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Four-Week, Home-Based, Robot Cognitive Intervention for Patients with Mild Cognitive Impairment: a Pilot Randomized Controlled Trial

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ABSTRACT

Background and Purpose: Previous studies suggest that cognitive intervention can mitigate the development of dementia in patients with mild cognitive impairment (MCI). However, the previous cognitive intervention was mostly provided as a group session, in which MCI patients sometimes had difficulty in regularly attending sessions or were reluctant to participate in group-based classes. Additionally, experienced instructors for traditional cognitive intervention may be unavailable in some chronic-care facilities or community centers. Considering these reasons, we have developed 5 programs for home-based cognitive intervention using a personal robot for MCI patients. In this preliminary study, we aimed to demonstrate the effects of our newly developed home-based cognitive intervention with robots on cognitive function in MCI patients.
Methods: We conducted a single-blind randomized controlled trial enrolling 46 MCI patients. Participants were randomized into 2 groups: the robot cognitive intervention (robot) (*n*=24) group and without cognitive intervention (control) (*n*=22) group. The interventions comprised 60-min sessions per day for 4 weeks. The primary outcome was the change in cognitive function measured using the Cambridge Neuropsychological Test Automated Battery.
Results: There were no significant baseline demographic or clinical differences between the robot and control groups. After the 4-week cognitive intervention, the robot group showed greater improvement in working memory than did the control group.
Conclusions: Our home-based cognitive intervention with a personal robot improved the working memory in MCI patients. Further studies with larger samples and longer study periods are required to demonstrate the effects of these programs in other cognitive domains in MCI patients.

Keywords: Cognitive Intervention; Mild Cognitive Impairment; Working Memory; Home-Based; Personal Robot

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Conflict of Interest
Geon Ha Kim & Jee Hyang Jeong hold a co-ownership of patents with Robocare company. All other authors report no conflicts of interest relevant to this article.

Author Contributions
Conceptualization: Lee EH, Park HK, Park KD, Jeong JH, Kim GH; Data curation: Kim BR, Kim H, Kim SH, Chun MY, Park HK, Park KD, Jeong JH, Kim GH; Formal analysis: Lee EH, Kim GH; Funding acquisition: Kim GH; Investigation: Kim BR, Kim H, Kim SH, Chun MY, Park HK, Kim GH; Project administration: Kim GH; Supervision: Park KD, Jeong JH, Kim GH; Visualization: Lee EH, Kim GH; Writing - original draft: Lee EH, Kim GH; Writing - review & editing: Jeong JH, Kim GH.

INTRODUCTION

It has been reported that 50 million people have been diagnosed with dementia worldwide.[1] It has been forecast that the number of patients diagnosed with dementia will increase rapidly, with approximately 152 million patients diagnosed with this disease by 2050, which would triple the current dementia population.[1] Despite efforts to develop pharmacological treatments for dementia, none of the treatments have successfully overcome the cognitive or functional dysfunction in patients with dementia.

Mild cognitive impairment (MCI) is a prodromal stage of dementia. Patients with MCI have a 10 times higher risk of developing dementia than do cognitively normal individuals at the same age.[2] Therefore, recent studies have focused on multiple non-pharmacological strategies to mitigate the progression to dementia in patients with MCI, including cognitive intervention or lifestyle changes (i.e., exercise).[3,4]

Fortunately, accumulating evidence indicates that cognitive intervention could benefit cognitive performance and might delay the progression to dementia in patients with MCI.[4-18]

Additionally, depression and anxiety are among the most common comorbid neuropsychiatric problems in MCI patietns,[19,20] and MCI patients with such mood symptoms had an higher risk of progression to dementia than did those without mood problems.[20,21] Several prior studies have shown that cognitive intervention also improves mood symptoms in MCI patients.[4,10-12,14,22-24]

Traditionally, cognitive interventions have usually been group-based or face-to-face programs that require qualified therapists, sufficient space, and convenient locations for accessibility. However, experienced instructors who do cognitive interventions are not always available in small local hospitals and community centers. Additionally, given that we suspect there might be a lack of qualified personnel in the near future because of a dramatic increase in the aging population, provision of cognitive interventions for patients with MCI may be challenging.

