of family members coresiding with older parents. Thus, Japan's experience in implementing a national LTC policy may provide useful insights into how to cope with increasing demands for family caregiving in other aging societies.

### **STUDIES OF THE EFFECTS OF THE JAPANESE LTC POLICY ON CAREGIVING**

To explore the impact of the LTC policy on family caregivers and the wider population, the results of four studies conducted by one of the authors (YA) and her colleagues are described in this paper. The goals of these studies were fourfold: (i) to ascertain whether caregivers' attitudes towards family caregiving had changed from those held before the implementation of LTC insurance; (ii) to investigate whether the use of services provided under the LTC scheme alleviate caregiver burden; (iii) to explore the attitudes of the general public towards and their understanding of family caregiving; and (iv) to determine the extent of the general public's knowledge of dementia. Prior to the discussion of the details of each study, the

current situation in Japan, including the LTC insurance scheme, is briefly described.

### **The LTC insurance scheme in Japan**

Japan is the fastest graying society in the world. By 2020, one-quarter of the population will be over 65 years of age.<sup>7</sup>

Traditionally, older Japanese people lived with their children, particularly the eldest son and his wife. Caregiving emerged naturally under this arrangement. This arrangement was an integral part of the Confucian principles that were used to order families and society. With modernization, these traditions are changing rapidly. Over the past 60 years, the percentage of older people residing with their children has been decreasing constantly in Japan, as well as in other countries.<sup>8</sup> Rates of coresidence in Japan started at a much higher level than in Western countries, and are still much higher, but the relative drop for Japan has been substantial, from 80% in 1952 to 43% at present. In summary, the traditional normative pattern of care in the same household is no longer available for over half of Japan's older residents. The new residential patterns reflect the emergence of new norms and values that are eroding the traditional responsibility that daughters-in-law had for their husbands' parents. With women increasingly employed outside the home, they are less likely to take on the obligation to be the main care provider for their in-laws, although they still may want to help their own parents. In addition, some older people may prefer maintaining their independence, rather than moving in with their children. Thus, the change in residential patterns, combined with other social changes and a rapidly growing older population, complicates the situation for caregiving.

The LTC insurance program was developed explicitly to address the changes in the age of the population and in family structure. The LTC scheme covers home-based and institutional care for those aged 65 years or older who require it. It also provides for people over 40 years of age who have 'age-related' diseases, such as dementia. Municipal governments are the insurers and the level of services is determined by the clients' severity of disability by using an index called the Government-Certified Disability Index (GCDI); under the LTC insurance program, care services are allocated based on this GCDI.<sup>9</sup> One of the most important features of this scheme is that the

extent of informal care available to clients is not taken into account when eligibility is determined. For Japan, this is an incredibly radical departure from the traditional belief that families are the prime resource for long-term care.<sup>10</sup>

The LTC insurance scheme is financed by insurance premiums and tax revenue. Half the funding comes from premiums paid by people over 40 years of age. The other half of the funding comes from taxes.

We now turn to the four studies that address the effects of the LTC insurance scheme on family caregivers and the broader population.

### **Attitudes towards family caregiving among caregivers**

The objective of the first study was to ascertain whether caregivers' attitudes towards family caregiving had changed from those before the implementation of the LTC insurance scheme.<sup>11</sup> Specifically, family caregivers who looked after disabled elderly served by a private agency in Osaka prefecture were asked on two occasions about who should care for disabled elders, once before the LTC insurance scheme was implemented (in 2000) and then after the scheme was in place (in 2001). The choices for responses were family only, family and society, mainly society, and society only. The responses showed greater endorsement of the responsibility of society for the care of older people in 2001 than in 2000. The proportion of those who answered 'mainly society' increased from 12.4% to 22.8%, whereas those responding 'society only' increased from 3.7% to 6.2%. These changes were statistically significant and meaningful in a society with strong cultural traditions of filial piety.

These results suggest that in a short period of time the LTC insurance scheme had demonstrably changed the attitudes of caregivers. More caregivers came to believe that society must be involved in the care of older people after the implementation of the LTC insurance scheme. There was a shift from the traditional way of thinking that the care of disabled older people falls to the family to the acceptance that society must help in the care of disabled older people in Japan.

