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The Effect of Cognitive Training in Patients with Mild Cognitive Impairment and Early Alzheimer's Disease: A Preliminary Study

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Background and Purpose The objective of this study was to determine the benefits of cognitive training in patients with amnesic mild cognitive impairment (aMCI) and those with early Alzheimer's disease (AD).

Methods Eleven patients with aMCI and nine with early AD (stage 4 on the Global Deterioration Scale) participated in this study. Six participants with aMCI and six with AD were allocated to the cognitive training group, while five participants with aMCI and three with AD were allocated to a wait-list control group. Multicomponent cognitive training was administered in 18 weekly, individual sessions. Outcome measures were undertaken at baseline, and at 2 weeks and 3 months of follow-up.

Results In the trained MCI group, there were significant improvements in the delayed-recall scores on the Seoul Verbal Learning Test at both the 2-week and 3-month follow-ups compared with baseline (baseline, 1.6 ± 1.5 ; 2 weeks, 4.4 ± 1.5 , $p=0.04$; 3 months, 4.6 ± 2.3 , $p=0.04$). The phonemic fluency scores (1.0 ± 0.8 vs. 5.0 ± 1.8 , $p=0.07$) and Korean Mini-Mental State Examination scores (18.8 ± 0.5 vs. 23.8 ± 2.2 , $p=0.07$) also showed a tendency toward improvement at the 2-week follow-up compared to baseline in the trained AD group.

Conclusions This study provides evidence of the effectiveness of cognitive training in aMCI and early AD. The efficacy of cognitive training programs remains to be verified in studies with larger samples and a randomized design.

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Key Words Alzheimer's disease, cognitive therapy, memory, mild cognitive impairment, training.

Introduction

The transitional state between the cognitive changes of normal aging and mild dementia is referred to as mild cognitive impairment (MCI).¹ It is a heterogeneous clinical condition with several subtypes and multiple etiologies.² The amnesic sub-

type of MCI (aMCI) is defined as a significant impairment in memory with no impairment in the activities of daily living.¹ An interventional study of patients meeting the Petersen criteria for aMCI¹ found that 16% progress to dementia each year, 99% of whom are ultimately diagnosed with Alzheimer's disease (AD).³ aMCI is often a degenerative condition that may represent prodromal AD.⁴ Therefore, it is crucial to develop and evaluate treatment strategies for this population. However, no pharmacological treatments are currently available to improve the symptoms or slow down the disease progression in

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patients with aMCI.^{3,5}

Clinicians have been interested in other potential treatment alternatives for patients with aMCI, such as cognitive interventions. Patients with aMCI differ from patients with dementia in terms of their relatively preserved insight⁶ and metamemory.⁷ Therefore, cognitive intervention may be a more effective treatment for aMCI than for AD. However, previous studies have failed to show consistently that cognitive intervention is efficacious in aMCI.⁸⁻¹⁵ Objective measures of memory have revealed statistically significant improvements after cognitive intervention in only approximately one-half of the published studies.⁸ Furthermore, the subjective measures of memory, quality of life, and mood/anxiety were also statistically improved after cognitive intervention in half of all of the relevant published studies.⁸ Although follow-up evaluation is crucial for assessing the longitudinal course of the efficacy data because aMCI is a degenerative condition in a certain proportion of individuals, a follow-up evaluation was not conducted in many previous studies.^{7,12,16,17} Therefore, the efficacy of cognitive intervention programs in aMCI remains to be verified.¹⁸

The effect of cognitive intervention in AD patients is more uncertain.^{19,20} One study showed a beneficial effect of a computerized cognitive training program in mild dementia as well as in MCI.¹² Since AD is a progressive neurodegenerative disorder, cognitive training may be more effective at the earliest stage of AD, during the time directly after conversion from MCI.

Cognitive training programs should be adjusted according to the cultural and social background of the patient. To our knowledge there have been no reports of the effects of cognitive training in patients with aMCI or early AD²¹ in Korea. The objective of this study was to determine the benefits of a multicomponent cognitive training program in patients with aMCI and in those with early AD.

