Figure 2 Total number of words recalled by patients in the reminiscence (■) and conversation (□) groups at the first and fifth evaluations of therapy.

Thus, changes in non-verbal communication differed based on differences in the type of session (Table 2; Fig. 4).

Evaluation of subjective feelings after each session indicated an interaction only in the happiness scores for the two groups between the first and final sessions ($F_{(1,14)} = 14.40$, $P = 0.002$). These results confirm that the degree of happiness differed based on the type of session (Table 2; Fig. 5).

Evaluation of daily appearance based on the Daycare Evaluation Table (total score of 10 items) revealed an interaction between the two groups before and after the sessions ($F_{(1,14)} = 8.44$, $P = 0.012$). Accordingly, it was confirmed that changes in the items on the Daycare Evaluation Table were related to the content of the session (Table 2; Fig. 6).

Participants' appearance during the sessions

Participants in the reminiscence group were observed to be uneasy during the beginning of the first session, but gradually they became closer to each other as they recalled nostalgic memories with the group. The participants did not always actively converse, but they still enjoyed conversing with others. The staff observing the session was encouraged by the appearance of the participants in the reminiscence group. Conversely, in the conversation group, although resistance did not increase from the first session onwards,

the conversations were difficult to start, there was no progression in group development, and the staff felt that the therapeutic intervention was difficult and that it should be conducted in line with the abilities of the participants.

Correlations among the scales for the reminiscence group

We used correlation analysis to ascertain whether there were any relationships among the scales indicating significant changes for the reminiscence group. After the reminiscence therapy had been performed five times, compared with the first therapy session, significant changes were found in the following scales: the total words recalled on the verbal fluency task, 'non-verbal communication' of TORS, the feeling of 'happiness' at each session, and the Daycare Evaluation Table. We investigated correlations among the scales using the results of the final evaluations (Table 3). The results revealed a significant negative correlation ($r = -0.94$, $P < 0.01$) between the Daycare Evaluation Table and the feeling of 'happiness' at each session. Furthermore, the correlation coefficient for the number of words recalled and the feeling of 'happiness' each time was $r = 0.68$, revealing no significant difference. Thus, no clear correlation was observed.

DISCUSSION
Changes based on session content and evaluation method

It was expected that participants in the reminiscence group would not only come to feel more secure, but that communication with their families and care-giving staff would also improve. The present study revealed an interaction between the number of words recalled on the first and final evaluations using the verbal fluency task and the type of intervention, either reminiscence therapy or conversation only.

In the reminiscence group, interest in the other group members increased with each session. Non-verbal communication was undertaken with no trouble with participants nodding their heads as they appeared to enjoy listening to each other. After the sessions, they reported feeling happier than did participants in the conversation (control) group. For elderly people with dementia who have impaired recall of recent memories, it is easier to recall and talk about nostalgic memories from the distant past. Therefore, it

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**Table 2** Comparison of changes between the reminiscence and conversation groups

Evaluation	Mobilizing factor (intrasubject)	Type III sum of squares	Degrees of freedom	Mean square	F value	P value
Verbal fluency						
Total	Pre–post	36.13	1	36.13	2.91	0.110
	Pre–post × therapy	171.13	1	171.13	13.79	0.002
	Error (pre–post)	173.75	14	12.41		
Todai-shiki Observational Rating Scale						
Verbal communication	Pre–post	5.28	1	5.28	16.66	0.001
	Pre–post × therapy	0.78	1	0.78	2.47	0.139
	Error (pre–post)	4.44	14	0.32		
Non-verbal communication	Pre–post	3.78	1	3.78	9.74	0.008
	Pre–post × therapy	5.28	1	5.28	13.60	0.002
	Error (pre–post)	5.44	14	0.39		
Attentiveness/interest	Pre–post	0.28	1	0.28	0.44	0.518
	Pre–post × therapy	0.28	1	0.28	0.44	0.518
	Error (pre–post)	8.94	14	0.64		
Emotions	Pre–post	3.13	1	3.13	2.85	0.114
	Pre–post × therapy	0.50	1	0.50	0.46	0.511
	Error (pre–post)	15.38	14	1.10		
Subjective feelings						
Mood	Pre–post	0.28	1	0.28	0.84	0.375
	Pre–post × therapy	1.53	1	1.53	4.57	0.051
	Error (pre–post)	4.69	14	0.34		
Happiness	Pre–post	1.13	1	1.13	3.60	0.079
	Pre–post × therapy	4.50	1	4.50	14.40	0.002
	Error (pre–post)	4.38	14	0.31		
Daycare Evaluation Table						
Total of 10 items	Pre–post	51.26	1	51.26	19.70	0.001
	Pre–post × therapy	21.95	1	21.95	8.44	0.012
	Error (pre–post)	36.42	14	2.60		