In this regard, service robots have been considered as a way to provide home-based cognitive intervention for patients with MCI since service robots could interact with humans and offer appropriate services as programmed.

For this reason, we have developed home-care robots that can provide cognitive intervention. Therefore, in this study we aimed to demonstrate the effects of our newly developed cognitive intervention with home-care robots on cognitive performance in patients with MCI. Specifically, we hypothesized that our robot cognitive intervention could improve the attention, working memory, and memory performance of MCI patients, since previous studies have reported that multi-domain cognitive intervention in MCI patients has predominantly improved those 3 cognitive domains.[4,25]

METHODS

Study design
This was a 4-week, prospective, single-center, rater-blind, and controlled trial conducted from September 20, 2018 to February 27, 2020 in the Memory Disorder Clinic of Ewha

Womans University Mokdong Hospital. We randomly allocated participants in a 1:1 ratio into 2 groups: those with cognitive intervention with a personal robot (robot) and those without cognitive intervention (control) groups.

Participants

We initially recruited the 47 volunteers aged 60 years or older diagnosed with MCI from the Ewha Womans University Mokdong Hospital. These participants were diagnosed with MCI based on the operationalized Petersen criteria.[26] As assessed by a neurologist, the participants included in the study were ones who:

    had not been diagnosed with dementia,
    were considered literate,
    had no known history of dementia,
    had no visual or hearing impairment severe enough to interfere with cognitive testing/ cognitive intervention,
    had no history of major neurological or psychiatric illnesses,
    had no history of medication that could affect cognitive function, and
    had no major medical problems.

All patients underwent neuropsychological testing using a standardized neuropsychological battery called the Seoul Neuropsychological Screening Battery.[27] This battery assesses attention, language, praxis, elements of Gerstmann syndrome, visuospatial/constructive function, verbal and visual memory, and frontal/executive function.

Of the 47 participants, one participant was excluded because of withdrawal of consent. Therefore, the final sample comprised 46 participants (**Fig. 1**) who were randomly allocated into the following 2 groups: the robot intervention group (robot) (*n*=24) and the control group (control) (*n*=22). All participants provided written informed consent, and the study protocol was approved by the Institutional Review Board (IRB) of Ewha Womans University Mokdong Hospital (IRB EUMC 2018-08-034).

Cognitive intervention

All participants received 1 hour of education about dementia prevention after undergoing the baseline assessment. This education included the definition, diagnosis, and current treatments of dementia and lifestyle modifications for dementia prevention encompassing the importance of cognitive training, healthy foods for the brain, aerobic exercise, and stretching that could be done at home.[28,29]

