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Review Article

The Effects of Cognitive-Based Interventions in Older Adults: A Systematic Review and Meta-Analysis

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Abstract

Background: Cognitive-based intervention is divided into three types: Cognitive Stimulation (CS), Cognitive Training (CT), and Cognitive Rehabilitation (CR). This study was conducted to identify systematically the effects of cognitive-based interventions in randomized controlled trials (RCTs) applied to older adults in the following three groups: cognitively healthy, mild cognitive impairment (MCI), and dementia.

Methods: This search was carried out using the Ovid-MEDLINE, EMBASE, Cochrane library, CINAHL, ProQuest, and Korea databases. The effectiveness of the intervention was verified using the CMA 2.0 program.

Results: A total of 54 RCTs were included in systematic reviews and 38 studies were analyzed by meta-analysis. Meta-analysis showed that cognitive-based interventions were effective in improving the cognitive function (SMD=0.39, 95% CI=0.32-0.44) of older adults. The subgroup analysis of cognitive function revealed that CT was the most effective in the cognitively healthy (SMD=0.40, 95% CI=0.33-0.46) and the MCI (SMD=0.45, 95% CI=0.27-0.63) groups, and CS was the most effective in the dementia group (SMD=0.57, 95% CI=0.43-0.70).

Conclusion: In order to improve the cognitive function of older adults in each group, the most effective intervention type needs to be considered first. Evidence on the appropriate type of Cognitive-based intervention will be helpful in nursing practice.

Keywords: Older adults; Cognitive; Education; Rehabilitation; Systematic review

Introduction

The number of older adults suffering from cognitive function decline due to aging is on the rise (1). The sub-types of cognitive function can be classified into memory, executive function and overall cognitive function (1). Gradual decline in cognitive function adversely affects the lives of older adults by reducing independence of physical and emotional functions and reducing social participation (2). In addition, cognitive decline in old age is known to be a major predictor of dementia (3) and it is reported that 10-15% of the mild cognitive impairment (hereinafter referred to as MCI) older adults are diagnosed with Alzheimer's dementia every year, and 80% of them develop dementia after 6 years (4). In the case of dementia, memory impairment not only greatly affects self-confidence, but can lead to depression and loss of activity, which can lead to worse cognitive decline

(5). Delaying cognitive decline in the elderly is very important in preventing dementia, and if it helps delay the onset of dementia, it will be effective in reducing the burden of disease (6).

Currently, cholinesterase inhibitors are the main treatments for cognitive improvement in older adults suffering from Alzheimer's dementia and MCI (7). However, pharmacological treatment is showing limited efficacy in preventing dementia or improving cognitive decline and shows some adverse effects. Therefore, non-pharmaceutical approach that can compensate for the limitations of drug therapy is very important (7-9).

Among non-pharmacological approaches, cognitive-based intervention aims to improve and maintain cognitive function directly, rather than intervention that indirectly affects cognitive function such as relaxation therapy or music therapy (3). According to the Clare & Woods classification, cognitive-based intervention is divided into three types: Cognitive Stimulation (CS), Cognitive Training (CT), and Cognitive Rehabilitation (CR) (10). CS includes programs such as reality orientation, reminiscence therapy, and discussion. CT involves learning on a set of standard tasks such as reading, counting, and computer cognitive training and is designed to train specific cognitive domains with varying levels of difficulty. CR is an approach to selecting and prioritizing meaningful activities to improve the performance of daily activities by optimizing compensatory and environmental strategies (5, 10).

Effect can vary depending on what and how cognitive-based intervention was used (11). While CS and CT was effective in improving cognitive function in 3 groups of older adults (12-15), CR shows no effect on improving cognitive function in older adults with MCI (16).