$P < 0.05$ was considered significant (two-way ANOVA).
Pre–post, evaluation at first session and final sessions; Therapy, reminiscence group or conversation group.
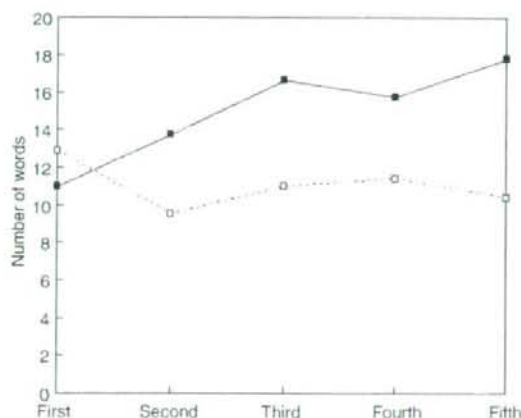
Figure 3 Changes in the total number of words recalled by patients in the reminiscence (■) and conversation ( ) groups after each therapy session.
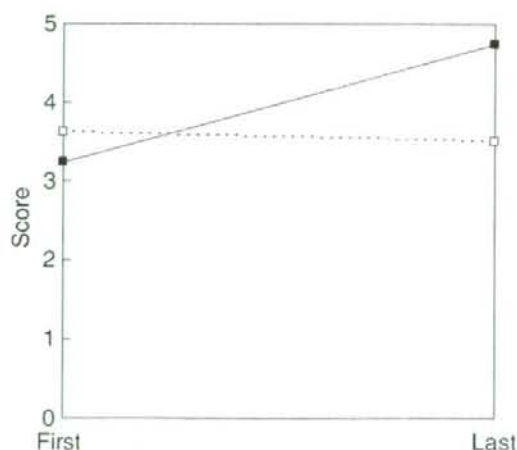
Figure 4 Changes in non-verbal communication, as assessed by the Todai-shiki Observational Rating Scale, in patients in the reminiscence (■) and conversation ( ) groups at the first and fifth evaluations of therapy.
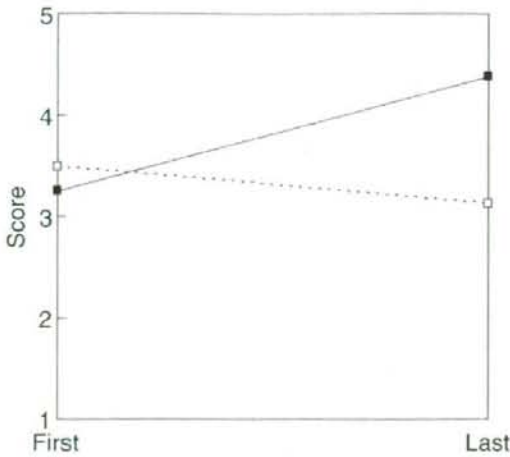
Figure 5 Changes in the impression of 'happiness' in patients in the reminiscence (■) and conversation (□) groups at the first and fifth sessions of therapy.
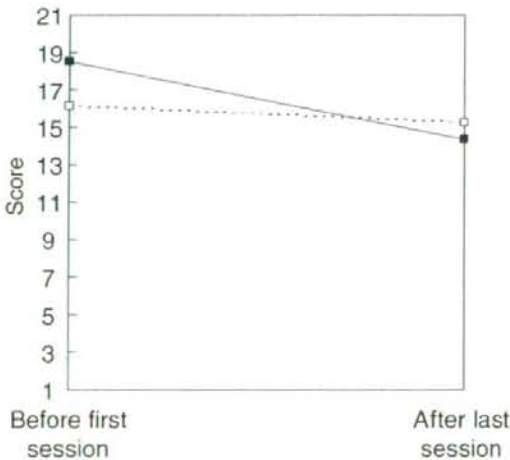

Figure 6 Scores (total 10 items) for the Daycare Evaluation Table in the reminiscence (■) and conversation (□) groups before the first and after the last session of therapy.

is likely that the number of words recalled, as well as the happiness of this group, was promoted through reminiscence therapy. The present study did not find a significant difference in the verbal communication scores during the sessions based on TORS. However, there was an increase in non-verbal communication,

including sensitivity, turning one's ear, and smooth exchanges with others. Therefore, improvements resulting from therapy were not limited to fluency in recalling memories. It is possible that the introduction of appropriate topics to release memories that the elderly with dementia could relate to easily facilitated the sharing of experiences.