A robot named Bomy (Robocare, Seongnam, Republic of Korea) that included 5 cognitive training programs was set at each MCI patient's home within a week of the baseline evaluation (**Fig. 2**). Each program was used for training specific cognitive domains, such as memory, language, visuospatial function, calculation, and frontal executive function. We asked the participants in the robot group to play cognitive training programs with the robot for at least 60 minutes a day, 5 days a week, for 4 weeks. Each training session of a day comprised at least 2 different programs, one for memory training. the other for other cognitive domain training, including language, visuospatial function, calculation, and frontal executive function. From Monday to Friday, we scheduled the robot to provide 2 cognitive training programs at the appointed times. Each cognitive program usually took about 30 minutes. Therefore, the robot group received at least 40 training sessions during the 4 weeks: 20 sessions for memory, 5 for language, 5 for calculation, 5 for visuospatial function, and 5
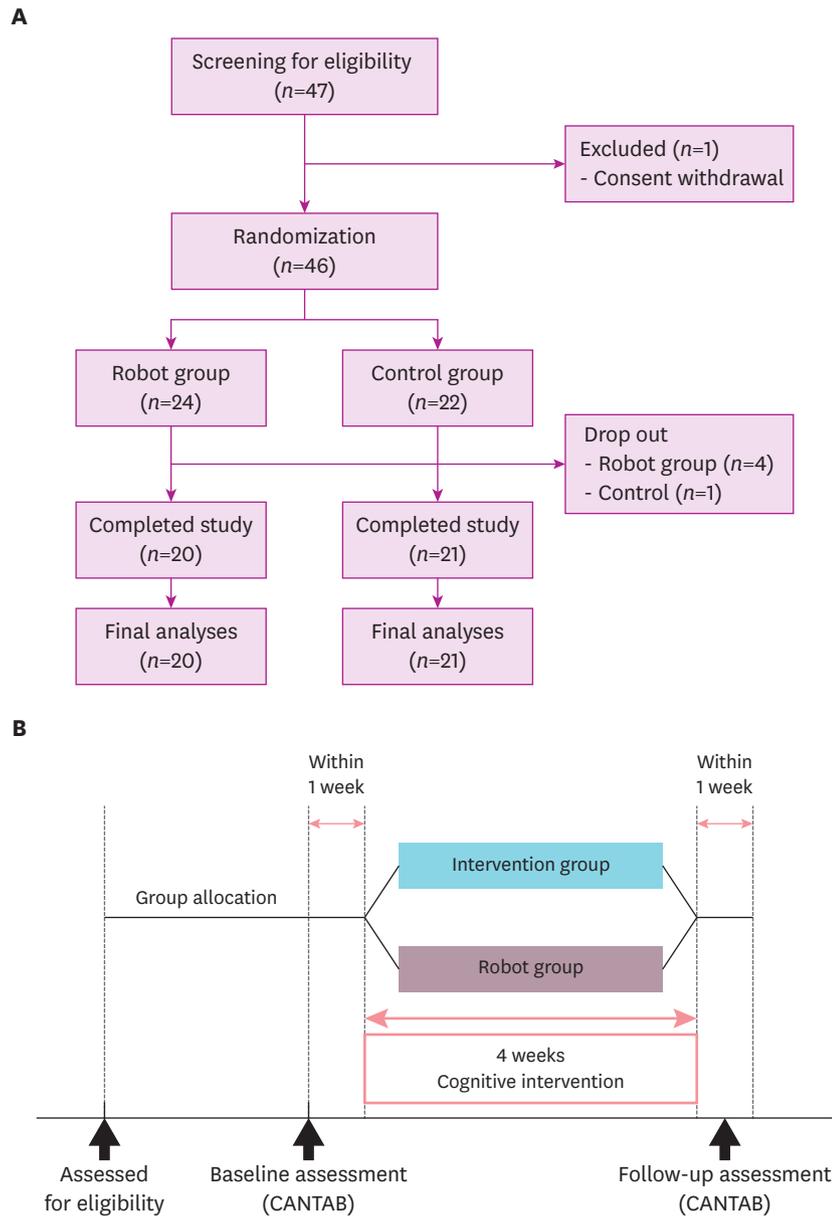
Fig. 1. Study design and flow of the study. (A) Forty-six patients diagnosed with mild cognitive impairment aged 60 years or older volunteered for this single-blind randomized controlled trial. They were randomized into the control and robot intervention groups. Moreover, 4 of the 24 participants in the robot group and 1 of the 22 participants in the control group dropped out; we included the remaining 20 and 21 volunteers for each group in the final analyses. (B) After group allocation, we used the CANTAB scores for baseline assessment. Cognitive intervention was done for 4 weeks, and within a week after termination of the intervention period, we remeasured the CANTAB scores for primary outcomes, and used the Geriatric Depression Scale and Geriatric Anxiety Inventory to assess the secondary outcomes.
CANTAB: Cambridge Neuropsychological Test Automated Battery.