Studies on the effect of cognitive-based intervention in older adults have been reported steadily. However, parameters such as subject, method, variables, measurement tool, and etc. are diverse and there are many contradictory results. Therefore, it is necessary to perform systematic review and meta-analysis of randomized controlled trials (RCTs) considered as golden standard for interventional research (17). According to the systematic review and meta-analysis on the effects of cognitive-based intervention (1, 18-20), the age group was diverse and comprehensive information on cognitive-based intervention applied to the 3 groups (cognitively healthy, MCI and dementia) was insufficient because only subjects of a specific cognitive level were included in the review. In particular, since brain pathology progresses before symptoms appear in dementia patients, approach to delay cognitive decline in not only older adults with MCI or dementia but also in cognitively healthy older adults (21). In addition, in order to clarify the clear evidence for the improvement or maintenance of cognitive function in older adults, it is also important to analyze what types of cognitive-based intervention are most appropriate according to the cognitive level, how to establish appropriate criteria for the composition of cognitive-based intervention.

Therefore, based on systematic review and meta-analysis, we aimed to identify the effects of cognitive-based intervention applied to older adults and identify types of individual cognitive-based intervention suitable for older adults who are cognitively healthy, MCI and dementia.

Methods

Eligibility criteria

Participants: The inclusion criteria were for older adults (≥60 years old), and cognitively healthy older adults refers to those without cognitive impairment in cognitive tests including MMSE. Older adults with MCI refer to those who have been diagnosed with MCI according to the Petersen criteria and other criteria (22). Older adults with dementia are those diagnosed with dementia according to the DSM-4 diagnostic criteria (23).

Interventions: It referred to the CS, CT and CR programs classified by Clare & Woods (5, 10), and includes multiple interventions in which two or more types of cognition-based intervention are mixed.

Control: Subject who did not get cognition-based intervention and referred as no treatment control and usual care.

Outcome: Variables of cognitive-based intervention included everything without limitation. **Study Design:** RCTs.

Ethical approval

The study was conducted after getting approval (1801203-**-017-01) from the institutional life review committee for exemption of review

Study selection and data extraction

Data search

All papers published before January 12, 2019 were searched. Search period was from January 3 to 12, 2019. To reduce publication bias, both academic thesis and journal papers were included, and keywords were selected by conducting a preliminary search based on PICO-SD. Search strategy was established by using synonyms, alternative words, Medical Subject Headings (MeSH) and EMTREE of the identified keywords. A search was carried out using the Ovid-MEDLINE, EMBASE, Cochrane library, CINAHL, ProQuest, and Korea databases (KISS, NDSL, KMBASE, KoreaMed, and RISS).

Search strategy was as follows. ('aged' [MeSH] OR 'elderly' OR 'healthy older adults' OR 'elderly individuals' OR 'elderly people' OR 'cognitive dysfunctions' [MeSH] OR 'mild cognitive impairment' [EMTREE] OR 'mild neurocognitive disorder*', OR 'cognitive declin*' OR 'mental deterioration*' OR 'MCI' OR Dementia [MeSH, EMTREE] OR Amentia* OR 'Senile Paranoid Dementia*' OR 'Familial Dementia*') AND ('cognitive stimulation' [EMTREE] OR 'reality orientation' OR 'memory stimul*' OR 'mental stimul*' OR 'cognitive intervention' OR 'global stimul*' OR 'cognitive psychostimulation' OR 'cognitive support' OR 'memory therap*' OR 'memory group*' OR 'memory support' OR 'cognitive training' [EMTREE] OR 'cognitive exercis*' OR 'cognitive retraining', 'memory training' [EMTREE] OR 'memory retraining' OR 'brain training' OR 'memory strateg*' OR 'memory management' OR 'memory aid*' OR 'mental training' OR 'cognitive rehabilitation' [EMTREE])

Data selection

Three people including the author and two assistant researchers independently performed the literature selection process. In case of disagreement, discussion with research methodology expert was performed and final result was applied.

Data extraction

Data extraction was first performed by the author and then reviewed by assistant researcher. For inconsistent items, original study was reviewed and revised together to make no more disagreements.

Quality assessment

Quality assessment was performed using the Cochrane's Risk of Bias tool (RoB 2.0) (24). Three evaluators including author and two assistant researchers, conducted independently, and for items that were not consistent, review of the original study and re-examination by research methodology expert were done to lead consistent conclusion.

Publication bias test

Publication bias of the study was tested by Funnel plot and Trim & fill of Duvall and Tweedie.