This is one of the most meaningful changes initiated by the LTC insurance scheme. The lesson here is that many people may oppose change, fearing what it

may mean, but come to accept a new program when it proves useful.

### **Effectiveness of service use on reducing caregiver burden**

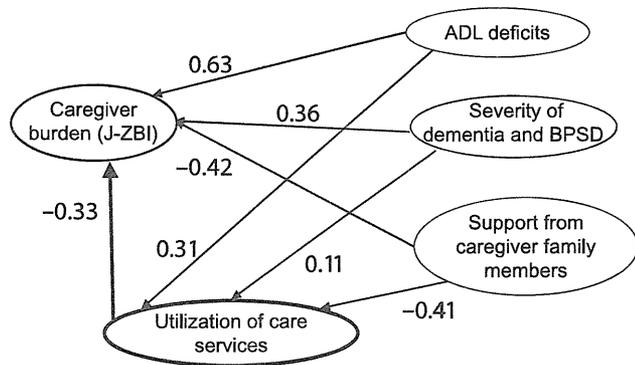
Because relatively few observational studies had been conducted on the impact of home care services on burden or other aspects of the caregiver's experience, the second study investigated whether the use of services provided under the LTC scheme alleviated caregiver burden.<sup>12</sup>

The study tested three hypotheses:

1. That the severity of impairment and the dementia among the disabled elderly increases the feelings of burden among family caregivers and that support from family members decreases burden.
2. That the amount of services used by older people and their caregivers is affected by the severity of dementia and deficiencies in activities of daily living (ADL) among the disabled elderly and the amount of support from family members.
3. Controlling for severity, that the use of care services under the LTC insurance scheme serves to reduce the feelings of burden among family caregivers.

The study used data obtained from community-dwelling disabled elderly and their principal family caregivers. A structural equation model was used to test the hypotheses. The model included the following variables: age of the disabled elderly; the severity of the ADL deficiency and behavioral disturbances; the use of formal (public) care services; support from family members; and feelings of burden among family caregivers. After adjusting for the severity of impairment, it was found that greater service utilization under the LTC insurance scheme was associated with less caregiver burden (Fig. 1).<sup>12</sup>

These findings suggested that care services provided under the LTC insurance scheme had been successfully reducing burden among family caregivers. This study was one of the first to show that the use of services can reduce caregiver burden in a non-experimental setting,<sup>12</sup> that is, in a real community setting. More studies of this type are needed to expand our understanding of how services provided under the LTC insurance scheme may be helping family caregivers.



**Figure 1** Structural model of the caregiver burden for family caregivers. Controlling for severity, the use of care services under the National Long-Term Care (LTC) insurance scheme serves to reduce the feelings of burden among family caregivers ( $\chi^2 = 34.46$ ; d.f. = 26;  $P = 0.12$ ; adjusted goodness of fit index (AGFI) = 0.85; comparative fit index (CFI) = 0.92; root mean square error of approximation (RMSEA) = 0.06). J-ZBI, Japanese version of the Zarit Burden Interview; ADL, activities of daily living; BPSD, behavioral and psychological symptoms of dementia.

### Attitudes towards family caregiving among the general public

The third and the fourth studies were targeted at the general public and these studies were conducted with a view that an understanding of the general public's perception of caregiving is indispensable if we are to reduce 'caregiver burden' at the societal level.

The goal of the third study was to explore how the general public in Japan feels about caring for older people at home.<sup>13</sup> Participants in the study were asked to report to what extent they agree with the following statement: 'Caring for older people at home can be a greater burden on family caregivers than at care facilities.' It was revealed that 85% of the Japanese general public believes that caring for older people at home is a great burden on family caregivers. This indicates a high level of concern and although we do not have data on similar concerns prior to the implementation of the LTC insurance scheme, it would seem that the LTC insurance scheme has yet to allay apprehensions about caring for older family members among the general public in Japan.