for executive function. If the participants did not perform the scheduled programs, the robot provided a message to encourage participation in the cognitive training. If the participants did not perform the programs even after 3 encouraging messages, then the robot sent an alarm to the designated caregiver in order to directly encourage MCI patients to run the cognitive training programs.
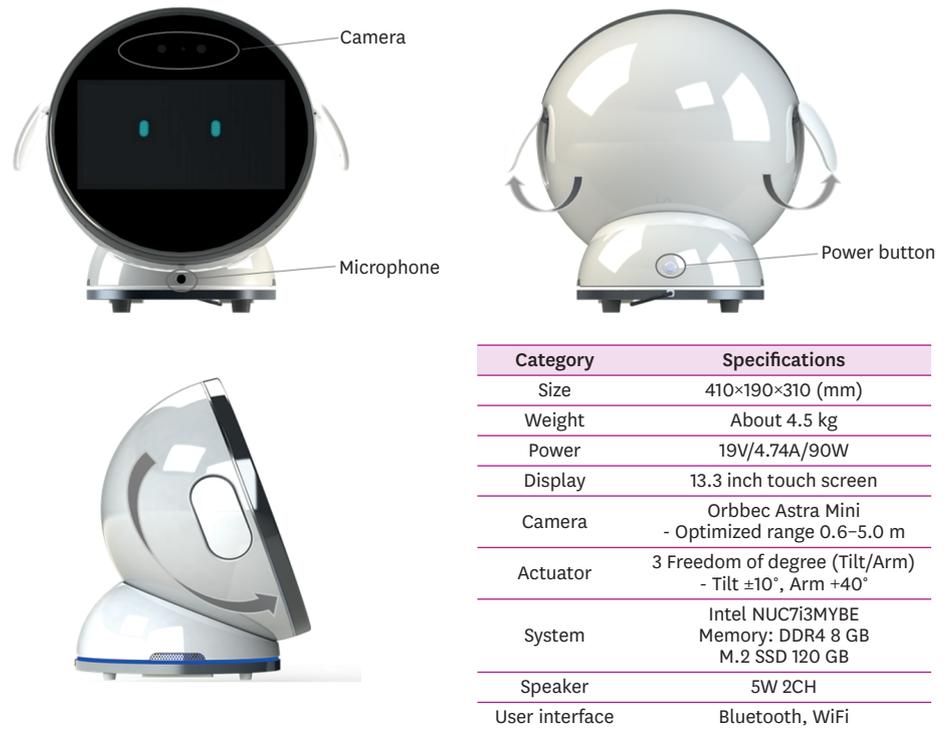
Category	Specifications
Size	410×190×310 (mm)
Weight	About 4.5 kg
Power	19V/4.74A/90W
Display	13.3 inch touch screen
Camera	Orbbec Astra Mini - Optimized range 0.6–5.0 m
Actuator	3 Freedom of degree (Tilt/Arm) - Tilt ±10°, Arm +40°
System	Intel NUC7i3MYBE Memory: DDR4 8 GB M.2 SSD 120 GB
Speaker	5W 2CH
User interface	Bluetooth, WiFi

Fig. 2. The appearance and the specifications of the robot (Bomy).

Outcome measures

Primary outcome variables were changes in mean scores in the 3 tests based on the Cambridge Neuropsychological Test Automated Battery (CANTAB), which included Spatial Working Memory (SWM), Paired Associates Learning (PAL), and Rapid Visual Information Processing (RVP) (detailed descriptions of the tests are available on the website http://www.cambridgecognition.com/academic/cantabsuite/tests). In brief, SWM evaluates the visual working memory function to retain spatial information and to manipulate the remembered items. The between error of the SWM task is defined as the times that the participant revisits a box in which a token has previously been found. The lower the error in the SWM task, the better the performance. The PAL task measures simple visual memory and visuospatial associative learning. We used the total number of errors from the PAL task to measure performance, with lower scores representing better performance. The RVP task assesses the function of sustained attention by measuring the participant's ability to efficiently detect the target sequence. The outcome measure of the RVP includes the probability of sensitivity ranging from 0 to 1, which represents the signal detection rate. We converted the raw scores of each of the 3 tasks mentioned above to standardized Z-scores using the baseline mean scores and standard deviation of the control group. If necessary, we reversed the scores so that positive Z-scores represented better performance.

Secondary outcome variables included changes in the scores for anxiety and depression, which were measured using the Korean version of the Geriatric Anxiety Inventory (GAI)[30] and the Geriatric Depression Scale (GDS): Short Form,[31] respectively.

Statistical analyses

We compared demographic and clinical characteristics using *t*-tests for continuous variables and chi-squared tests for categorical variables. We applied the analysis of covariance test to compare the baseline neuropsychological tests using age, sex, and years of education as covariates. We used a linear mixed model with unstructured covariance to estimate group differences in the changes of CANTAB scores before and after the intervention, where we included the treatment group, visit, and visit-by-group interaction as fixed effects. We considered the within-subject factor to be a random effect. We included age, sex, and years of education as covariates. Significance for all tests was set at α=0.05, 2-tailed. We did all statistical analyses using Stata version 13.0 (Stata Corp., College Station, TX, USA).