The reminiscence group also showed positive changes in daily life, as indicated by the Daycare Evaluation Table for estimating changes in communication with others and other psychological variables. This suggested that reminiscence therapy may have an effect on the daily life of elderly people with dementia, even after the reminiscence session.

Previous studies have used a variety of scales to evaluate the efficacy of reminiscence therapy in the elderly with dementia. It should be noted that a certain degree of communicative ability is necessary for subjects to participate in reminiscence therapy. Moreover, because there are a number of ways to participate in the sessions, such as recalling experiences of the self, representing experiences, listening closely to others' recollections, there could also be individual differences in the manifest efficacy of therapy, depending on the type and degree of participation. In the present study, we measured the number of words produced on a verbal fluency task as an index of the efficacy of reminiscence therapy. We suggest that future research should also consider the effects of changes in interest and exchanges with others when evaluating the efficacy of such therapy.

Methods of implementing treatment

Usually reminiscence therapy is conducted in closed groups over eight to 10 sessions, and participants are reported to actively participate and change positively as they develop smoother interpersonal relationships with others.[3-6] The present study took into consideration the circumstances of those in a hospital, group home, or visiting a daycare center, and conducted the treatment over a short five-session regimen. Moreover, the group members were fixed (closed group) in order to compare the reminiscence group with the conversation group. In the reminiscence group, significant positive changes, such as an increase in the number of words recalled and an improvement in daily living condition, were revealed. Improvements in the participants observed in the present study suggest

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Table 3 Correlations among the scales in the reminiscence group

	Verbal fluency (total)	TORS	Impression of 'happiness'	The Daycare Evaluation Table
Verbal fluency (total)	–	0.28	0.68	−0.49
TORS		–	0.31	−0.34
Impression of 'happiness'			–	−0.94**
The Daycare Evaluation Table (total)				–

Pearson correlation coefficient, **$P < 0.01$

TORS, non-verbal communication (Todai-shiki Observational Rating Scale).

that reminiscence therapy could be introduced to the elderly with dementia, even over a short time span.

Moreover, investigation of the correlations among the scales in which significant changes were observed after the reminiscence therapy had been performed revealed a significant negative correlation between the feeling of 'happiness' at each session and the Daycare Evaluation Table. These results show that happiness while participating in reminiscence therapy is related to a change in everyday life. In addition, the results reveal that it is possible that elderly patients with dementia are not emotionally impaired. However, no significant correlations were revealed on either of the scales for the number of words recalled on the verbal fluency task. Therefore, it is possible that reminiscence therapy is helpful in activating the frontal and temporal lobes, even in patients who did not enjoy the therapy. The difficulties in evaluating the effectiveness of reminiscence therapy are possibly related to the distinctive characteristics of the therapy. Although it is very important that the elderly participants in reminiscence therapy enjoy reminiscing, the findings of the present study indicate the importance of investigating multiple meanings of reminiscence therapy beyond simply happiness. Even though there was a tendency for a correlation between the number of words and enjoyment, this was not significant. However, because the number of participants in the present investigation was limited, we hope to increase the number of subjects in further studies to examine any possible connection.

From the perspective of continuing the therapy, it may be easier to offer this to participants using group-work techniques (planning, formation, development, closure) to devlop the group over time[2] for long-term treatment. Moreover, the present study found a significant increase in the number of words from the third session onwards. It is thought that patients suffering from dementia are able to adapt easily, even with a short period of practice, such as in the present study,

which took place over a course of five sessions only. However, the results also indicate that positive changes are limited and that the patients did not have sufficient pleasant feelings at an adequate level. This may possibly have been caused by the shortness of the treatment period, which prevented the group from maturing. In addition, because the participants' degree of dementia was not mild, it is possible that the degree of reminiscence achieved was not sufficient.

Based on the results of the present study, it is concluded that reminiscence therapy is an effective method of providing care to a wide range of elderly people, including those with dementia. It could be introduced as a part of the daily exchange at care facilities. For example, it may be implemented quickly in group homes with the goal of improving care in accordance with the wishes of elderly with dementia.[22] The present study revealed the usefulness of introducing such therapy over a short period of time.