One possible explanation is that this 'expected burden' would be a lack of familiarity with the LTC insurance scheme among the general public. Therefore, we asked whether respondents knew how to use the services provided under the LTC insurance scheme. More than 60% of the general public did not know how to use the program and another 17% were

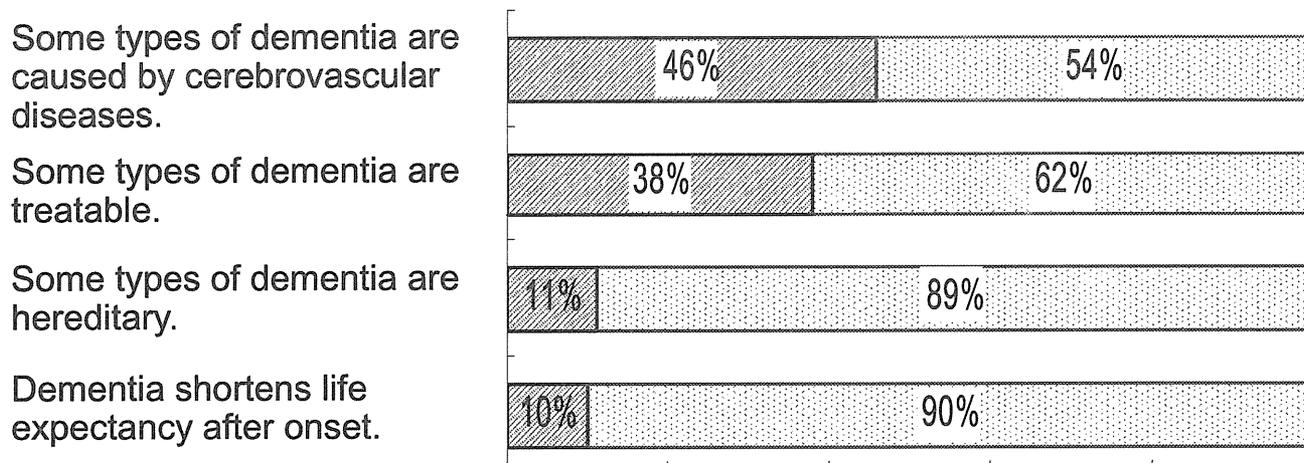
not sure if they knew how to use the program.<sup>13</sup> Moreover, the proportion of people who did not know how to use the program was higher among those younger than 40 years of age. People under 40 years of age may not know much about how to use the LTC insurance scheme because they do not pay the compulsory monthly insurance premium. Of course, they are also less likely to be assisting a parent than are middle-aged adults. Nonetheless, increased understanding of the program in this age group could be useful. Family caregiving can befall anyone; most individuals are exposed to this risk or possibility of becoming 'a family caregiver', and some people under 40 years of age do take on this role. Thus, a lack of knowledge about the services provided under the LTC insurance scheme needs to be improved and apprehensions regarding caregiving among the general public need to be allayed, particularly in younger generations. This lack of knowledge may increase the difficulties these people may encounter if they become caregivers or it dissuade them from taking on the role of caregiver in the first place. Lack of knowledge could also undermine support among the general public of the LTC program.

### Knowledge of dementia among the general public

The objective of the fourth study was to determine the extent of the general public's knowledge of dementia in Japan.<sup>14</sup> We focused on dementia because of the number of people affected, particularly at advanced ages, and the considerable impact that dementia has on the family. As with knowledge about the LTC insurance scheme, knowledge about dementia represents an essential component for recognizing and supporting older people with this problem and their caregivers.

A 'dementia knowledge' survey was conducted targeted at the general public across the country, aged 20 years or older. A self-administered questionnaire was used to assess the level of understanding of dementia among the general public. Specifically, the survey comprised true-false assessments for 11 statements concerning dementia that addressed the categories 'general aspects', 'symptoms', and 'biomedical aspects including cause, treatment, and prognosis'.

The following two points became clear from the results. First, people understood the general aspects



**Figure 2** Knowledge of the 'biomedical aspects of dementia' in the general public aged 20 years or older ( $n = 2115$ ). (■), correct answers; (▨), incorrect answers. The causes, treatment and prognosis of dementia were not well understood.

of dementia (e.g. the role of aging as well as symptoms of dementia). Second, the proportion of participants who showed proper understanding of items regarding the biomedical aspects of dementia was remarkably low; less than half the respondents gave correct answers in this area of questioning. For example, two of the items concerning heredity (cause) and life expectancy (prognosis) were answered correctly by only 10% and 11% of the sample, respectively. In addition, only 38% responded with the correct assessment of the statement regarding treatment for dementia ('some types of dementia are treatable'; Fig. 2). Overall, the causes, treatment and prognosis of dementia were not well understood among the general public, although the people generally knew about the role of age and types of symptoms manifested in dementia.<sup>14</sup>

This lack of understanding of dementia may prevent people from preparing for possible social and financial challenges if they become caregivers looking after a disabled family member. Indeed, family caregiving can befall anyone: becoming a family caregiver is a possibility for most individuals. Similarly, developing dementia can befall anyone.