RESULTS

For the baseline demographic characteristics, there was no statistical difference between the 2 groups in age, sex, or years of education (**Table 1**). Baseline cognitive function, such as the Korean version of the Mini-Mental State Examination scores and neuropsychological test scores, did not differ between the 2 groups (**Table 1**). Among the 46 participants, one participant in the control group and 4 participants in the robot group withdrew from the study. Therefore, a total of 41 participants (21 in the control group and 20 in the robot group) completed the study. The dropout rate between the 2 groups not significantly different (4.5% for the control group vs. 16.7% for the robot group, *p*=0.349). The robot group completed 38.8 (96.9%) of the total of 40 sessions and spent 60.5 minutes a day on average for the cognitive training programs.

Table 1. Baseline characteristics of participants

Characteristics	Control (*n*=22)	Robot (*n*=24)	*p*-value
Sex (female)	9 (40.9)	9 (37.5)	0.813
Age (yr)	74.5±1.5	73.6±1.4	0.653
Education (yr)	8.7±1.1	8.9±1.0	0.852
K-MMSE	25.6±0.5	25.4±0.5	0.762
Underlying disease			
Diabetes mellitus	8 (0.36)	9 (0.38)	0.936
Hypertension	10 (0.45)	9 (0.38)	0.584
Hyperlipidemia	6 (0.27)	8 (0.33)	0.655
Baseline cognitive function[a]			
Attention			
Digit span (forward)	4.6±0.2	5.1±0.2	0.124
Digit span (backward)	3.2±0.1	3.2±0.1	0.986
Visuospatial function			
RCFT	29.5±1.2	29.5±1.1	0.986
Memory			
RCFT delayed recall	9.2±1.4	8.6±1.4	0.764
SVLT delayed recall	3.4±0.5	2.9±0.5	0.525
Frontal/executive function			
COWAT (animal)	11.6±0.6	12.0±0.6	0.652
COWAT (gout)	6.4±0.6	6.3±0.6	0.913

Data are shown as number (%) or mean ± standard deviation.
K-MMSE: Korean version of Mini-Mental State Examination, SVLT: Seoul Verbal Learning Test; RCFT: Rey-Osterrieth Complex Figure Test; COWAT: Controlled Oral Word Association Test.
[a]*p*<0.05, adjusted by age, sex, and years of education.

Table 2. Changes in cognitive function after 4-week intervention

Z-score	Control		Robot		b (SE)	p for group by visit interaction
	Baseline (n=22)	Week 4 (n=21)	Baseline (n=24)	Week 4 (n=20)		
SWM	0±1	−0.2±1.3	−0.3±1.3	0.4±0.2	1.0±0.5	0.037*
PAL	0±1	0.1±1.1	−0.2±0.2	0±0.2	0.1±0.3	0.744
RVP	0±1	0.2±0.7	0.1±0.6	0.1±0.5	−0.2±0.3	0.366

SWM: spatial working memory, PAL: paired associates learning, RVP: rapid visual information processing.
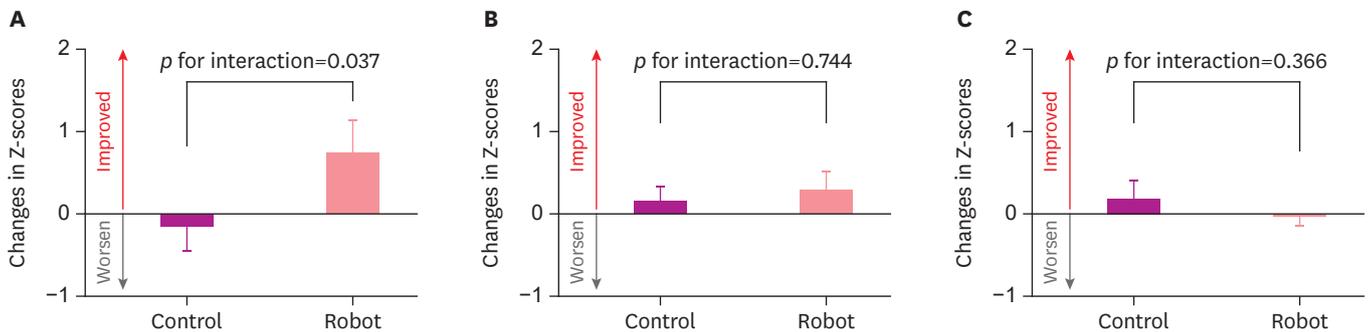*p<0.05.