It is suggested that introducing reminiscence therapy could serve a number of purposes, such as a recreational activity providing an enjoyable time for everyone over a longer period of time. As the number of therapy sessions changes, the purpose of the group, the condition of the patients, and the intervention point to keep in mind may also change. In addition, based on the results obtained over short and long periods of therapy, a variety of concrete plans for developing this method could be developed.

Further research is necessary to examine the effectiveness of reminiscence therapy based on differences in the number of sessions and the progression of the disease. Studies should also be designed to investigate the relationship between reminiscence therapy and other non-pharmacological therapies.

REFERENCES

1 Kiernat JM. The use of life review activity with confused nursing home residents. *Am J Occup Ther* 1979; **33**: 306–310.

2 Nomura T. Application of reminiscence to group work with institutionalized elderly. *Soc Gerontol* 1992; **35**: 32–46 (in Japanese with an English abstract).

3 Nomura T. Reminiscence. *Jpn J Geriatric Psychiatry* 1995; **6**: 1476–1484 (in Japanese).

4 Nomura T. *Reminiscence and Life Review.* Tokyo: Chuohouki Syuppan, 1998 (in Japanese).

5 Kurokawa Y. Reminiscence group approach for the cognitively impaired elderly. *Jpn J Geriatr Psychiatry* 1994; **5**: 73–81 (in Japanese).

6 Kurokawa Y. Reminiscence group with Japanese dementia patients. *J Jpn Clin Psychiatry* 1995; **13**: 169–179 (in Japanese with an English abstract).

7 Okumura Y, Fujimoto N, Narita M. Rehabilitation program for mild dementia patients of Alzheimer type. *Jpn J Geriatric Psychiatry* 1997; **8**: 951–963 (in Japanese).

8 Mihara S, Okumura Y, Sugimura Y *et al.* Reminiscence at dementia wards. *Resume Second Conf Jpn Soc Dement Care* 2000; 25 (in Japanese; Abstract).

9 Imai Y. The concept of non-pharmacological therapy for dementia. *Jpn J Gerontol* 2004; **26**: 5–14 (in Japanese).

10 Merriam SB. The concept and function of reminiscence: A review of the research. *Gerontologist* 1980; **20**: 604–609.

11 Molinari V, Reichlin RE. Life review reminiscence in the elderly; a review of the literature. *Int J Aging Hum Dev* 1984–1985; **20**: 81–92.

12 Kurokawa Y, Saito M, Matsuda O. The evaluation of the efficacy of psychotherapy for the elderly: A literature review of reminiscence and life review. *Jpn J Geriatr Psychiatry* 1995; **6**: 315–329 (in Japanese).

13 Nomura T. Application of evaluative framework on reminiscence practice. *Jpn J Gerontol* 2004; **26**: 24–31 (in Japanese).

14 Merriam SB. The structure of simple reminiscence. *Gerontologist* 1989; **29**: 761–767.

15 Hashimoto R, Suzuki A, Konno K *et al.* Effect of group work (reminiscence) for institutionalized patients with Alzheimer's disease. *Jpn J Geriatr Psychiatry* 2005; **16**: 337–346 (in Japanese with an English abstract).

16 Ota Y. What kind of assessment tool is appropriate for reminiscence? In: Reminiscence Life Review Research Group (ed.). *Handbook for Reminiscence.* Tokyo: Chuohouki Shuppan, 2001; 108–109 (in Japanese).

17 Okumura Y, Tanimukai S, Kuze J. The study of evaluation method and frequency of the reminiscence group for the elderly with dementia. *J Jpn Soc Dement Care* 2005; **4**: 24–31 (in Japanese with an English abstract).

18 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.

19 Kurokawa Y, Matsuda O, Maruyama K, Saito M. *Manual for Reminiscence Groups.* Tokyo: World Planning, 1999 (in Japanese).

20 Matsuda O, Kurokawa Y, Saito M *et al.* Interrater reliability of the Todai-shiki Observational Rating Scale (TORS) for group psychotherapy of elderly patients with dementia. *Psychogeriatrics* 2001; **1**: 133–138.

21 Hasegawa K. *Nursing and Day Care for Elderly People with Dementia.* Tokyo: Igaku Shoin, 1986 (in Japanese).

22 Nomura T, Takahashi Y, Miyazawa K. The fact and effect of reminiscence at group homes. *Resume Second Conf Jpn Soc Dement Care* 2001; 109 (in Japanese; Abstract).