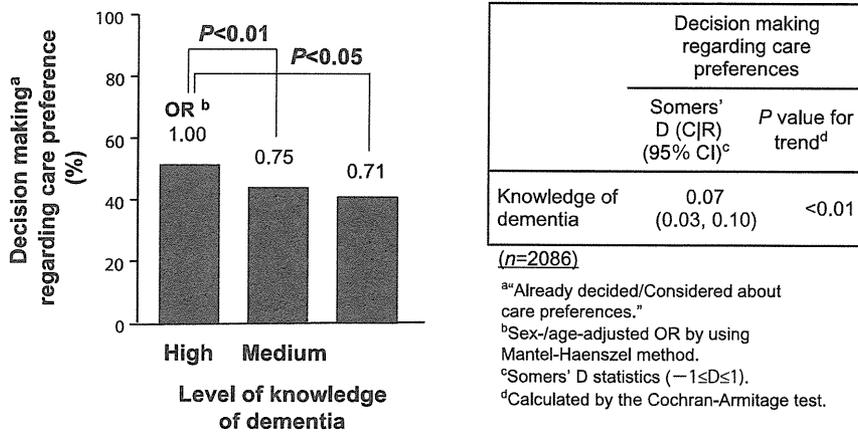
To explore these findings further, we developed the following hypothesis: people who have more knowledge about dementia will be more likely to have done some advanced care planning for themselves. We examined the association between one's degree of knowledge of dementia and the proportion of those who have made decisions regarding care preferences

(i.e. advance care planning). For this study, we used a representative sample of 2000 people.<sup>15</sup> We found that less than 60% of participants had decided about their care preferences on their own if extra assistance was required, regardless of their level of understanding about dementia (Fig. 3). However, using a Cochran–Armitage test for trends, we found that those with a better understanding of dementia were more likely to have already decided their own care preferences, should they need help in the future. In addition, this relationship was significant even after controlling for age and gender (Fig. 3).<sup>15</sup>

This result indicates that those who have sufficient knowledge of dementia are more likely to decide their own care preferences. This should allow them and their family caregivers to be 'more ready' for any social and medical challenges resulting from dementia. Thus, dissemination of knowledge of dementia among the general public is important because it may lead to a reduction in, or even a prevention of, caregiver burden by allowing them to seek early diagnosis and the provision of proper care in a timely manner.

## CONCLUSIONS

The overall conclusions from these studies are as follows. First, preliminary studies suggest that Japan's National LTC insurance scheme appears an effective measure for alleviating the burden of care among family caregivers. The LTC insurance scheme has involved the general public (those over 40 years of



**Figure 3** Association between advanced care planning and knowledge of dementia. Sixty percent of participants had decided on their own care preference if extra assistance was required, regardless of their level of understanding about dementia. OR, odds ratio; CI, confidence interval; CIR, row variable x (knowledge of dementia) is regarded as an independent variable, whereas the column variable y (decision making regarding care preferences) is regarded as a dependent variable.

age) by sharing the burden of caregiving through the compulsory payment of a monthly premium.

Second, the implication for other countries is that a system of burden sharing at the societal level may have a positive effect on reducing, and possibly preventing, the burden of care of ‘present day’ caregivers. More importantly, such a system can get the general public accustomed to the idea of sharing the burden of caregiving before any individual actually needs assistance, although that has not happened as much as it could have in Japan. Successful long-term care programs in the Scandinavian countries are built on long-standing cultural patterns of shared responsibility (see Sundström *et al.*<sup>16</sup>), but in countries such as Japan, where the LTC insurance scheme reflects changes in values, it may be important to combine policy initiatives with public education. Such an approach can be a useful strategy for preventing burden because people are then more prepared to become a family caregiver. In addition, it may encourage people to take on care responsibilities without feeling that they will be overwhelmed by having to do all the caring themselves.

Third, there are differences in the degree of apprehension felt about caregiving among different age groups. This appears to be based on the age for starting to pay the premium for the LTC insurance scheme. Thus, dissemination of information should be tailored to target different age groups in different ways.

