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Original Article

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Effect of Tablet-based Cognitive Intervention on Cognition in Patients With Mild Cognitive Impairment: A Pilot Study

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Conflict of Interest
Sung Hoon Kang and Chi Kyung Kim have stock in the Brain Academy Company. All other authors report no conflicts of interest.

ABSTRACT

Background and Purpose: Growing evidence has shown that cognitive interventions can mitigate cognitive decline in patients with mild cognitive impairment (MCI). However, most previous cognitive interventions have been group-based programs. Due to their intrinsic limitations, group-based programs are not widely used in clinical practice. Therefore, we have developed a tablet-based cognitive intervention program. This preliminary study investigated the feasibility and effects of a 12-week structured tablet-based program on cognitive function in patients with MCI.
Methods: We performed a single-arm study on 24 patients with MCI. The participants underwent a tablet-based cognitive intervention program 5 times a week over a 12-week period. The primary outcome was changes in cognitive function, measured using the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K). Outcomes were evaluated at baseline, within two weeks of the last program (post-intervention), and at the six-month follow-up session.
Results: The completion rate of the tablet-based program was 83.3% in patients with MCI. The program improved cognitive function based on the CERAD-K total score (p=0.026), which was maintained for at least three months (p=0.004). There was also an improvement in the depression scale score (p=0.002), which persisted for three months (p=0.027).
Conclusions: Our 12-week structured tablet-based program is feasible for patients with MCI. Furthermore, although further studies with a double-arm design are required, the program appears to be an effective strategy to prevent cognitive decline in patients with MCI.

Keywords: Cognitive Training; Cognition; Mild Cognitive Impairment

INTRODUCTION

Mild cognitive impairment (MCI) is regarded as a prodromal stage of dementia, as patients with MCI are ten times more likely to develop dementia than cognitively unimpaired individuals.[1] To delay the onset of dementia, physicians seek to diagnose MCI at an early

Author Contributions

Conceptualization: Kang SH; Data curation: Park JY, Choi SA, Kim JJ, Park YJ, Kim CK, Cho GJ, Koh SB; Formal analysis: Park JY, Kang SH; Investigation: Choi SA, Kang SH; Methodology: Park YJ, Kang SH; Visualization: Park JY, Kang SH; Writing - original draft: Park JY, Kang SH; Writing - review & editing: Kang SH.

stage. However, no pharmacological treatments are available to slow cognitive decline in patients with MCI. Recent studies have investigated the effects of nonpharmacological interventions on the mitigation of cognitive decline and dementia conversion in patients with MCI. Specifically, growing evidence shows that cognitive interventions may delay dementia conversion in patients with MCI.[2-4]

Patients with MCI frequently have depressive symptoms, and may be at higher risk for progression to dementia.[5] Depressive symptoms in patient with MCI or dementia are partially responsive to anti-depressant medication.[6,7] In this regard, nonpharmacological approaches, including cognitive interventions, emerge as an alternative to improve depressive symptoms. Several studies have found that cognitive interventions may have beneficial effects on depression in patients with MCI.[8,9]

Generally, cognitive interventions are performed using group- or home-based study programs. However, experienced teachers are required to conduct group-based programs. Furthermore, the quality of cognitive interventions may depend on the expertise of teachers. Encouraging patients to participate in home-based study programs and checking the adherence rate can be challenging. As an alternative to the traditional programs, recent studies have focused on computerized or tablet-based cognitive intervention programs.[10-14] Individuals can perform tablet-based cognitive interventions regardless of the time and place, and repeated practice is always possible. Qualified personnel are not required during the intervention, which may increase cost efficiency. Additionally, a tablet-based cognitive intervention program can provide personalized training tasks according to the cognitive level of the participants, increase the training motivation of the participants by providing immediate feedback on the training results, and easily evaluate training performance by comparing and analyzing continuously recorded training data.