Prevalence of Mild Cognitive Impairment in a Japanese community: Toward more workable MCI criteria

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Running title: Prevalence of MCI

Key words; MCI, dementia, depression, APOE4

Background: More than 20 population-based studies of prevalence of Mild Cognitive Impairment (MCI) have been reported. However, the results have widely varied according to the criteria of MCI. Although a more general approach to the diagnosis of MC was proposed recently, few epidemiological studies based on the approach have been published

Methods: As the first wave of the longitudinal study of a community sample, we assessed the cognitive function of Japanese elderly aged 65 years and older. We attempted to estimate the prevalence of 4 subtypes of MCI based on the recent diagnostic approach. For each of the 4 MCIs, we estimated the prevalence using two cutoffs (1 and 1.5 SD below norms). It has been reported that presence of apolipoprotein E4 allele (APOE4) known as a strong risk factor for Alzheimer disease (AD) is associated with high convert risk from MCI to AD. Thus, we calculated the frequency of APOE4 carriers for each MCI subtype.

Results: 1916 (70%) of 2730 baseline samples were enrolled in this project. After excluding the subjects who had been diagnosed as having dementia, the prevalence of subtypes of MCI ranged from 1.7% to 13.5% depending on the criterion applied. The prevalence of MCI using 1 SD cutoff is higher than that of 1.5 SD, and the prevalence of amnestic MCI single 1.5 SD is lowest among subtypes of MCI. The frequency of APOE4 is higher for amnestic MCIs than that for non-amnestic MCIs and cognitively normal group.

Conclusion: Prevalence of MCI is highly dependent on the diagnostic criteria applied. Amnestic MCI is more likely to convert to AD, while non-amnestic MCI might take different clinical course. For future intervention to delay the onset of dementia, it might be desirable to

target individuals with amnestic MCI multiple 1 SD.

INTRODUCTION

Mild Cognitive Impairment (MCI) has been used to describe a distinct state of abnormal cognition that does not amount to dementia, but is distinguishable from normal cognitive decline associated with aging (Petersen, 1996). Although Petersen's MCI (amnestic MCI single) is assumed to be a core subtype of MCI and pre-stage of dementia, some counterevidence has been produced. For example, its prevalence in a community-based cohort was very low compared to the established incidence rate of AD. (Jungwirth S, et al. 2005) More than 20 of community-based epidemiological studies of MCI and similar conditions have been reported and their results have varied widely according to different diagnostic criteria (Panza, et al., 2005). Recently, a more general approach to the diagnosis of MCI was proposed, which includes the consideration of multiple types of cognitive impairment in addition to the memory impairment that characterizes amnestic MCI. The approach distinguishes four clinical subtypes: amnestic MCI single, amnestic MCI multiple, nonamnestic MCI single, and nonamnestic MCI multiple (Petersen et al., 2004). To our knowledge, only two epidemiological studies employing the newly proposed general approach to the diagnosis of 4 subtypes of MCI have as yet been published (Busse A, et al. 2003, Jungwirth et al., 2005).

The significance of the entity of MCI depends on its high specificity and sensitivity for the conversion to dementia including Alzheimer disease (AD), in other words, its predictive validity. Regarding this issue, there appears to be a lack of consensus concerning the diagnosis of MCI. Namely, two cutoffs – 1.0 SD and 1.5 SD – for cognitive domains including memory have been used in the previous studies (Busse A, et al. 2003, Jungwirth et al., 2005).

It is said that there are several clinical and etiological heterogeneities among subtypes of MCI, and amnestic MCI has been assumed to share the clinical features of AD including overrepresentation of apolipoprotein E 4 allele (APOE4) known as a strong risk factor (Morris JC. 2006). In fact, some clinic-based researches have shown a relationship between the possession of APOE4 and the risk of conversion to AD (Petersen et al., 1995). Furthermore, a recent community studies showed diagnosis of amnestic MCI is associated with higher probability of later conversion to AD (Busse, et al., 2006, Fisher, et al., 2007,). Therefore, the data of APOE4 frequency for each MCI could provide some information about its clinical characteristics to a certain extent.

As the first wave of a prospective longitudinal study of an elderly community sample, we have set out to estimate the prevalence of subtypes of MCI using two cutoffs (1 and 1.5 SD below age-, sex-, and education-controlled mean) among Japanese population of elderly persons. Combining APOE4 frequency with the demographic data, the clinical utility of the subtypes of MCI will be discussed.

METHODS

The present research was conducted in Tone town, Ibaraki, Japan. This town is located approximately 40 kilometers northeast of central Tokyo, and consists of 22 districts. On May 1st, 2001, 3103 inhabitants aged 65 years and older lived in the town. These 3103 inhabitants are hereafter referred to as the potential candidates. This population composition compares to the composition of Japan's total population in 2001.