Methods

Study participants

Twenty patients, comprising 11 with aMCI and 9 with early AD, participated in this study. They were recruited consecutively from outpatients visiting a memory clinic in the Department of Neurology at Inha University Hospital between May 2008 and May 2009. The subjects with AD 1) met the criteria for dementia according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,²² and the criteria for probable AD established by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association,²³ 2) had received a stable dose of an acetylcholinesterase inhibitor for

at least 8 weeks before the start of the study, and 3) were at stage 4 on the Korean version of the Global Deterioration Scale (GDS).²⁴ aMCI was diagnosed using the criteria defined by Petersen and colleagues:¹ 1) memory complaint corroborated by an informant, 2) delayed-recall score on the Seoul Verbal Learning Test (SVLT) at or below 1.5 standard deviations from the mean of the age and education-normative values among the Korean population,²⁵ 3) at stage 3 on the GDS, 4) at or above 1.5 standard deviations from the mean of normative data of the respective age- and education-matched population on the Korean Mini-Mental State Examination (K-MMSE),²⁶ 5) normal functional activities, and 6) not diagnosed with dementia.

Subjects were 50-80 years of age, were ambulatory, and had brain magnetic resonance imaging scans showing no clinical evidence of other diseases capable of producing cognitive impairment (i.e., normal-pressure hydrocephalus, brain tumor, and cerebrovascular disease). Subjects were also required to have a reliable caregiver who met with the patient at least once a week and could provide the investigator with accurate information about the patient. The doses of psychotropic medication or any drugs able to affect cognition were kept constant throughout the study period among all participants.

Exclusion criteria included any primary neurodegenerative or psychiatric disorder other than AD (i.e., Parkinson's disease, schizophrenia, or major depressive disorder), clinically significant laboratory abnormalities such as an abnormal thyroid function test, abnormally low level of vitamin B₁₂ or folate, positive venereal disease research laboratory test, any history of drug or alcohol addiction during the past 10 years, any severe or unstable medical disease that could prevent the patient from completing all of the study requirements (i.e., unstable or severe asthma or cardiovascular disease, active gastric ulcer, or severe hepatic or renal disease), any hearing or visual impairment that could significantly impair the evaluation of the patient, illiteracy, and an involvement in other clinical trials or exposure to treatment by any experimental drug within the previous 4 weeks.

Six participants with aMCI and six with AD were allocated to the cognitive training group, while five with aMCI and three with AD were allocated to a wait-list control group. The study protocol and informed consent form were reviewed and approved by the institutional review board of Inha University Hospital. All subjects gave their written informed consent to participate in the study.

Cognitive training

The cognitive training was administered via 18 weekly sessions, at hospital-based outpatient memory clinics. Each session lasted approximately 50 minutes. The cognitive training

program, which was offered in the form of individual sessions, was a multicomponent cognitive training program, targeted largely at memory training. There was one instructor, who was an experienced clinical neuropsychologist. The cognitive training program was conducted in a standardized manner, but the difficulty level was individualized.

In brief, sessions included a welcome and checking-homework period (5 minutes), reality orientation techniques (10 minutes), attentional training (10 minutes), and cognitive exercises (25 minutes). The cognitive exercises were designed to stimulate one specific cognitive function during each session (eight sessions focused on memory, five sessions focused on visuoconstructional abilities, and five sessions focused on executive functions and abstract thinking). The contents of the components of the intervention are described in Table 1. The goal of the sessions was to improve the participants' daily function. Homework was assigned at every session in order to encourage the patients to practice and apply any strategies learned from the program in their daily life.

The methods selected for the intervention were reflective of current evidence-based scientific research in cognitive training.^{7,10,16,27} Strategies for improving organizational and attention skills in learning and remembering were practiced during memory training. The following easily implemented memory strategies that could be used for specific daily tasks (e.g., face-name recall or remembering a story or shopping list) were also

practiced: verbal categorization,²⁷ hierarchical organization,¹⁰ visual imagery,¹⁶ errorless learning,⁷ finding key words of a story or news item, giving a title to a story or news item, and face-name association.¹⁶