Therefore, we developed a tablet-based cognitive intervention program. In this preliminary study, we aimed to investigate the feasibility and effects of a 12-week structured tablet-based program on cognitive function and depression in patients with MCI.

METHODS

Study design and participants

This was a single-center, single-arm study conducted to check the feasibility and effects of a tablet-based cognitive intervention program called the Mind Rx. We prospectively recruited participants with amnestic MCI aged ≥60 years from a dementia prevention center in Geumcheon-gu, Seoul, Korea, to participate in a cognitive intervention program over a 12-week period. All participants underwent neuropsychological testing using the Korean version of the Consortium to Establish a Registry for Alzheimer Disease Assessment Packet (CERAD-K),[15] and met the modified Peterson's criteria,[16,17] as follow: 1) subjective cognitive complaints by the participant or caregiver; 2) objective memory impairment below –1.0 SD on verbal or visual memory tests; 3) no significant impairment in activities of daily living; and 4) non-demented. We excluded participants with the following: 1) severe or unstable medical diseases that interfered with participation in the program; 2) diagnostic history of other neurodegenerative diseases, psychiatric disorders, or alcohol or drug addiction; 3) less than six years of education; and 4) hearing or visual impairment.

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This study was approved by the Institutional Review Board of Korea University Guro Hospital. Written informed consent was obtained from all the participants.

Mind Rx program

The Mind Rx cognitive training program was used as the treatment condition in this study. The program was developed for cognitive training at home, and was composed of cognitive training games targeting a particular cognitive domain, grouped into five categories: memory, attention, language, visuospatial perception, and frontal executive function. Initially, participants visited the facility 1 a week for 4 weeks, and were trained on how to play the games (**Fig. 1**). Afterward, the participants performed daily training session freely at home 5 days per week over a 12-week period. According to predetermined criteria, 8 new games were selected in 5 cognitive domains every 2 weeks. Over the course of 2 weeks, participants were given 10 daily training sessions (5 days per week), and in the first half of the course, the curriculum was structured to train 8 games evenly to one daily training session. In the second half of the course, a tailored curriculum was provided to strengthen weak cognitive domains by analyzing the training records of the first half.

One 4-game session typically took approximately 12 minutes to complete (**Fig. 2**). Outside this session, participants could perform additional training games with any of the 96 available games. Detailed information of and experience with the Mind Rx cognitive training program are presented on the website (https://mindrx.care).

Outcomes

Assessments were performed at baseline, within 2 weeks of the last program (post-intervention), and at the 24-week follow-up session (long-term effect). The primary efficacy outcome was the change in CERAD-K total score from baseline to post-intervention.[15] Secondary outcomes were the Mini-Mental State Examination (MMSE),[18] Word List delayed recall, 15-item Boston Naming Test (BNT-15), Constructional Praxis, Verbal Fluency, Trail Making Test Part B (TMT-B), Stroop Test color reading, and 15-item Geriatric Depression Scale (GDS-15) scores.[19]

Statistical analyses

The demographics of participants were described using descriptive statistics. Continuous and categorical variables are presented as the mean ± standard deviation, and frequency (%),

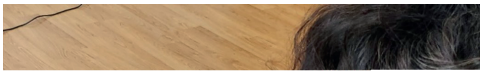

Fig. 1. Participants self-training with Mind Rx installed on a tablet.

