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The Effect of Cognitive Intervention on Cognitive Improvement in Patients with Dementia

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ABSTRACT

Background and Purpose: The effect of cognitive intervention in patients with dementia is inconsistent. This study sought to find out the effect of cognitive intervention by measuring interval change between before and after intervention.

Methods: We evaluated cognitive changes according to clinical diagnostic group across Gangwon province for 940 patients with dementia diagnosed at hospital clinics and 2,975 subjects without dementia. All subjects were treated with cognitive intervention. They underwent a cognitive and mood assessment before and after intervention. We used interval change of Mini-Mental State Examination (MMSE) scores as a primary measure of interventional outcome.

Results: Changes in mean MMSE score were significantly different between the non-dementia group and the dementia group (p=0.016), with changes of 0.7±2.4 and 1.0±3.7 points (±standard deviation), respectively. Cognitive improvement regarding completion of session was significantly higher in the dementia group (p=0.001), with changes of 0.41±4.51 for uncompleted group and 1.30±3.22 points for completed ones. Lower initial MMSE scores, lower age, and type of intervention were found to be independent predictive factors of subsequent cognitive changes as indicated by mean MMSE scores.

Conclusions: These findings suggest that cognitive intervention might be useful for patients with dementia. Their response to treatment might be related to the type of intervention.

Keywords: Cognitive Therapy; Dementia

INTRODUCTION

The number of elderly people with dementia is increasing rapidly. It is expected to reach 1.5 billion in 2050.[1] Dementia patients usually have multiple disabilities in cognition, including memory, language, judgement, and visuospatial function, resulting in loss of independence and decreased social activities.[2] These factors can lower the quality of life for caregivers as well as patients themselves, increasing social burden with deep impact at physical, economical, and psychological levels.[3,4]

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Currently available drugs for dementia can only lead to modest improvement for cognitive function. There is still a strong unmet need for novel and effective strategies that are preventive and therapeutic.[5]

Previous studies have demonstrated that cognitive intervention is effective in improving cognition in patients with mild cognitive impairment or dementia[6-9] from either single domain or reasoning training.[10] A recent study recruiting 1,994 Korean community-dwelling elderlies has also reported that cognitive training can improve their cognitive function, depression level, and quality of life regardless of gender, age, or family support.[6] Despite these results, the efficacy of non-pharmacological intervention has not been conclusively established due to heterogeneity of interventional modality.[11] A consensus on standard method for cognitive intervention by expert group is urgently needed.[12]

The purpose of this study was to investigate the efficacy of a cognitive intervention by comparing general cognitive score after the intervention. Relatively large number of community-dwelling elderlies were recruited for this purpose. Their levels of cognition and depression were measured between pre- and post-cognitive intervention. Mini-Mental State Examination (MMSE) is widely used to examine mild to moderate stages of dementia.[13-15] It was used in this study to measure cognitive changes.

METHODS

Participants

Participants were drawn from the elderly who visited eighteen public health centers between March 2015 and December 2016 across cities and counties of Gangwon province; including Gangneug, Donghae, Samcheok, Sokcho, Wonju, Chuncheon, Taebaek, Goeseong, Yanggu, Yangyang, Yeongwol, Inje, Jeongseon, Cheorwon, Pyeongchang, Hongcheon, Hwacheon, and Hoengseong. Initial screening test by simple history taking, MMSE, and Geriatric Depression Scale (GDpS) were performed. Elderly people with possible cognitive decline were sent to hospitals for diagnosis of dementia. This is an early dementia detection program supported by the Ministry of Health and Welfare. The Korean version of the Alzheimer's disease (AD), neuropsychological battery, a brain computed tomography (CT) scan, and laboratory tests were used to diagnose dementia. Initially, 5,758 subjects were enrolled for cognitive interventional program. Among them, 1,843 participants were not followed up and excluded from the current study. As a result, 940 subjects were enrolled as dementia patients and 2,975 subjects were enrolled for the non-dementia group. Patients in both groups were evaluated before and after the cognitive intervention with the Korean version of the MMSE. Participants were consecutively registered. Their clinical data were analyzed retrospectively.