Fig. 3. The effects of cognitive intervention on cognitive function. (A) Spatial Working Memory scores were significantly better in the robot group than in the control group after the 4-week cognitive intervention (p for group by visit interaction=0.037). There was no difference between the groups by time interaction in (B) Paired Associates Learning (p for group by visit interaction=0.744) and (C) Rapid Visual Information Processing (p for group by visit interaction=0.366) scores.

Primary outcomes

The baseline scores of CANTAB were not different between the robot and control groups (**Table 2**). After the 4-week cognitive intervention, the robot group showed greater improvement in the SWM scores than did the control group (p for group by visit interaction=0.037). However, there was no significant group by time interaction in terms of PAL (p for group by visit interaction=0.744) or RVP scores (p for group by visit interaction=0.366) (**Table 2**, **Fig. 3**).

Secondary outcomes

The baseline scores of GAI and GDS were not different between the robot and control groups. Anxiety scores were significantly improved in the robot group more than in the control group after 4 weeks (p for group by visit interaction=0.035). There were no significant changes in depression scores between the 2 groups after 4 weeks (p for group by visit interaction=0.114) (**Table 3**).

DISCUSSION

First, we found that a 4-week, home-based multi-domain cognitive intervention with a personal robot may help improve working memory in patients with MCI. This finding may be consistent with the previous findings showing that computerized or conventional multi-

Table 3. Depression and anxiety scores after 4-week cognitive intervention

Variables	Control		Robot		b (SE)	P for group by visit interaction
	Baseline (n=22)	Week 4 (n=21)	Baseline (n=24)	Week 4 (n=20)		
GAI	3.2±5.1	5.0±5.8	4.7±5.1	3.9±5.7	−2.6±1.2	0.035*
GDS	2.5±3.1	2.8±3.6	4.2±4.6	3.2±4.3	−1.3±0.8	0.114

GAI: Geriatric Anxiety Inventory, GDS: Geriatric Depression Scale.
*p<0.05.

domain cognitive intervention brought about benefits for working memory in patients with MCI,[4,14,32] although these interventions did not focus on working memory only.

It is noteworthy that cognitive intervention has both direct effects and transfer effects on cognitive improvement.[8,32] Direct effects, also known as training effects, refer to a function of trained cognitive-domain improvement after cognitive intervention, whereas transfer effects are defined as improvement of untrained cognitive functions and trained ones.[33,34]

We can explain the improvement of working memory in this study as rather a transfer effect than a direct effect, given that our cognitive intervention targeted memory, language, visuospatial function, calculation, and frontal executive function, possibly because working memory is a unique domain that has the largest effect size and showed statistically significant results different from those for the other cognitive domains in the previous studies.[4,6,14,25,32,35,36] Considering that previous studies reported that various cognitive domains did not equally improve after cognitive intervention,[6,12,16,23,32] our results confirm that working memory could be one of the most effective cognitive domains after cognitive intervention. In addition, although we did not specifically target working memory training, it could be also plausible that working memory could be trained additionally while participants participated in multi-domain cognitive training. It is noteworthy that working memory is necessary for maintaining task-relevant information[37]; so working memory could also be required to pay attention and complete cognitive training in other cognitive domains. However, further studies with larger samples and longer durations are required to demonstrate the effects of these programs in other cognitive domains in patients with MCI.

Contrary to our expectation, there were no significant effects of cognitive intervention on other cognitive domains except for working memory, perhaps because there was insufficient training time for each cognitive domain. Our cognitive intervention consisted of 60 minutes a day for 4-week training with 5 cognitive domains; thus the training time for each single-domain might not have been sufficient to change performances in each domain, considering that previous study has shown that the training effect was associated with the total time of cognitive training.[38]