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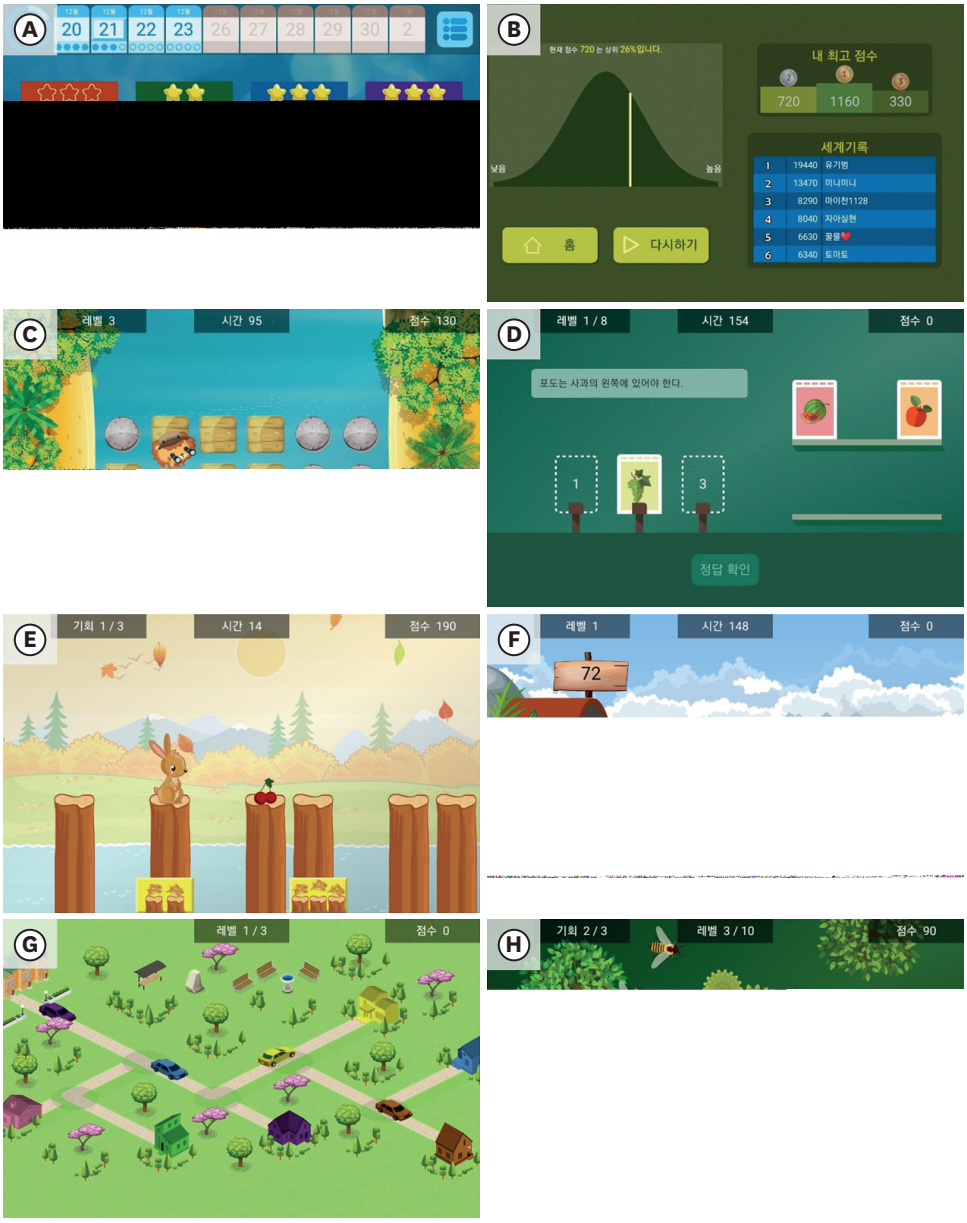

Fig. 2. Screenshot of the cognitive intervention game in Mind Rx.
(A) Mind Rx was designed to present 4 tasks per day, (B) Learning management system showing the trainer's cognitive level immediately after the game is over, (C) Lion Jones game in the memory category, (D) Gardener's Dilemma game in the language function category, (E) Bunny Hop game in the attention category, (F) Cargo Train game in the frontal executive function category, (G) After School game in the visuospatial category, and (H) Feeding Bee game in the memory category. Each category consists of at least 20 new games.

respectively. The Wilcoxon signed-rank test was performed to evaluate post-intervention changes from baseline (post-intervention vs. baseline) and long-term effects of intervention (24-week follow up vs. baseline).