Cognitive intervention

The program for cognitive intervention was performed as a specialized project in Gangwon province since 2014 with the goal to expand these programs, to provide professional services to prevent dementia and delay the onset of symptom. The program included exercise, music, cooking, storytelling, play therapy, and recall therapy. Instructors who were in charge of the program were composed of general or specialized occupational therapist for dementia, undergraduate or graduate students with major in occupational therapy, and those who have completed the educational training program provided by and those who have completed the educational training program provided by Gangwon Provincial Dementia Center. There

Table 1. Models for cognitive intervention program

Programs*	Model 1	Model 2	Model 3
Personal therapy	1 person × within 40 sessions × 20 groups	1 person × within 36 sessions × 15 groups	1 person × more than 30 sessions × 10 groups
Group therapy I (public health center program)	15 people × 24 sessions × 3 groups	15 people × 16 sessions × 3 groups	15 people × 12 sessions × 3 groups
Group therapy II (institution visiting program)	25 people × 16 sessions × 3 groups	25 people × 16 sessions × 2 groups	25 people × 12 sessions × 2 groups

Each model includes the regions follow as: model 1: Chuncheon, Wonju, Gangneung, Taebaek, Samcheok, Hongcheon, Hoengseong; model 2: Donghae, Sokcho, Yeongwol, Pyeongchang, Jeongseon, Cheorwon; model 3: Hwacheon, Yanggu, Inje, Goeseong, Yangyang.
*With reference to this example, cities and counties autonomously organized the actual cognitive intervention programs that included exercise, music, cooking, storytelling, play therapy, and recall therapy with 90 minutes per session.

are 2 types of cognitive intervention: personal therapy and group therapy. Each therapy was provided for more than 90 minutes per session (**Table 1**). After finishing the final session of cognitive intervention, follow-up MMSE and GDpS were measured to detect interval changes. If the program was not completed, the most recent test was used. The study protocol was approved by the Ethics Committee of the Kangwon National University Hospital (KNUH) for studies involving human subjects (approval number: KNUH-2017-09-010).

Statistical analyses

Cognitive changes over time were measured by MMSE change which was calculated as difference between two scores (before and after cognitive intervention). Independent t-tests were performed to examine potential differences between groups for continuous variables while χ^2 tests were used to evaluate differences for categorical variables. Associations between clinical groups and mean MMSE changes were assessed by univariate and multivariate analysis using linear regression analysis with age, sex, education, initial cognitive test scores, initial depression scores, type of intervention, and number of intervention as covariates. Variables with p value <0.2 in univariate analyses were included in multivariate analysis. All tests were 2-sided. Statistical analyses were performed with R (Version 3.4.1, 64-bit platform; The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 3,915 subjects were enrolled in the study. The study group consisted of subjects without dementia (n=2,975), and patients with dementia (n=940). Demographic and baseline characteristics of patients were different between the 2 groups. Patients with dementia were older with lower education levels compared to those without dementia (**Table 2**).

Most subjects in the control group received group therapy while as half of subjects in the dementia group received group therapy. Most instructors were certified ones in both groups. Total number of cognitive intervention was significantly higher in the total number of cognitive intervention was significantly higher in the dementia group compared to that in the control group (p<0.001).