Statistical analysis

For meta-analysis, Standardized Mean Difference (hereinafter, SMD) was calculated using CMA 2.0 (Comprehensive Meta-Analysis 2.0). First, after calculating the total effect size, sensitivity analysis was performed to confirm the change in statistical significance and heterogeneity according to the difference in residence type, quality assessment result and effect size. After sensitivity analysis, studies that showed high heterogeneity in terms of effect size were removed and total effect size was recalculated and an analysis model was selected. Heterogeneity between each study was evaluated by Higgins I^2 statistic. If I^2 value was judged to be more than 50%, Random-effect model was used for analysis) (25). The effect size was used as an analysis unit in subgroup analysis, and individual studies were used as an analysis unit in calculating total effect size to avoid loss of information and violation of the assumption of independence (26).

Results

Study selection

As a result of review of electronic database and search by hand, a total of 7243 studies were searched. Of the 7243 studies, 54 were finally selected that met the selection criteria. Of the final 54 studies, 38 studies, which could calculate the effect size and reported cognitive function, were used for meta-analysis (Fig. 1).

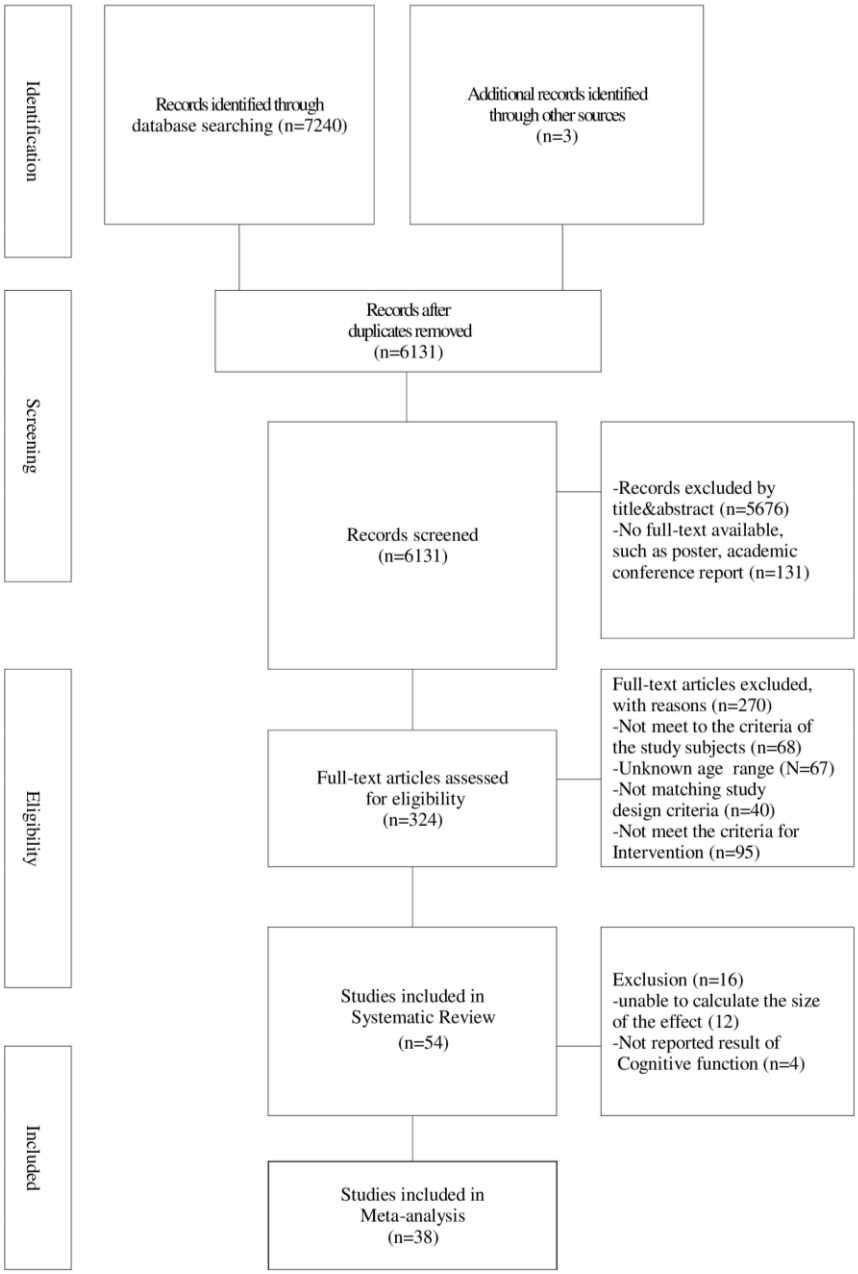

Fig. 1: Study flow diagram of a systematic review

Methodological quality

Fifty-four selected literatures were evaluated for their methodological quality using RoB 2.0 tool. As a result of bias judgement in randomization process, 12(22.2%) had low risk of bias, while 42(77.8%) showed some concern. Two out of 10 studies with high risk of bias were not included in the meta-analysis since they effect size could not be calculated or did not report cognitive function or depression. Remaining 8 studies with high risk of bias were included in the final meta-analysis as it was confirmed not to affect study results through sensitivity analysis (Table 1).

Table 1: Descriptive analysis of included studies (n=54)

Category					*N*	*%*	*Mean(SD) (Age/sessions)*