Outcome measures

Outcome measures were recorded at baseline, and after 2 weeks and 3 months of cognitive training in the trained group, and twice at an interval of 20 weeks in the wait-list control group. Cognition was assessed using the K-MMSE and the Seoul Neuropsychological Screening Battery-dementia version (SN-SB-D),²⁵ an extensive neuropsychological test battery including the SVLT of a 12-word list consisting of 4 household items, 4 flowers, and 4 stationery words, the short form of the Korean version of the Boston Naming Test (K-BNT), consisting of 15 black-and-white line drawings, Rey Osterrieth Complex Figure test, digit span forward and backward tests, semantic and phonemic verbal fluency, and the Stroop Color-Word Test. The Korean version of the Quality of Life-AD questionnaire was administered to assess the quality of life of the participants.²⁸

The Self-Assessment of Cognition questionnaire (SAC) and Satisfaction Questionnaire were administered only to the participants in the trained group. The SAC consists of the following six self-assessment items: 1) I know the date; 2) I recall the name of someone, message for someone, or what I am about to do; 3) I concentrate on some stimuli; 4) I understand what

Table 1. Components and content of the cognitive training

Component	Content
Welcome and checking homework	Inquire about what happened during the previous week regarding any difficulties with the homework assignment, any help from family members or others for homework, feelings and perceived changes brought about by participation in the program, and the responses of individuals close to the patient. The instructor also checked the participants' homework assignments.
Reality orientation	Inquire about the current date, place, weather, what happened today, departure time from home and arrival time at the hospital, and directions to the hospital; asking him/her what he/she expects during this training time.
Attention training	Computer-assisted attention training, paced auditory serial addition, paced auditory serial calculation with a calculator, clapping when a specific number or word was spoken out by the instructor, coloring a picture according to the auditory direction.
Memory training	Use of mnemonics and strategies, story-recall training, training the recall of shopping lists, face-name associations, reproduction of the locations of furniture miniatures, reproduction of a previously directed coloring of a picture, and remembering the location of objects in the room.
Visuoconstruction training	Drawing up a floor plan for his/her house, changing the floor plan for his/her house as he/she wants, drawing polygons, making a doll, and copying drawings of various ball types (i.e., football and basketball).
Executive function training	Planning a week's worth of meals, vocalizing a food recipe, semantic word fluency, mapping out a trip, and making a daily timetable.
Abstract thinking	Sorting pictures of animals and plants according to various categories.
Homework	Memorizing a poem, writing a letter, making a model robot, making a calendar and writing a note about the daily activities on it, writing many words that he/she thinks about a specific word (i.e., Korea or May), drawing up a floor plan for his/her house accurately, and any activity that was not accomplished during the training time.

someone is speaking about, book content, or television program; 5) I plan what I have to do and conduct myself to fit the occasion; and 6) I can find my way. The responses for each item were given on the following 5-point scale: 1, 'very impaired'; 2, 'impaired'; 3, 'fair'; 4, 'good'; and 5, 'very good'. The Satisfaction Questionnaire consists of eight items: 1) this program was helpful for reducing anxiety, 2) this program was helpful for adapting to my social life, 3) this program was helpful for gaining confidence, 4) this program was helpful for human relationships, 5) this program was interesting, 6) I will participate in a program like this again, 7) I will recommend this program to others, and 8) my family or friends said that my memory, function or mood was improved after I finished this program. Again, the responses for each item were given on a 5-point scale: 1, 'never'; 2, 'a little'; 3, 'fair'; 4, 'much'; and 5, 'very much'. The SAC and Satisfaction Questionnaire were scored by averaging each participant's ratings (range 1-5), with higher scores indicating greater satisfaction with the training program.

Statistical analysis

The patient's demographic and clinical characteristics were compared using the Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables. The post-training and baseline scores of the outcome measures were compared using the Wilcoxon signed-rank test in each group. The continuous variables measured in this study are expressed as mean $\pm$ SD values. Statistical analyses were performed using SPSS version 18.0 software. Significance was considered to be present when $p < 0.05$.