All reported *p*-values were two-sided, and the significance level was set at 0.05. All analyses were performed using R version 4.3.0 (Institute for Statistics and Mathematics, Vienna, Austria; www.R-project.org).

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RESULTS

The study was conducted between September 2022 and April 2023. Thirty individuals were screened for eligibility in September 2022. Nine participants withdrew their consent before the program initiation. Ultimately, 24 individuals participated in the program. Twenty of the 24 participants (83.3%) completed the 12-week program. Two participants discontinued the program through withdrawing their consent. One participant discontinued because he was diagnosed with unstable angina. One participant discontinued because she underwent an operation due to severe osteoarthritis. One participant was lost to follow up. The mean number of total games played and each game per day was (69.7±36.1) and (17.5±9.1), respectively. No adverse events were observed during the study period.

Table 1 shows the baseline demographic characteristics of the study participants. The mean age was (73.8±5.1) years, and 17 out of the 19 (89.5%) participants were female. The mean years of education was (11.5±3.1). In terms of baseline cognitive function, the mean CERAD-K total score was (66.7±7.6). The mean MMSE and GDS-15 scores were (26.3±2.0) and (7.2±4.3), respectively.

Post-intervention, as shown in **Table 2**, there were significant improvements in the CERAD-K total score (5.3 point increase, p=0.026) and the GDS–15 score (−3.4 point decrease, p=0.002; **Fig. 3**). In terms of the subdomain scores of the CERAD-K, the Word List delayed recall (1.2 point increase, p=0.005), BNT-15 (0.9 point increase, p=0.016), TMT-B (−37.0 point decrease, p=0.028), and Stroop Test color reading (5.9 point increase, p=0.026) scores improved post-intervention. However, there were no significant improvements in the MMSE (1.1 point increase, p=0.061), constructional praxis (0.1 point increase, p=0.878), or verbal fluency (0.2 point increase, p=0.823).

Table 1. Demographics of the study participants at baseline (n=19)

Participants with MCI	Values
Demographics	
Age (yr)	73.8±5.1
Female	17 (89.5)
Education (yr)	11.5±3.1
Baseline evaluation	
CERAD-K total score	66.7±7.6
MMSE score	26.3±2.0
GDS-15 score	7.2±4.3

Values are presented as the mean ± standard deviation, or number (%).
MCI: mild cognitive impairment, CERAD-K: Korean Version of the Consortium to Establish a Registry for Alzheimer Disease Assessment Packet, MMSE: Mini-Mental State Examination, GDS-15: 15-item Geriatric Depression Scale.

Table 2. Changes in the outcome measures post-intervention

Variables	Scores at baseline	Scores at PI	Changes from baseline to PI	p-value*
CERAD-K total	66.7±7.6	72.1±8.5	5.3±9.1	0.026
MMSE	26.3±2.0	27.4±1.9	1.1±2.5	0.061
Word List delayed recall	4.4±1.6	5.6±1.8	1.2±1.4	0.005
BNT-15	10.6±2.5	11.5±2.4	0.9±1.4	0.016
Constructional Praxis	6.5±2.3	6.5±3.0	0.1±3.5	0.878
Verbal fluency	12.9±2.8	13.1±3.1	0.2±3.5	0.823
TMT-B	183.9±40.5	146.9±54.7	−37.0±35.7	0.028
Stroop Test color reading	29.5±11.5	35.4±13.0	5.9±10.6	0.026
GDS-15	7.2±4.3	3.8±3.2	−3.4±3.9	0.002

PI: post-intervention, CERAD-K: Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet, MMSE: Mini-Mental State Examination, BNT-15: 15-item Boston Naming Test, TMT-B: Trail Making Test Part B, GDS-15: 15-item Geriatric Depression Scale.
*p-values were obtained using the Wilcoxon signed-rank test.