Participant†	Type		Cognitively healthy		40	59.7	70.6(4.80)
			MCI		10	14.9	72.1(3.62)
			Dementia		17	25.4	73.7(4.53)
	Sample size		≤60		35	52.2	
			61-120		17	25.4	
			≥121		15	22.4	
	Residence		Community		62	88.6	
			Day centers		5	7.1	
			Nursing home		3	4.3	
Intervention†	Type		CS		17	25.4	
			CT		37	55.2	
			CR		10	14.9	
			Mixed (CS+CT)		3	4.5	
	Contents	CS	Basic computer skills program		3	4.8	
			RO (reality orientation) Therapy		6	9.0	
			RT (reminiscence therapy)		5	7.5	
			Reading & Discussion		2	3.0	
			Education & Discussion		1	1.5	
		CT	Computer cognitive training		20	29.9	
			Structured cognitive domain training		12	17.9	
			Program using reading and		3	4.8	
		CR	Choose and prioritize meaningful activities		10	14.9	
		Mixed	RT & Computer Cognitive Training		3	4.5	
	Period		Total sessions (times)				30.7(41.89)
			Weekly sessions (times)				2.3(1.28)
			Session length (min)				65.0(27.72)
			Total period (weeks)				16.8(22.08)
Participant &			Cognitively healthy	CS	11	16.4	
				CT	28	41.8	
Intervention type†				Mixed	1	1.5	
			MCI	CS	1	1.5	
				CT	5	7.5	
				CR	3	4.5	
				Mixed	1	1.5	
			Dementia	CS	5	7.5	
				CT	4	6.0	
				CR	7	10.4	
				Mixed	1	1.5	
Outcome†			Variables				Statistical significance
			Cognitive function		49	90.7	33(+)
			Depression		13	24.1	7(+)
			Quality of life		8	14.8	5(+)
			IADL		7	13.0	4(+)
			ADL		6	11.1	3(+)

	Health status (general, physical, nutrition)	5	9.3	2(+)
	Gait, balance	4	7.4	2(+)
	Others	32	59.3	
Publication year	2000-2005	4	7.4	
	2006-2010	5	9.3	
	2011-2015	26	48.1	
	2016-2018	19	35.2	
Research countries	Asia	14	25.9	
	Europe	21	38.9	
	America	14	25.9	
	others	5	9.3	

Risk of Bias

Type of Bias	***n (%)***		
	Low	***High***	***Some concern***
The randomization process	12(22.2)		42(77.8)
Deviations from the intended interventions	10(18.5)		44(81.5)
Missing outcome data	40(74.0)	5(9.3)	9(16.7)
Measurement of the outcome	49(90.7)	5(9.3)	
Selection of the reported result	54(100)		
Overall bias	3(5.6)	10(18.5)	41(75.9)

†= Duplicate count, CS=Cognitive Stimulation, CT= Cognitive Training, CR=Cognitive Rehabilitation, MCI =Mild Cognitive Impairment, '+'=There is statistical significance.