Results

Group characteristics

Of the original 20 participants, 17 (85%) completed the final follow-up; 1 participant with aMCI and 2 with AD in the trained group were excluded from the study. The aMCI participant withdrew from participation because the distance from

home to hospital was too far, while one of the AD patients dropped out due to an injury sustained in an accident and the other withdrew her consent. The age, gender, educational level, and the K-MMSE score did not differ significantly between the participants who withdrew from the study and their counterparts with aMCI and AD who completed the study. The demographic characteristics and baseline K-MMSE and Korean version of the Geriatric Depression Scale (GDS-K)²⁹ scores are given in Table 2. The age, gender, education level, K-MMSE score, GDS-K score, and baseline scores of each item of the SNSB-D did not differ significantly between the trained group and the control group for either the participants with aMCI or those with AD. The duration of receiving a stable dose of an acetylcholinesterase inhibitor did not differ significantly between the trained AD group and the control group (8.3 ± 0.5 weeks vs. 8.7 ± 1.2 weeks; $p = 0.86$). The AD participants took various acetylcholinesterase inhibitors; however, the mean dosages were about two-thirds of the maximal treatable dosage in both groups and did not differ significantly between them ($62.5 \pm 25.0\%$ vs. $72.3 \pm 25.4\%$; $p = 0.63$).

Outcome variables

In the trained MCI group, there were significant differences between the delayed-recall scores on the SVLT at baseline and those at both the 2-week and 3-month follow-ups (1.6 ± 1.5 vs. 4.4 ± 1.5 , $p = 0.04$; 1.6 ± 1.5 vs. 4.6 ± 2.3 , $p = 0.04$) (Table 3, Fig. 1). The immediate recall scores on the Rey Osterrieth Complex Figure (11.9 ± 9.2 vs. 15.8 ± 9.4 ; $p = 0.04$) and the SAC (3.5 ± 0.7 vs. 4.5 ± 0.5 ; $p = 0.04$) were significantly improved at the 2-week follow-up in the trained MCI group. There was a tendency toward improvement of the digit span forward scores (6.2 ± 1.1 vs. 7.8 ± 1.3 ; $p = 0.07$) at the 2-week follow-up and the short-form K-BNT scores (10.6 ± 1.9 vs. 12.0 ± 2.0 ; $p = 0.07$) at the 3-month follow-up compared to the baseline scores in the trained MCI group (Table 3). The KQOL-AD score was improved after cognitive training, but the difference did not reach statistical significance (23.3 ± 7.5 vs. 27.9 ± 7.7 ; $p = 0.23$).

The short-form K-BNT score had declined significantly at

Table 2. Demographic data of the participant groups (observed cases)

	aMCI			Early AD		
	Trained group (n=5)	Control (n=5)	<i>p</i>	Trained group (n=4)	Control (n=3)	<i>p</i>
Age (years)	63.4 $\pm$ 9.4	67.2 $\pm$ 8.8	0.69	70.5 $\pm$ 3.5	75.3 $\pm$ 4.7	0.23
Females (%)	80	60	0.50	75	100	0.57
Education (years)	6.8 $\pm$ 4.1	6.5 $\pm$ 3.6	0.99	3.0 $\pm$ 3.5	3.7 $\pm$ 2.1	0.86
K-MMSE score	26.2 $\pm$ 3.6	25.0 $\pm$ 3.1	0.55	18.8 $\pm$ 1.5	19.3 $\pm$ 4.7	0.63
GDS-K score	8.4 $\pm$ 2.9	6.0 $\pm$ 5.6	0.31	4.8 $\pm$ 1.0	9.0 $\pm$ 7.2	0.28

Data are mean $\pm$ SD values.

AD: Alzheimer's disease, aMCI: amnesic mild cognitive impairment, GDS-K: Korean version of the Geriatric Depression Scale, K-MMSE: Korean Mini-Mental State Examination, SD: standard deviation.

the follow-up examination compared to the baseline score in the MCI wait-list control group (11.2 ± 1.9 vs. 10.0 ± 2.2 ; $p=0.046$). There were no significant differences between the

baseline and follow-up scores in other outcome measures in the MCI wait-list control group.