The mean MMSE score change was +0.7 points in the non-dementia group and +1.0 points in the dementia group. The difference between the two groups was statistically significant (p=0.016). A subgroup comparison was performed depending on whether subjects completed the minimal sessions for cognitive intervention. Analyses were performed between completed group (more than 10 sessions) and uncompleted group (less than 10 sessions). In patients with dementia, the mean MMSE score change was +0.41 points in the uncompleted group and +1.30 points in the

Table 2. Demographic variables according to diagnostic group

Variables	Non-dementia (*n*=2,975)	Dementia (*n*=940)	*p*
Mean age (yr)	76.7±6.7	79.1±6.6	<0.001
Sex (female)	2,384 (80.1)	707 (75.2)	<0.001
Years of education	4.4±4.1	3.4±3.9	<0.001
Type of intervention			<0.001
Personal	144 (4.8)	449 (47.8)	
Group	2,831 (95.2)	491 (52.2)	
Total number of intervention	12.7±9.0	20.4±16.9	<0.001
Completed session	1,638 (55.1)	619 (65.9)	<0.001
Initial MMSE	24.1±4.6	17.4±5.2	<0.001
Follow-up MMSE	24.8±4.4	18.4±5.8	<0.001
Follow-up duration (day)	114.6±74.7	143.1±84.4	<0.001
Initial GDpS	4.3±4.0	6.0±4.1	<0.001
Mean change of MMSE	0.7±2.4	1.0±3.7	0.016
Mean change of GDpS	−0.5±2.9	−0.7±3.4	0.062

Values are means±standard deviation or numbers of cases with percentages in parentheses.
MMSE: Mini-Mental Status Examination, GDpS: Geriatric Depression Scale.

completed group (*p*=0.001). The non-dementia group experienced a mean MMSE score change of 0.65 point for the uncompleted group and +0.68 points for the completed group (*p*=0.666) (**Fig. 1**). GDpS score change was −0.5 points in the non-dementia group and −0.7 in the dementia group without statistical significance (*p*=0.062). Subgroup analysis depending on session completion failed to reveal any significant difference between groups (**Fig. 2**). Univariate analysis was conducted to determine demographic and clinical factors (age, sex, education, initial MMSE, initial GDpS, type of intervention, and number of intervention) predicting general cognitive decline. Results are summarized in **Table 2**. Subsequent multivariate analysis revealed that lower age (*p*<0.013), lower initial MMSE (*p*<0.001), and type of intervention (*p*<0.001) were significant factors predicting improved cognitive abilities, as indicated by mean MMSE change (**Table 3**).

DISCUSSION

Nowadays, lots of cognitive interventions are being used to support elderly patients with dementia. However, utility of it remains unclear.[16] Although systemic reviews have failed to
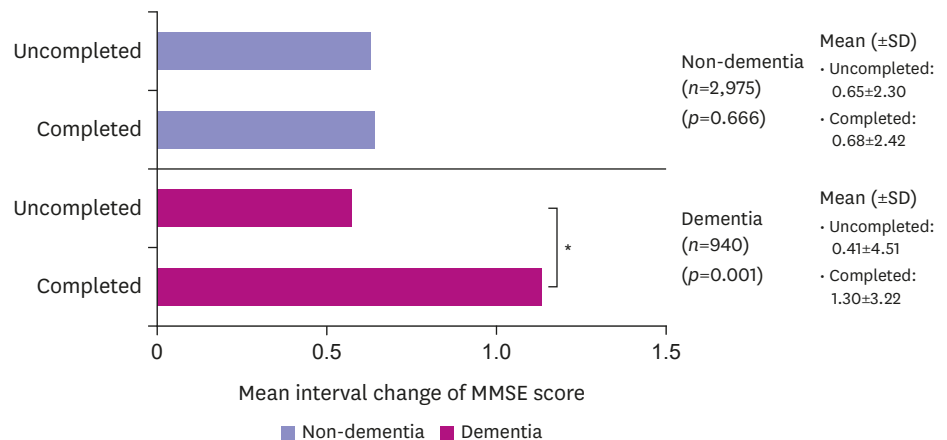