Systematic review of Cognitive-based intervention

Total number of subjects in experiment group and control groups was 5,238 and 5,079, respectively. Among intervention types, 37(55.2%), 17(25.4%), and 10(14.9%) studies dealt with CT, CS, and CR, respectively. As for the distribution of intervention types by study subjects, 28(41.8%) and 5(7.5%) CT studies were conducted in cognitively health group and group with MCI, respectively. Seven (10.4%) CR studies were conducted in group with dementia.

Outcome variables were cognitive function, depression, ADL, IADL, etc. Cognitive function was reported as an intervention outcome in 49 studies (90.7%) (Table 1).

Effect of cognitive-based intervention

Total of 38 studies reported cognitive function were included in the meta-analysis. After removing 3 studies with highly heterogeneous effect size by sensitivity analysis, 35 studies were tested for homogeneity again. Even after removing outliers, I^2 values were 71.2%. Thus, effect size was calculated using Random-effect model that presumes heterogeneity between studies (Table 2).

Table 2: Effect of Cognitive-based Interventions on Cognitive Function

Total Effect							
NS		d(ES)	SE	*P*	95% CI	Heterogeneity	
						I^2	*P*
35		0.39	0.03	<.001	0.32-0.44	71.2	<.001
Subgroup Analysis							
Categories	***K***	***d(ES)***	***SE***	***P***	***95% CI***	***Heterogeneity***	
						I²	***P***
CS	81	0.44	0.04	<.001	0.37-0.52	65.2	<.001
CT	180	0.40	0.03	<.001	0.35-0.46	29.3	<.001
CR	52	0.38	0.05	<.001	0.27-0.48	0.0	.750

Mixed		6	0.23	0.13	.029	0.03-0.05	0.0	.642
Cognitively Healthy		167	0.38	0.03	<.001	0.33-0.44	39.6	<.001
MCI		52	0.42	0.06	<.001	0.32-0.53	3.1	.410
Dementia		100	0.45	0.04	<.001	0.37-0.53	52.1	<.001
Cognitively Healthy	CS	44	0.36	0.05	<.001	0.25-0.46	35.5	.012
	CT	121	0.40	0.03	<.001	0.33-0.46	42.1	<.001
	Mixed	2	0.27	0.20	.182	-0.13-0.67	0.0	.571
MCI	CS	8	0.39	0.13	.004	0.12-0.65	0.0	.746
	CT	21	0.45	0.09	<.001	0.27-0.63	0.6	.449
	CR	21	0.44	0.05	<.001	0.32-0.55	22.6	.171
	Mixed	2	0.36	0.15	.019	0.06-0.66	49.0	.161
Dementia	CS	29	0.57	0.05	<.001	0.43-0.70	63.2	<.001
	CT	38	0.43	0.08	<.001	0.27-0.58	0.0	.925
	CR	31	0.34	0.08	<.001	0.17-0.50	0.0	.987
	Mixed	2	0.18	0.07	.484	-0.33-0.69	0.0	.543

*NS=Number of Studies, K=Number of effect size, d(ES)=Effect Size, SE=Standard Error, 95% CI=95% Confidence Interval, MCI= mild cognitive impairment, CS=Cognitive Stimulation, CT=Cognitive Training, CR=Cognitive Rehabilitation

Unless there are significant number of studies, it is very unlikely that subgroup analysis will produce meaningful findings (26). Other variables except cognitive function were judged to be not enough in the number of studies to conduct subgroup analysis, so the meta-analysis of these was not performed.

1) Total effect: Total SMD for the cognitive function of cognitive-based intervention in 35 studies were 0.39(95% CI=0.32-0.44) (Table 2).

2) Subgroup analysis: Result of subgroup analysis according to the subject's cognitive level and cognition-based intervention type are as follows. In the case of cognitively healthy and MCI, CT was analyzed as 0.40(95% CI=0.33-0.46) and 0.45(95% CI=0.27-0.63), respectively, showing the significant effect. In the case of older adults with dementia, effect size of CS was 0.57(95% CI=0.43-0.70) which was significantly the largest (Table 2).