Fourth, policy makers should recognize that the LTC insurance scheme contains effective measures for reducing or even preventing caregiver burden at a societal level rather than regarding it as only contain-

ing measures for reducing caregiver burden. Such recognition could be used as part of a universal primary prevention approach to provide education about how the LTC insurance scheme can help people meet caregiving responsibilities, if and when they have to assume such a role.

### ACKNOWLEDGMENTS

The author’s research reported herein was supported, in part, by grants provided by the Ministry of Education, Culture, Sports, Science and Technology, Japan (no. 14570375; principal investigator: YA) and by the Ministry of Health, Labour and Welfare, Japan (no. H19-025; principal investigator: YA; and no. 21A-9; principal investigator: YA).

### REFERENCES

- Mittelman MS, Ferris SH, Shulman E *et al.* A family intervention to delay nursing home placement of patients with Alzheimer disease: A randomized controlled trial. *JAMA* 1996; **276**: 1725–1731.
- Mittelman MS, Roth DL, Coon DW, Haley WE. Sustained benefit of supportive intervention for depressive symptoms in caregivers of patients with Alzheimer’s disease. *Am J Psychiatry* 2004; **161**: 850–856.
- Mittelman MS, Roth DL, Clay OJ, Haley WE. Preserving health of Alzheimer caregivers: Impact of a spouse caregiver intervention. *Am J Geriatr Psychiatry* 2007; **15**: 780–789.
- Zarit SH, Stephens MAP, Townsend A *et al.* Stress reduction for family caregivers: effects of adult day care use. *J Gerontol B Psychol Sci Soc Sci* 1998; **53**: B267–B277.
- Zarit SH, Leitsch SA. Developing and evaluating community based intervention programs for Alzheimer’s patients and their caregivers. *Aging Ment Health* 2001; **5** (Suppl): S84–S98.
- Gaugler JE, Jarrott SE, Zarit SH, Stephens MAP, Townsend A, Greene R. Adult day service use and reductions in caregiving hours: Effects on stress and psychological well-being for dementia caregivers. *Int J Geriatr Psychiatry* 2003; **18**: 55–62.

- 7 Ministry of Health, Labor and Welfare/Care of Elderly Study Group. *Elderly Care in 2015: Establishing Care that Supports the Dignity of the Elderly*. Available from: <http://www.mhlw.go.jp/topics/kaigo/kentou/15kourei/3.html> [accessed 3 December 2009].
- 8 National Institute of Population and Social Security Research. *Household Projections for Japan by Prefectures: 1995–2020 Reported on March 2000*. Available from: <http://www.ipss.go.jp/pp-ajsetai/e/chk2000/chk.html> [accessed 3 December 2009].
- 9 Arai Y, Zarit SH, Kumamoto K, Takeda A. Are there inequities in the assessment of dementia under Japan's LTC insurance system? *Int J Geriatr Psychiatry* 2003; **18**: 346–352.
- 10 Arai Y. Japan's new long-term care insurance. *Lancet* 2001; **357**: 1713.
- 11 Arai Y, Ueda T. Paradox revisited: Still no direct connection between hours of care and caregiver burden. *Int J Geriatr Psychiatry* 2003; **18**: 188–189.
- 12 Kumamoto K, Arai Y, Zarit SH. Use of home care services effectively reduces feelings of burden among family caregivers of disabled elderly in Japan: Preliminary results. *Int J Geriatr Psychiatry* 2006; **21**: 163–170.
- 13 Arai A, Sasaki M, Arai Y. The general public's attitudes towards and their understanding of the long term care insurance. *Geriatr Med* 2007; **45**: 139–144 (in Japanese).
- 14 Arai Y, Arai A, Zarit SH. What do we know about dementia? A survey on knowledge about dementia in the general public of Japan. *Int J Geriatr Psychiatry* 2008; **23**: 433–438.
- 15 Arai A, Arai Y. Advance care planning among the general public in Japan: association with awareness about dementia. *Jpn J Geriatr* 2008; **45**: 640–646 (in Japanese).
- 16 Sundström G, Malmberg B, Johansson L. Balancing family and state care: Neither, either or both? The case of Sweden. *Ageing Soc* 2006; **26**: 767–782.