Seven psychiatrists and eight psychologists, who were trained for this study by the authors, along with public health nurses, conducted this research. The protocol of this study was approved by the ethics committee of the University of Tsukuba (Miyamoto, et al 2008)

THE FIRST STUDY

The general design of the project is shown in Figure 1. The first study was conducted between December 2001 and April 2002. Before the baseline examination, we sent the letter to each potential candidate and explained the objectives of the project. One week before the group screening, we telephoned each candidate and asked him or her to participate. We also asked the local welfare commissioners (*Minsei-iin*: persons who are vested with promoting social welfare in each local area) to recommend individual residents to participation in the research. We excluded individuals with whom a local welfare commissioner could not meet or contact despite three telephone (uncontactable individuals).

We visited each of the 22 districts once per week and conducted two group screenings in the

morning and afternoon. In addition to the group screenings at the 22 districts, we visited 44

individuals who were institutionalized in a long-term care facility and examined them using the

same methods described below.

ASSESSMENT PROCEDURES

Prior to the series of examinations, one of the authors explained the aims of the present

study. Subsequently, the eligible subjects provided informed written consent to participate in

the study. After providing their informed consent, all participants underwent a screening

interview.

Demographics and Medical and Psychiatric issues

The interview consisted of a structured questionnaire assessing age, sex, education,

previous medical and psychiatric diseases, current medication use, and dementia risk factors

including alcohol and tobacco consumption. The subjects were also asked to provide blood

samples for routine tests and genotyping of apolipoprotein E (APOE). (Corder, et al., 1993) We

also measured height and weight of each participant.

Mood Status

This interview was followed by the 15-item short version of the Geriatric Depression Scale

(Brink, et al., 1982) for mood assessment. Those who scored 6 or more were considered to be

depressive symptoms cases.

Perceived Memory Difficulty

Participants were asked whether they had memory difficulties in general, as well as difficulties in specific areas according to the 19 items of the Deterioration de Cognitive Observe (DECO) which had been originally developed for an objective assessment of memory difficulty (Ritchie, et al., 1992). Participants were considered to have memory complaints if they indicated that they had problems on 1 or more of the items.

Assessment of Activities of Daily Living

Basic activities of daily living was measured using Nishimura's Activities of Daily Living (NADL) 12), which determines the level of independence in five activities: walking/transferring, going outside, dressing/bathing, feeding, and toileting. Responders were considered to be functionally intact if they reported no difficulty on any of the 5 items of the NADL.

Neuropsychological Battery

After completing the interview, all participants underwent a group assessment which used a set of 5 tests which measures the following cognitive domains: attention; memory; visuospatial function; language; and reasoning. We named this set of tests thereafter the 5-Cog.

We evaluated attention using a Japanese version of the set dependency activity (Sohlberg and

Mateer, 1986). This test assesses alternating attention, which refers to the capacity for mental

flexibility that allows individuals to shift their focus of attention and move between tasks with

different cognitive requirements, thus controlling which information will be selectively

processed. In order to assess the memory ability, we used a Category Cued Recall test

(Grober, et al, 1988). The Clock Drawing test, which requires subjects to draw the hands of a

clock to depict the time at "ten after eleven" (Freedman, et al, 1994), was used to assess

visuospatial function. We examined language ability using a category fluency test (Soloman

and Pendlebury, 1998). The subjects were asked to generate as many examples as possible in 2

minutes from the semantic category 'animal'. The total number of animals named is the score

for the test. To assess abstract reasoning ability, we employed the similarity subset of the

Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1981).

This cognitive assessment was conducted in a group setting (maximum 50 participants) by

an examiner with the use of a projector. All participants were asked to record their answer on

the answer sheet. Each screening was supervised by approximately ten members of our

research team. The mean length of the 5-Cog examination was 35 minutes. For participants

who had difficulty in understanding the tasks or impaired hearing or vision, we conducted the

examination using the individual version of the 5-Cog in a face-to-face setting.

During the interview and examinations, we estimated the visual acuity and hearing and

speech ability of each subject. We also identified those who could not respond to our

instructions and/or some of the scales because of obvious cognitive impairment.

Consensus Diagnosis

After each assessment, a group of psychiatrists and neuropsychologists reviewed the functional, medical, neurologic, psychiatric, and neuropsychological data and reached a consensus regarding the presence or absence of dementia by diagnosis of dementia according to the DSM-IV (American Psychiatric Association, 1994) criteria. Only those who were not diagnosed as having dementia were considered for a diagnosis of MCI.