3) Meta-regression by intervention period: Effect size showed statistically significant (P<.001) decrease as the number of sessions per week increased, the. In terms of slope, effect of the program was higher when the number of sessions per week was about 2 (Table 3).

Table 3: Meta-Regression by Intervention Dose and Sensitivity Analysis on Cognitive Function

Variables		***Coefficients***	***SE***	***95% CI***	***Z***	***P***
Weekly Sessions	Slope	-0.04	0.01	-0.07~-0.02	-3.86	<.001
Session Length(min)	Slope	-0.00	0.00	-0.00~-0.00	-0.44	.656
Total Sessions	Slope	-0.00	0.00	-0.00~-1.51	-1.50	.13
Total Period(week)	Slope	-0.00	0.00	-0.00~0.00	-1.04	.30

Sensitivity Analysis Variables	***NS***	***d(ES)***	***SE***	***p***	***95% CI***	***Heterogeneity***	
						I^2	***p***
Residence	33	0.42	0.02	<.001	0.39-0.45	81.0	<.001
Risk of Bias	31	0.45	0.04	<.001	0.37-0.53	80.9	<.001

*NS=Number of Studies, d(ES)=Effect Size, SE=Standard Error, 95% CI=95% Confidence Interval

Publication bias test

Because of funnel plot, it can be predicted that there was no publication bias. Result of Trim & fill analysis predicted the same (Fig. 2).

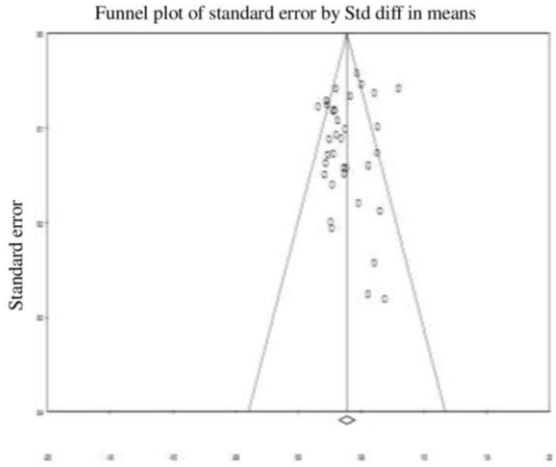

Figure 2-A. funnel Plot of Cognitive function

		Studies Trimmed	d(ES)	Q	95% CI
Cognitive function	observed values		0.42	630.05	0.38-0.47
	adjusted values	0	0.42	630.05	0.38-0.47

Figure 2-B. Duvall & Tweedie's Trim & Fill

Fig. 2: Funnel Plot and Duvall & Tweedie's trim & fill

Discussion

As a result of systematic review, there were studies that did not report on the number of total and weekly intervention, and average time per intervention, , and also studies in which statistics were not properly presented, thus included in the systematic review, but later excluded from meta-analysis. In addition, there were many cases where detailed and specific information on the operating procedure of cognitive-based intervention programs was not available, which could hinder the use of the study that guides interventions to be actually used in practice. Providing accurate information on the research based on objective and proven evidence will be more helpful in practice.

When looking at the methodological quality of the literature selected for this study, quality of the literature was not excellent while showing some concern. Especially, there were also many cases where information on the 'randomization method' and 'allocation concealment' was not sufficiently reported. Most of the cases of blinding of caregiver and the subject were also of some concern. It can be resulted from the fact that there were many passive control groups in which the control group did not contact caregiver or subject of the experimental group. Nevertheless, researchers performing RCTs need to perform accurate reporting on randomization and 'allocation concealment,' and procedures of blinding of caregivers, subjects, and outcome evaluators. This is because well-designed,

well-performed and well-reported RCTs can only provide the best evidence (17).

As a result of meta-analysis, total effect size of cognitive-based intervention on cognitive function of older adults and effect size of the cognitive function according to the cognitive level of the subject and the type of cognitive-based intervention was medium. This was similar to the results of previous studies on meta-analysis of the effect of cognitive-based intervention (1, 18-19) and it is confirmed that cognitive-based intervention is consistent evidence showing important and meaningful improvement in cognitive function.