The phonemic fluency (1.0 ± 0.8 vs. 5.0 ± 1.8 ; $p=0.07$) and

Table 3. Changes in outcome variables in the participants with aMCI

	Trained aMCI group			aMCI wait-list control	
	Baseline	2-week follow-up	3-month follow-up	Baseline	After 20 weeks
SVLT, immediate recall	15.4 ± 4.3	14.4 ± 1.9	16.6 ± 5.1	15.0 ± 3.1	12.8 ± 5.9
SVLT, delayed recall	1.6 ± 1.5	$4.4 \pm 1.5^*$	$4.6 \pm 2.3^*$	2.2 ± 1.5	2.4 ± 2.6
SVLT, recognition	5.6 ± 2.2	7.0 ± 1.9	6.4 ± 2.3	7.4 ± 1.9	7.4 ± 0.9
ROCF copy	34.6 ± 1.3	36.0 ± 0.0	34.2 ± 1.6	28.9 ± 8.5	26.2 ± 8.8
ROCF, immediate recall	11.9 ± 9.2	$15.8 \pm 9.4^*$	10.0 ± 3.4	7.0 ± 4.7	9.3 ± 5.4
ROCF, delayed recall	11.6 ± 9.4	16.3 ± 8.9	15.4 ± 8.1	7.2 ± 4.6	9.6 ± 5.6
ROCF, recognition	6.6 ± 2.9	7.0 ± 2.8	7.4 ± 2.5	6.0 ± 1.4	5.0 ± 0.7
Digit span forward	6.2 ± 1.1	$7.8 \pm 1.3^{\dagger}$	7.2 ± 1.1	5.8 ± 1.1	6.4 ± 1.5
Digit span backward	3.8 ± 0.8	4.0 ± 1.6	3.6 ± 0.9	2.2 ± 1.3	2.6 ± 0.5
Stroop, color reading	73.4 ± 35.2	80.6 ± 26.8	86.2 ± 23.3	70.6 ± 23.4	59.8 ± 39.9
Animal fluency	10.6 ± 2.2	13.4 ± 5.7	13.2 ± 4.4	11.2 ± 4.3	11.6 ± 4.8
Phonemic fluency	7.4 ± 3.6	5.6 ± 4.8	5.6 ± 2.9	6.0 ± 3.4	6.0 ± 5.0
Calculation	9.0 ± 3.7	10.2 ± 2.5	10.0 ± 2.6	8.8 ± 5.1	8.8 ± 5.0
Short-form K-BNT score	10.6 ± 1.9	11.4 ± 2.4	$12.0 \pm 2.0^{\dagger}$	11.2 ± 1.9	$10.0 \pm 2.2^*$
K-MMSE score	26.2 ± 3.6	28.2 ± 2.5	27.0 ± 2.6	25.0 ± 3.1	23.6 ± 4.6
KQOL-AD score	23.3 ± 7.5	27.9 ± 7.7	19.7 ± 4.4	34.2 ± 1.6	34.0 ± 3.1
SAC score	3.5 ± 0.7	$4.5 \pm 0.5^*$	4.1 ± 0.7		
Satisfaction questionnaire score		4.0 ± 0.5	3.8 ± 0.4		

* $p < 0.05$, $^{\dagger}p = 0.07$ vs. baseline by Wilcoxon signed-rank test.

aMCI: amnesic mild cognitive impairment, K-BNT: Korean version of the Boston Naming Test, K-MMSE: Korean Mini-Mental State Examination, KQOL-AD: Korean version of Quality of Life-Alzheimer's Disease questionnaire, ROCF: Rey Osterrieth Complex Figure, SAC: Self-Assessment of Cognition, SVLT: Seoul Verbal Learning Test.

Fig. 1. Changes in the delayed recall scores on the Seoul Verbal Learning Test (SVLT) (A) and Korean Mini-Mental State Examination (K-MMSE) (B). A: In the trained mild cognitive impairment (MCI) group (●), the delayed recall scores on the SVLT showed a significant improvement at both the 2-week and 3-month follow-ups compared to the baseline score (1.6 ± 1.5 vs. 4.4 ± 1.5 , $p=0.04$; 1.6 ± 1.5 vs. 4.6 ± 2.3 , $p=0.04$). B: The K-MMSE score showed a tendency to improve at the 2-week follow-up compared to baseline in the trained Alzheimer's disease (AD) group (○; 18.8 ± 0.5 vs. 23.8 ± 2.2 , $p=0.07$).