Fig. 1. Effect of completed session of cognitive intervention on patients with dementia based on mean changes in MMSE scores.
MMSE: Mini-Mental State Examination, SD: standard deviation.
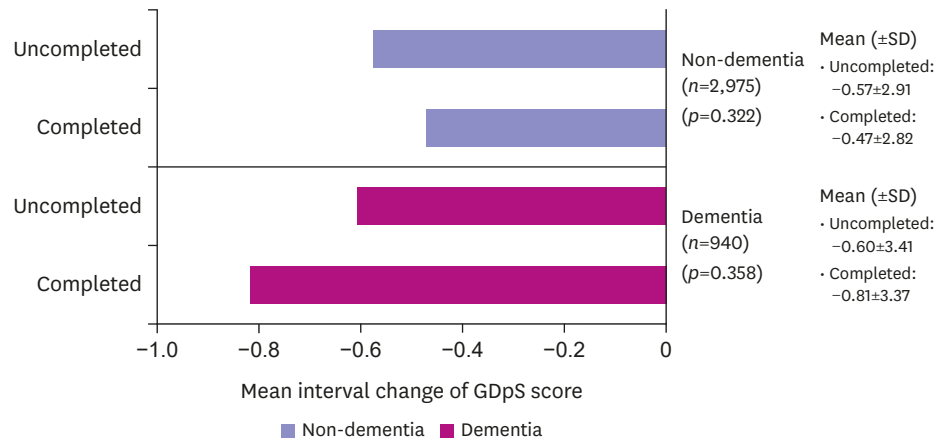*Significant difference between uncompleted and completed groups (p<0.001).

Fig. 2. Effect of cognitive intervention on depression as measured by mean changes in GDpS scores. GDpS: Geriatric Depression Scale, SD: standard deviation.

consistently reveal a positive effect of cognitive intervention on dementia patients, recent studies have suggested that patients undergoing structured cognitive intervention can be improved compared to untrained patients.[17] Based on the practical point that cognitive intervention has been already widely used in nursing home or elderly caring facilities in Korea, the objective of our study is to examine the effect of interventional activity on cognitive improvement represented by MMSE score. A relatively large number of elderly people with or without dementia were included in this study to find out general correlation between cognitive intervention and cognitive improvement across Gangwon province.

In the current study, patients with dementia who received cognitive intervention had significantly higher MMSE score changes compared to subjects without dementia (+1.0 vs. +0.7 points). Although we should avoid hasty generalization, increased mean MMSE score in both groups might be worthy of attention considering the continuous decrement of longitudinal MMSE score over time even in pharmacological treatment group in previous studies.[18,19] These findings suggest that cognitive intervention is efficacious for both of elderly people with or without dementia, at least in the short term. This interesting finding of cognitive improvement in both groups, although it was greater in the dementia group, was consistent with previous reports.[16,20] A greater improvement could be expected in patients with dementia who had more cognitive dysfunction at initial state as they could get more benefit from the intervention. On the contrary, the potential for improvement might be lower in non-dementia subjects who were already better at initial state. Although there was no significant difference in mean interval change between completed and uncompleted

Table 3. Multivariate analysis of factors predicting mean MMSE changes in dementia group

Variables	Univariate analysis		Multivariate analysis	
	β (SE)	p	β (SE)	p
Age	−0.03 (0.01)	0.161	−0.05 (0.02)	0.013
Education	−0.02 (0.03)	0.587	-	-
Sex	−0.33 (0.28)	0.248	-	-
Initial MMSE	−0.14 (0.02)	<0.001	−0.15 (0.02)	<0.001
Initial GDpS	0.03 (0.03)	0.375	-	-
Type of intervention	−1.20 (0.24)	<0.001	−1.11 (0.24)	<0.001
Number of intervention	0.02 (0.01)	0.023	0.01 (0.01)	0.185

Mean MMSE change were entered as dependent variables with others as independent variables.
MMSE: Mini-Mental Status Examination, SE: standard error, GDpS: Geriatric Depression Scale.

subgroups of non-dementia group, cognitive benefit was significantly higher in the completed subgroup compared to that in the uncompleted group of dementia subjects, implying that clinical benefits of cognitive intervention are greater for patients with dementia subjects, especially if they completed minimal sessions (**Fig. 1**).