MCI Diagnostic Criteria

Criteria for MCI were retrospectively applied among nondemented individuals after the consensus conference. Consistent with the standard criteria, for all subtypes of MCI described below, those considered for MCI were required to have: (1) objective impairment in at least 1 cognitive domain based on the average of the scores on the neuropsychological measures within that domain and 1 SD and 1.5 SD cut-off using normative corrections for age, years of education, and sex; (2) essentially preserved activities of daily living (defined above); (3) presence of the memory complaints (defined above); and (4) no diagnosis of dementia at the consensus diagnosis.

First, for our subtype of amnestic MCI single, memory impairment was defined as a score less than 1 or 1.5 SD below the demographically corrected mean on the category cued recall test, and performance on scores from all other cognitive domains (ie, attention, language, visuospatial,

and reasoning) was required to fall within normal limits (score must be more than 1 or 1.5 SD

below the demographically corrected mean). Second, a diagnosis of amnestic MCI multiple

was made if there was objective impairment on the memory domain score and if there was

impairment on 1 or more cognitive domains. Third, a diagnosis of nonamnestic MCI single

had a cognitive impairment in a single nonmemory domain and performance on scores in all

other cognitive domains fell within normal limit. Finally, the diagnosis of non-amnestic MCI

multiple was assigned if there was impairment in 2 or more of the 4 nonmemory domains, and if

the memory domain score was within normal limits. The classification into the 4 MCI

subtypes was mutually exclusive. Thus, we estimated the prevalence of the 8 types (2 cutoffs

(1SD, 1.5SD) $\times$ 4 subtypes) of MCI.

SECOND STUDY (Investigation of delayed-responders)

At the completion of the first study, we had identified a total of 1035 non-participants who

were contacted but had refused to participate, excluding the above-defined uncontactable

individuals. We attempted a door-to-door survey of those non-participants. This portion of

the study was conducted with the aid of the general practitioners and local welfare

commissioners of Tone town in the hope that their invitations would encourage the participation

of new-comers from among non-participants. We asked them to contact and explain our

project to individuals that appeared on the non-participants list. Subsequently, between April

and June 2002, 225 of the non-participants agreed to participate. These 225 non-participants

are termed 'delayed-responders' hereafter. A psychiatrist (T. A.) and the psychologists visited

each delayed-responder's home and conducted the same interview and tests that had been used

on the first study. The individual version of the 5-Cog was used for cognitive assessment.

After each assessment, we discussed the case on the basis of the consensus diagnosis described

above.

STASTICAL ISSUES AND ANALYSIS

For the normative data, we excluded data from participants who did not complete the series

of interview and examinations and had had a diagnosis of dementia. Test-retest reliability of

the 5-Cog was confirmed (mean value of Pearson's correlation coefficient was 0.70, $p < 0.01$ for

all of the five tests) using data from randomly selected 38 1st study participants collected at a

mean interval of 64 (SD: 28) days.

The participants' characteristics and cognitive status were analyzed using a t-test and

chi-square test for continuous and categorical variables, respectively. For analyses in which the

expected frequency was less than 5, Fisher's exact probability test was used. The data were

analyzed using SPSS 15.0J (SPSS Inc, Chicago, IL, USA). The results for continuous

variables are given as mean $\pm$ SD. All analyses were conducted with significance established

at the $p < 0.05$ level.

RESULTS

Basic issues

As Figure-1 shows, 132 of the 3083 potential candidates were excluded. Specifically, 87 had died and 45 had moved before the initial examination. Additionally, 253 residents were 'uncontactable individuals'. Thus, the remaining 2698 residents were considered the candidate at the baseline. Of the 1035 residents refused to participate (non-participants), 225 became 2nd study participants. Consequently, 1888 (1619 1st study and 225 2nd study participants, and 44 nursing home residents) (70%) of 2698 baseline candidates were enrolled.

Prevalence rate of MCI

As the results of the consensus diagnosis, we estimated 6.5 % prevalence for any types of dementia combined among 1888 participants. After excluding those who had been diagnosed as having dementia, 1433 subjects with complete data remained for the final analysis. The basic data for the subjects are shown in Table1, and the prevalence of the 8 subtypes of MCI among the subjects is shown in Table 2.