Table 4. Changes in outcome variables in the participants with early AD

	Trained early AD group			Early AD wait-list control	
	Baseline	2-week follow-up	3-month follow-up	Baseline	After 20 weeks
SVLT, immediate recall	14.0±3.7	13.3±4.0	15.3±2.4	10.3±2.5	10.3±5.9
SVLT, delayed recall	0.0±0.0	2.0±2.8	1.0±1.4	0.0±0.0	0.0±0.0
SVLT, recognition	3.5±3.1	4.3±4.3	5.3±2.2	2.7±4.0	4.3±2.3
ROCF copy	21.5±12.1	24.8±12.0	27.5±7.9	2.5±2.2	13.5±2.6
ROCF, immediate recall	4.0±3.0	7.0±4.1	4.9±4.9	1.3±2.3	1.0±1.3
ROCF, delayed recall	4.3±4.2	4.3±6.1	3.6±4.3	1.2±2.0	0.2±0.3
ROCF, recognition	3.3±1.0	5.3±2.5	5.0±2.6	2.3±4.0	2.7±1.5
Digit span forward	5.8±1.3	6.5±0.6	6.0±1.4	7.3±1.2	7.0±2.0
Digit span backward	1.5±1.0	2.0±1.4	3.0±0.8	3.0±0.0	1.0±1.7
Stroop, color reading	13.0±13.1	41.8±36.4	29.0±9.4*	31.7±18.0	30.3±23.5
Animal fluency	7.3±3.4	10.8±4.6	12.0±7.3	9.0±2.6	7.7±1.5
Phonemic fluency	1.0±0.8	5.0±1.8*	2.0±0.0	3.0±1.0	1.3±1.5
Calculation	4.5±0.6	5.5±0.6	6.5±0.6*	3.7±1.5	4.0±1.0
Short-form K-BNT score	9.3±2.2	8.8±3.3	9.3±2.2	7.7±1.2	8.0±1.0
K-MMSE score	18.8±0.5	23.8±2.2*	21.8±4.1	19.3±4.7	17.7±3.8
KQOL-AD score	16.9±4.4	17.0±4.2	16.4±4.1	22.7±4.2	25.0±6.1
SAC score	3.1±1.0	3.4±1.0	4.2±0.4		
Satisfaction questionnaire score		3.6±0.4	3.5±0.4		

* $p=0.07$ vs. baseline by Wilcoxon signed-rank test.

AD: Alzheimer's disease, K-BNT: Korean version of the Boston Naming Test, K-MMSE: Korean Mini-Mental State Examination, KQOL-AD: Korean version of Quality of Life-Alzheimer's Disease questionnaire, ROCF: Rey Osterrieth Complex Figure, SAC: Self-Assessment of Cognition, SVLT: Seoul Verbal Learning Test.

K-MMSE scores (18.8 ± 0.5 vs. 23.8 ± 2.2 ; $p=0.07$) exhibited a tendency toward improvement at the 2-week follow-up compared to the baseline scores in the trained AD group (Table 4, Fig. 1). The correct color reading of the Stroop test (13.0 ± 13.1 vs. 29.0 ± 9.4 ; $p=0.07$) and calculation scores (4.5 ± 0.6 vs. 6.5 ± 0.6 ; $p=0.07$) also exhibited a tendency toward improvement at the 3-month follow-up compared to baseline in the trained AD group (Table 4). The delayed-recall SVLT scores had improved at 2 weeks after cognitive training, but the difference did not reach statistical significance (0.0 ± 0.0 vs. 2.0 ± 2.8 ; $p=0.18$) (Table 4). There were no significant differences between the baseline and follow-up scores of any measures in the AD wait-list control group.

Discussion

The findings of this study show that cognitive training is effective in patients with aMCI or early AD. Participants with aMCI in the trained group exhibited a significant improvement in delayed recall of the SVLT after completing the cognitive training program, and improvements in episodic memory were maintained until 3 months after the end of the cognitive training (Table 3, Fig. 1). Cognitive training might therefore delay the conversion from aMCI to dementia. Global cognition was improved after cognitive training in early AD, but it declined slightly after completion of the cognitive training (Table 4, Fig.