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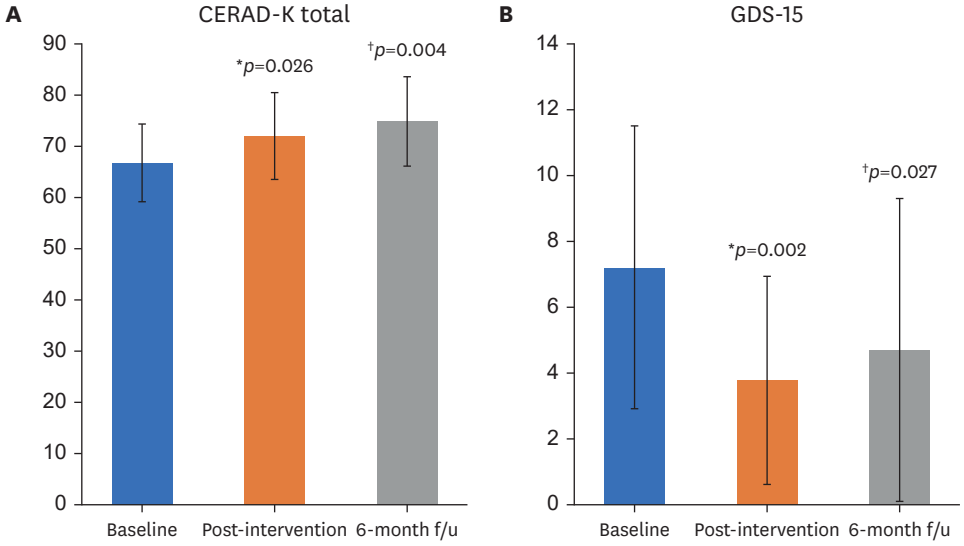

Fig. 3. Changes in the outcome measures post-intervention, and at the 6-month follow up.
The blue, orange, and gray bars represent the baseline, post-intervention, and 6-month follow-up scores, respectively. (A) Values depicted in the bar plot represent the mean CERAD-K total score, while values depicted in the error bar represent the standard deviation of the CERAD-K total score. (B) Values depicted in the bar plot represent the mean of the GDS-15, while the values depicted in the error bar represent the standard deviation of the GDS-15.
CERAD-K: Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet, GDS-15: 15-item Geriatric Depression Scale, f/u: follow-up.
*p-values were obtained from the comparison between baseline and post-intervention, using the Wilcoxon signed-rank test.
†p-values were obtained from the comparison between baseline and 24-week follow up, using the Wilcoxon signed-rank test.

At the six-month follow up, improvements were maintained in the CERAD-K total score (8.1 point increase, p=0.004), MMSE (1.9 point increase, p=0.006), and GDS-15 (−2.5 point decrease, p=0.027; **Table 3**, **Fig. 3**). Among the subdomain scores of the CERAD-K that improved post-intervention, the Word List delayed recall (1.6 point increase, p=0.003), BNT-15 (1.1 point increase, p=0.005), and TMT-B (−76.4 point decrease, p=0.043) scores were maintained. However, there was no sustained improvement in the constructional praxis (0.7 point increase, p=0.271), verbal fluency (0.2 point increase, p=0.726), or Stroop Test color reading (4.4 point increase, p=0.098) scores.

Table 3. Maintenance in the outcome measures at the 6-month follow-up visit

Variables	Scores at baseline	Scores at 6-month f/u	Maintenance from baseline to 6-month f/u	p-value*
CERAD-K total	66.7±7.6	74.8±8.7	8.1±10.4	0.004
MMSE	26.3±2.0	28.2±1.9	1.9±2.4	0.006
Word List delayed recall	4.4±1.6	5.9±1.8	1.6±1.8	0.003
BNT-15	10.6±2.5	11.6±2.2	1.1±1.4	0.005
Constructional Praxis	6.5±2.3	7.2±2.2	0.7±2.9	0.271
Verbal fluency	12.9±2.8	13.1±3.9	0.2±4.4	0.726
TMT-B	184.2±44.4	107.8±23.9	−76.4±42.8	0.043
Stroop Test color reading	29.5±11.5	33.8±9.2	4.4±11.5	0.098
GDS-15	7.2±4.3	4.7±4.6	−2.5±4.3	0.027