The main findings shown are as follows: 1) the prevalence of MCIs ranged from 1.7 to 16.5% depending on the diagnostic criteria applied, and the prevalence for the original MCI (amnestic MCI single 1.5SD) is lowest; 2) when cut-off of 1 SD and 1.5 SD were chosen, 19.5 to 39.3% of the study participants were operationally diagnosed as having any subtypes of MCI, respectively; 3) the prevalence of the MCI using 1SD cutoff is 1.5 to 3.5 times as high as that

using 1.5 SD for the 4 MCIs; 4) for amnestic MCI, the prevalence of the multiple is higher than that of the single, and highest prevalence is found in the MCI multiple 1SD (11.7%); 5) for non-amnestic MCI, the prevalence of the multiple is lower than that of the single.

Frequency of APOE4

The APOE genotyping revealed that 19.8% of the 1487 participants were APOE4 carriers (2/4, 3/4, 4/4). The frequency of APOE4 for each subtype of MCI is shown in Table 3. The frequency is higher for any types of MCI combined group than cognitively normal group. The APOE4 frequency of amnestic-MCI is higher than that of nonamnestic-MCI and normal groups. The frequncy is higher for 1.5 SD cutoff MCIs than that of 1 SD for all MCIs but the non-amnestic MCI multiple.

In the amnestic MCI group, the highest frequency of APOE4 (37.0%) is found in the multiple 1.5SD, whereas the lowest (23.3%) is found in the single 1SD. The frequency for the original MCI (amnestic MCI single 1.5SD) is 32.0%.

We compared the frequency among normal, amnestic MCI (single and multiple) and non-amnestic MCI (single and multiple) groups. For the purpose, we used chi-square analyses and Ryan's multiple comparison procedure as a post hoc analysis. As a whole, the highest frequency is found in the amnestic MCI group (single and multiple) (Fig 2)

DISCUSSION

General

The sample size of the present study seems to be comparable to the largest studies among previously reported population-based prevalence studies of pre-dementia syndromes including MCI from western countries (Panza et al., 2005). The reported prevalence of pre-dementia syndromes varies among the studies as a result of differences in diagnostic criteria, sampling and assessment procedure. About half of these studies used the amnestic MCI single as the diagnostic criteria, and most of these studies showed the prevalence rate of less than 6%. Thus our prevalence rate of 3.0 and 1.7% (1SD, 1.5SD) for the amnestic MCI single appears to be lower in comparison with the results of the previous studies. However, we believe the validity of our results on the following grounds. It has been reported that age, educational level, and gender are related to the prevalence of pre-dementia, however some of the previous studies estimating the prevalence did not control for the factors (Panza F et al., 2005). Our controlling for them might have contributed to the lower value.

To our knowledge, two previous studies have identified MCI subtypes using similar methods with ours (Busse et al., 2003, Jungwirth S, et al, 2005). General findings described in the results section bears resemblance to that of the two studies. Taking theses findings together, our estimated prevalence of MCIs including amnestic MCI single appear to be valid.

Regarding APOE4 frequency for Japanese, it is known that a little less than half of Japanese AD patients have at least one APOE4 allele and its value is about three times as much as that for

normal controls (Ueki A et al., 1993, Asada T et al., 1996). Thus distribution of 18.6% APOE4

for the non-MCI participants appears to be similar with that for Japanese healthy elderly, and the

37.0 % for amnestic MCI multiple 1.5SD subjects seems to be a little less than Japanese AD

patients. The individuals with amnestic MCI are assumed to be likely to convert to AD, thus

the latter value appears to be rational. To our knowledge, the only community-based study of

MCI estimating the frequency of APOE4 carriers found the association between APOE4 and the

original amnestic MCI (Lopez et al., 2003). In that study, the APOE4 frequency for amnestic

MCI and healthy participants was 33% (12/40) and 20% (101/552), respectively. The results

are very similar with ours. These findings together appear to support the validity of the results

of the present study.

Differences in amnestic and non-amnestic MCIs

The frequency of APOE4 is higher for amnestic MCI group (single plus multiple) than

non-amnestic group (single plus multiple) and normal elderly. Besides the pattern of cognitive

impairment, amnestic MCI is different in APOE4 frequency from non-amnestic MCI.

Many of clinic based studies which examined the utility of APOE4 in the prediction of AD

convert among patients with amnestic MCI have shown affirmative results (Tierney MC, et al.

1996, Fleisher A, et al. 2005, Devanand DP, et al. 2005). However, we must take notice of the

finding that there is an increased frequency of APOE4 in Lewy body dementia (DLB) but that

the effect is less prominent than in AD (Rapka, et al., 1998).