For the secondary outcomes, we found that the GAI scores in the robot group decreased after the 4-week intervention. Although the baseline anxiety scores of participants in both groups were not clinically significant, this may suggest that our robot cognitive intervention also had benefits for anxiety. Consistent with our findings, previous studies have also shown that patients with MCI receiving cognitive intervention demonstrated significant improvement in neuropsychiatric symptoms, including anxiety or depression.[11,22-24,39] Among these previous studies, only one case-control study showed that computerized cognitive training significantly improved anxiety in patients with MCI.[23] However, most previous studies have shown that cognitive intervention may affect depressive symptoms in patients with MCI.[22,39] Unexpectedly, cognitive intervention in this study did not show any effects on depressive symptoms in patients with MCI, perhaps because of the finding of a previous study stating that the effects of cognitive intervention on depressive symptoms were prominent for patients with clinically significant symptoms of depression.[40] Since the baseline scores of depressive symptoms in our current study were not clinically significant, it is plausible that no significant improvement in depressive scores was observed in the robot intervention group. However, further studies with longer durations may be necessary to demonstrate the effects of cognitive intervention on the improvement of neuropsychiatric symptoms in

patients with MCI, considering that targeting neuropsychiatric symptoms can help delay the transition from MCI to dementia.[41]

One of the distinctive features of our study is that robots have been used as a cognitive-intervention provider for patients with MCI. As mentioned earlier, cognitive intervention is usually provided by professional instructors. However, experienced instructors for cognitive intervention are not always available because of the dramatic increase in the aging population. Since the aging population is increasing and the number of younger health-care professionals has decreased, additional technological assistance is strongly desired to support maintenance of cognitive intervention for the elderly, specifically for those with cognitive impairment. Clearly, robots need less space and time than do specialized trained personnel providing conventional cognitive training. Additionally, multiple sensors of robots can recognize and monitor a variety of signals from patients with MCI at home, and can interact with the patients. From this point of view, robots could be proper assistants for cognitive intervention for patients with MCI at home. Robots can monitor the improvement of users, intelligently adjust the level of difficulty of training if necessary, and assess mood, interest, and engagement based on a variety of sensors, all of which could be difficult to achieve using only computer programs.[42] Furthermore, a robot can be shaped like a pet or humanoid and be programmed to express emotions with a human voice,[42,43] which might motivate patients with MCI to complete and succeed in cognitive training.

Until now, only a few studies have investigated the effects of cognitive intervention using robots in the elderly.[42,44-46] Most previous studies of cognitive intervention using robots were targeted for improvement of mood, such as depression, agitation and apathy, or quality of life in advanced dementia patients[44-46]; these studies found that most patients with dementia enjoyed the robots, which did improve stress or loneliness. To the best of our knowledge, ours is the first study to examine the effects of home-based cognitive intervention using robots in patients with MCI. Additionally, we found that the robot-based cognitive intervention can help improve working memory in patients with MCI.

This study has several limitations. First, since it was a preliminary study with a small sample and short study period, our findings cannot be generalized to the MCI population. Additionally, the effect size of the between-group changes in scores of SWM was only from small to medium (Cohen's f=0.12).[47] Therefore, further studies with larger samples and longer study periods are required to investigate the efficacy of home-based cognitive intervention in patients with MCI. Second, the 4-week intervention period in this study could have been too short to demonstrate the significant effects on improvement of cognitive function, considering that most previous cognitive intervention studies were conducted at least for 6–12 weeks.[5,10] Elongated study duration is considered beneficial for demonstrating more positive outcomes of robot cognitive interventions in patients with MCI. Third, since this study was a single-blinded design (rater-blinded), participants with MCI had recognized which group (robot group vs. control group) they participated in. Therefore, it may have been using the robot itself rather than the cognitive training that drew positive results in the robot group. Adapting mock programs that do not include targeted cognitive training, if possible, could help overcome this limitation. On a related note, since we did not compare the effects of robot cognitive intervention with an active control, such as conventional cognitive training using paper and pencil, the results of this study might have come from cognitive intervention itself, not from the effects of using a robot. Therefore, further studies with an active control should be warranted to examine the effects of the robot cognitive intervention compared to

those from conventional cognitive intervention using paper and pencil or computers. Finally, as mentioned before, we measured only 3 cognitive subtests, including working memory, attention, and visual memory tests, as primary outcomes. Therefore, other cognitive domains, such as language or calculation, might also be improved after cognitive training with robots, which was not investigated in this study.

Nonetheless, this pilot study demonstrated that using a personal robot for cognitive intervention at home in patients with MCI was beneficial to them in improving working memory.

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