f/u: follow-up, CERAD-K: Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet, MMSE: Mini-Mental State Examination, BNT-15: 15-item Boston Naming Test, TMT-B: Trail Making Test Part B, GDS-15: 15-item Geriatric Depression Scale.
*p-values were obtained using the Wilcoxon signed-rank test.

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DISCUSSION

In this preliminary study, we investigated the feasibility of a tablet-based program, and its effects on cognitive function and depression. The completion rate of the tablet-based program was 83.3% in patients with MCI. Importantly, the program improved cognitive function based on the CERAD-K total score as the primary efficacy assessment. The benefits of the program persisted for at least three months after discontinuation. Collectively, our findings suggest that a 12-week structured tablet-based program is feasible for patients with MCI. Furthermore, the program may be an effective strategy to prevent cognitive decline in patients with MCI.

The completion rate in the present study was higher than in a previous study,[3] even though we used a tablet-based program that may be unfamiliar to elderly individuals. This high completion rate can be explained by several factors. First, Mind Rx has been developed to be user-friendly through long-term usability testing, and has a detailed guidance system so that beginners can easily learn how to use it. Second, Mind Rx includes a learning management system that manages training records, and analyzes performance so that the therapist can monitor the training progress rate of the participant and encourage progress.

Our main finding was that the program improved cognitive function, as seen by the improvement in the CERAD-K total score as the primary efficacy assessment. The benefits of the program persisted for at least three months after discontinuation. Specifically, the program was effective in improving memory, language, and frontal executive functions. Given that patients with MCI and an amnestic presentation are more likely to develop dementia, and frontal dysfunction in patients with amnestic MCI has a high risk for dementia conversion,[20] a high proportion of the games focused on training the memory and frontal executive function. This proportion of the games may contribute to improvements in memory and frontal executive function. Consistent with our findings, previous studies have also shown that cognitive intervention using information and communications technology leads to significant improvement in general cognition in patients with MCI.[8,11-13,21-23]

We also found that as assessed using the GDS-15, the program was beneficial for depression. This result is consistent with the findings of previous studies. Several studies have shown that cognitive training improves depression in patients with MCI.[24,25] Depression is a common neuropsychiatric symptom observed in patients with MCI. Additionally, depressive mood is predictive of dementia conversion in patients with MCI. Therefore, a beneficial effect on depression may be associated with a good prognosis in patients with MCI.

This study had several limitations. First, as this was a pilot study, the sample size was relatively small. Second, the tablet-based program had only a modest effect on cognitive function and depression. In particular, we did not perform multiple comparison corrections, which might have been linked to a type I error. However, given that the design of the present study was exploratory, multiple comparison corrections might have lost the opportunity to find important associations during preliminary analyses. Further randomized controlled trials with larger sample sizes are needed to confirm our results. Third, depressive symptoms were evaluated using questionnaires. Considering that the participants could not be blinded to the program, our results did not confirm that the improvement in the GDS-15 was unrelated to the placebo effect. Finally, as participants were recruited from Geumcheon Center for Dementia, participants who live alone and have financial difficulties have a high

proportion. Thus, this study might have enrolled a more "depressive" population, which might limit the generalizability of this study to other populations. However, the internal validity of our findings should not have been affected by this issue. Nevertheless, this pilot study revealed that using a tablet-based application for cognitive intervention at home may be beneficial for improving cognitive performance in patients with MCI. Although further studies in clinical settings are necessary, these encouraging findings suggest that tablet-based programs may be an alternative therapy for the prevention of cognitive decline in patients with MCI.

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