The dementia group was used for multivariate analysis based on significant variables from univariate analysis. Younger age, lower initial MMSE score, and personalized intervention were favorable predictors for increase in MMSE. The number of intervention lost significance in multivariate analysis. This could be interpreted that it would be more important to complete sessions above threshold rather than just increasing the number of intervention. Regarding session completion, many subjects (44.9% for Non-dementia subjects and 34.1% for dementia subjects) failed to complete sessions. Although baseline variables such as age, sex, educational level, initial MMSE, or initial GDpS was not significantly different between completed and uncompleted groups (**Supplementary Table 1**), data from the uncompleted group could influence the result of cognitive intervention on the improvement as they were missing not at random. Lower initial MMSE score as good predictor could be explained by the similar reason desrcribed above in that there might be more potential for improvement when initial state is relatively deteriorated. Considering younger age as good predictor, the reason why such initial low cognitive state could be improved by cognitive intervention might be related to non-organic component such as mood. However, depressive symptom represented by geriatric depression scale failed to be proved as an independent marker for good outcome. The other possible explanation for cognitive improvement might be due to enhanced brain plasticity as an underlying mechanism.[20] Personalized training instead of group intervention was found to be an independent predictor for dementia patient, in line with previous studies.[21,22] However, many other studies[23-25] have reported that group therapy is more effective. Therefore, it is difficult to conclude that one method is better than the other.

In the current study, the MMSE follow-up duration was relatively different from each other according to public health centers due to diversities of interventional programs. In addition, the rate of deterioration in MMSE score is known to be more than 5.3 points a year for moderate to severe dementia patients but less than 2 points decrement a year for mild dementia patients.[26] This means that MMSE might be a more sensitive scale for relatively later stages of dementia compared to that for early stage dementia or normal elderly.[27] Therefore, it would be a limitation if only MMSE score is used without other clinical staging such as global deterioration scale, clinical dementia rating scale, or neuropsychological battery.[28] Other studies have shown some evidence for improved general cognitive function over the treatment based on more detailed neuropsychological test such as Alzheimer's Disease Assessment Scale-Cognitive subscale.[29,30] However, MMSE could be a convenient alternative measure to detailed neuropsychological testing. Its use allowed us to evaluate cognitive changes from large number of subjects.[28,31] Future studies would benefit from the use of a more comprehensive neuropsychology or other cognitive indices to evaluate patients with dementia managed by cognitive intervention and reflect disease progression not examined by MMSE. Another limitation is the possibility of including subjects with mild cognitive impairment or with dementia among non-dementia group. Although clinical diagnosis was made for dementia group by clinician at nearby hospital, non-dementia group only received screening test with MMSE and simple questionnaire at local health care center which could potentially miss some patients with mild cognitive impairment. Therefore, non-dementia group could not be classified as normal control. This means that we might not have an active control group. Therefore, observed effect of increased MMSE score in both groups might

be derived from nonspecific social relationship or learning effect instead of interventional program.[32] This study does not include classification of dementia such as AD or vascular dementia because it was not possible to obtain specific diagnosis from health care center based data. In addition, the heterogeneity of the interventional program and its instructor (e.g. occupational therapist, certified instructor, general instructor) might have influenced the result. Cognitive interventions in community dementia centers will increase in line with the national dementia policy. Therefore, it is necessary to apply a standardized program and measure detailed outcomes to prove its real efficacy.

In conclusion, general cognitive improvement based on mean MMSE score changes was observed for both non-dementia and dementia groups, with higher degree in the dementia group based on a large population. Interventional type, younger age, and lower initial MMSE were found to be independent predictors of subsequent cognitive changes indicated by mean MMSE scores. These findings suggest that cognitive intervention might be an effective management method for dementia.

SUPPLEMENTARY MATERIAL

Supplementary Table 1
Demographic variables according to session completion

Click here to view

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