As for the effect on cognitive function by intervention period, it was found that the effect of the program was significantly decreased as the number of interventions per week is increased, Effect of the program was found to be the highest when intervention was done about twice a week. This is similar to the meta-analysis study of CT on the elderly that 1-2 sessions per week were more effective than 3 or more sessions (19). Therefore, when planning cognitive-based intervention, it is necessary to consider a plan to operate session twice a week. In this study, after 60 minutes per operation and after 17 weeks of total operation period, effect size tended to decrease as the operation time and total operation period increased. This was similar to the result of the study that there was no clear linear relationship between total time provided for intervention and effect on cognitive function in a systematic review of CS conducted in subjects with dementia (10). Cognitive functions such as concentration and attention of the elderly, due to aging, tend to decrease over time (1, 27). This could be resulted in decrease in effect of cognitive-based intervention though duration of the intervention was increased. On the other hand, among literatures included in the meta-analysis, average dropout rate was 11.2% in studies conducted over 17 weeks, and the reasons for dropout were lack of time, loss of interest, admission to facilities, and other health reasons. It is possible that these factors also affected effectiveness of intervention period. Through this, it can be seen that when planning cognition-based intervention, time per session should be considered higher than the total cumulative time.

When designing cognitive-based intervention based on the results of this study, it seems necessary to consider one session to be 60 minutes and total operation period to be 16-17 weeks.

Factors to consider when developing intervention program include easy training, cost, long-term sustainability of the program, and adverse effects of intervention (19). Although there is no strong evidence for the cost-effectiveness of cognitive-based intervention, there were reports that annual medical expenditures for subjects who received CT have decreased (28), CS is likely to be cost-effective compared to usual care provided in nursing homes or day care centers, and that CR can also reduce patient's health care costs (10). As a result of this study, individual studies that conducted CT using a commercially developed computer program reported adverse effects such as headache, dizziness, and fatigue, but no adverse effects were reported in CS. CS, compared to CT or CR, is an intervention program that can be easily implemented in daily life without any special structural form. There is a broad consensus that staffs who provide CS do not require professional qualifications, and CS can be implemented in various situation (10). Considering all of the results discussed above, it seems necessary to use CS first in terms of cognitive-based intervention which is continuously accessible. On the other hand, given the situation that CT and CR, compared to CS, needs to evaluate the subject's condition, it is recommended that professional personnel who have received specialized and structured training on program perform CT and CR (29).

The strength of this study is that the number of individual effects as well as RCTs included in the meta-analysis is large, and that range of heterogeneity through subgroup analysis is 0-65% which is not high. Even in cases of high heterogeneity in meta-analysis, if the number of included studies is large, strict confidence interval can be obtained near estimate of random effect on average effect (25). For the elderly, change in their home resi-

dence may cause problems such as anxiety, depression, and social disconnection, which can negatively affect psychosocial well-being and survival (15, 30). Based on this, it is another strength of this study that it showed scientifically valid and robust results in estimating the overall effect size by sensitivity analysis of studies where the subject's residence is not the community and studies with high risk of bias.

Since depression and cognitive decline affect each other and are in organic relationship (31), the effect of cognitive-based intervention on depression needs to be investigated as well. However, due to the lack of research on depression and other variables, it was not possible to conduct a subgroup analysis of the elderly in the 3 group. Therefore, further studies on these are needed.

Conclusion

Cognitive-based interventions have been shown to be effective in improving cognitive function in older adults. CS and CT showed similar effects in the elderly with healthy cognition and those with MCI, and CS showed the greatest effect in the elderly with dementia. Therefore, even if the level of cognitive function of the older adults varies, cognitive-based intervention will be an effective approach. In addition, it will be possible to apply more effective types of cognitive-based interventions according to the cognitive levels. CS has the advantage that it can be easily applied to all elderly people. CT and CR will require additional efforts to train professionals who can plan and implement them in the nursing field. Evidence on the components of the intervention, including the type, dose, and delivery of intervention, will be helpful in nursing practice.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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