1). The early AD patients in the trained group showed a nonsignificant improvement of verbal episodic memory, but this improvement was reduced after the conclusion of cognitive training (Fig. 1).

Patients with early AD benefited less from cognitive training than did patients with aMCI. There are three likely explanations for modest effects of cognitive training in early AD: 1) the same training programs were applied to the aMCI and AD patients, and hence the level of difficulty of some of the components may have been set too high relative to the cognitive abilities of this group; 2) the absence of a significant difference could have been due to the small sample in this study; and 3) in AD (even early AD), episodic memory is severely impaired, which may make it difficult to improve episodic memory significantly by memory training.

While a multicomponent cognitive training program was employed in this study, cognitive training was effective on episodic memory in aMCI relative to other cognitive domains. This finding is in accordance with the results of previous studies on the effects of cognitive training in patients with aMCI.^{8,11,16} There are several possible interpretations for this finding. First, the improvement in episodic memory may be due to the memory training in the present study being performed more frequently than training of the other cognitive domains. A second possible interpretation is that the cognitive function of the other domains did not improve significantly after cognitive train-

ing because the other cognitive functions (aside from memory) were close to normal in the patients with aMCI.³⁰ A third possible interpretation is that the outcome measures might not be sensitive enough to detect improvements in cognitive functions other than memory because of a ceiling effect of the neuropsychological tests for those other cognitive functions in aMCI. The early AD patients showed improvements in global cognitive status and executive function after cognitive training, and this finding is in accordance with the results of a previous study.¹² However, we cannot exclude the possibility that this was a type of transient practice effect. It is therefore crucial to assess the longitudinal course of the efficacy data.

The training was standardized by having the same instructor administer the training using standardized instructions through all of the sessions in this study. The main advantage of individual programs is tailoring of the training to the needs and complaints of the individual patients. The satisfaction regarding the training program was high among the trained participants. The advantage of the standardized individual training may have contributed to a large improvement in episodic memory in the participants with aMCI. However, the individual training is limited by a single instructor being able to train only a few patients.

This is a preliminary study, and it has several limitations. First, the patient sample was small. In particular, the number of subjects was smaller in the AD wait-list control group than in the AD trained group. Furthermore, a few of the AD patients agreed to complete the intensive neuropsychological tests without any training, twice with an interval of 20 weeks. This limits the generalizability of the results. Second, this study was not a randomized blind trial. Third, the emotional state of the participants after the training program was not examined. According to some previous studies,^{11,12,15} depressive symptoms improve after cognitive interventions. However, none of the patients in the present study had significant depressive symptoms (GDS-K score ≥ 18) at baseline. Therefore, the observed improvement in episodic memory may not have been related to a reduction in depressive symptoms. Fourth, the effects of the training on the Instrumental Activities of Daily Living (IADL) score were not examined in this study. Although according to Petersen's criteria daily functioning must be intact in aMCI, there is some evidence that IADL is slightly impaired in aMCI.³¹ Given that MCI is a potentially degenerative condition, IADL scores are likely to deteriorate over time, at least in some patients with MCI. Therefore, the IADL score may be sensitive to early functional changes related to MCI, and this tool should thus be applied as an outcome measure. There was no improvement in the scores on the Functional Activities Questionnaire after intervention in either MCI or in mild to moderate AD,³² but a previous study showed that dai-

ly activities measured using the Bayer Activities of Daily Living scale—which is known to be a sensitive measure in MCI—were improved after cognitive intervention in MCI.¹⁵ Fifth, the 3-month follow-up evaluation was not conducted for the control patients.

Cognitive training had a positive effect on episodic memory in aMCI relative to other cognitive domains. The early AD patients showed improvements in global cognitive status and executive function after cognitive training. However, these findings should be interpreted with caution given the small sample. In conclusion, this study provides evidence of the effectiveness of cognitive training in aMCI and early AD. The efficacy of cognitive training programs remains to be verified in larger samples in randomized studies.

Conflicts of Interest

The authors have no financial conflicts of interest.

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