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Cognitive Stimulation as a Therapeutic Modality for Dementia: A Meta-Analysis

Kayoung Kim[1], Ji Won Han[2], Yoonseop So[3], Jiyeong Seo[4], You Joung Kim[2], Joon Hyuk Park[5], Seok Bum Lee[6], Jung Jae Lee[6], Hyun-Ghang Jeong[7], Tae Hui Kim[8], and Ki Woong Kim[1,2,9,10] ✉

[1]Department of Geriatric Psychiatry, National Center for Mental Health, Seoul, Republic of Korea
[2]Department of Neuropsychiatry, Seoul National University Bundang Hospital, Seongnam, Republic of Korea
[3]Department of Psychiatry, Evergreen Hospital, Goyang, Republic of Korea
[4]Department of Psychiatry, Changwon Gyeongsang National University Hospital, Changwon, Republic of Korea
[5]Department of Neuropsychiatry, Jeju National University Hospital, Jeju, Republic of Korea
[6]Department of Psychiatry, Dankook University Hospital, Cheonan, Republic of Korea
[7]Department of Neuropsychiatry, Korea University Guro Hospital, Seoul, Republic of Korea
[8]Department of Psychiatry, Wonju Severance Christian Hospital, Wonju, Republic of Korea
[9]Department of Psychiatry, Seoul National University College of Medicine, Seoul, Republic of Korea
[10]Department of Brain and Cognitive Science, Seoul National University College of Natural Sciences, Seoul, Republic of Korea

Objective Although cognitive stimulation (CS) is one of the most popular non-pharmacological interventions for people with dementia, its efficacy is still debatable. We performed a meta-analysis of randomized controlled trials (RCTs) on the efficacy of CS in people with dementia.

Methods Data sources were identified by searching PubMed, MEDLINE, Embase, psychINFO, and Cochrane Reviews Library. A total of 7,354 articles were identified, and of these, 30 RCTs were selected based on the selection criteria. Of these 30 RCTs, 14 were finally included in our meta-analysis [731 participants with dementia; 412 received CS (CS group) and 319 received usual care (control group)].

Results We found that the people with dementia had a moderate benefit from CS. The mean difference between the CS and control groups was 2.21 [95% CI (0.93, 3.49), Z=3.38, p=0.00007] in the Alzheimer's Disease Assessment Scale-Cognition and 1.41 [95% CI (0.98, 1.84), Z=6.39, p<0.00001] in the Mini-Mental State Examination. CS also improved quality of life in people with dementia [95% CI (0.72, 3.38), Z=3.02, p=0.003].

Conclusion CS is effective for improving cognition and quality of life in people with dementia; however, its effects were small to moderate.

Psychiatry Investig 2017;14(5):626-639

Key Words Cognitive stimulation, Dementia, Meta-analysis, Cognition, Quality of life.

INTRODUCTION

Dementia has become one of the most challenging global health problems. The number of people with dementia has been estimated to be 35.6 million, and the number has been predicted to double every 20 years and reach 115.4 million by 2050.[1] In Korea, one of the most rapidly aging countries in the world, the number of people with dementia is expected to double every 17 years.[2] People with dementia show gradual but progressive loss of cognition, and more than half of the people with dementia experience behavioral and psychological symptoms (BPSD).[3] These people need supervision or support for their instrumental and basic activities of daily living (ADL). Caregivers of people with dementia experience physical, emotional, and financial burdens. The efficacy of cholinesterase inhibitors for dementia has been reported to be limited,[4-6] and there is currently no cure for dementia. The importance of non-pharmacological interventions for people with dementia has increased.

Non-pharmacological interventions in combination with pharmacotherapies have been widely used in the management of people with dementia.[7,8] Neural plasticity and capacity for

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✉ **Correspondence:** Ki Woong Kim, MD, PhD
Department of Neuropsychiatry, Seoul National University Bundang Hospital, 82 Gumi-ro 173-gil, Bundang-gu, Seongnam 13620, Republic of Korea
Tel: +82-31-787-7432, **Fax:** +82-31-787-4058, **E-mail:** kwkimmd@snu.ac.kr

cognitive-deficit compensation may underlie the efficacy of non-pharmacological interventions.[9] Cognitive stimulation (CS) is one of the most popular non-pharmacological interventions for people with dementia.[10] It is usually provided in a group and more flexible than cognitive training as it does not have to match specific therapeutic modalities. Several previous studies reported that CS may delay functional impairments[11,12] and improve quality of life (QoL)[13-15] in people with dementia. The Scottish Intercollegiate Guidelines Network (SIGN) recommends the application of CS to people with dementia in the UK.[16] However, the therapeutic efficacy of CS in people with dementia has been in controversy because of the diversity of outcome measures and definition of CS employed in previous clinical trials. Several studies on CS were not clear with regard to the concepts of "training," "stimulation," and "rehabilitation."

We performed a meta-analysis to investigate the effectiveness of CS on cognition, BPSD, mood, ADL, and QoL in people with dementia. In this meta-analysis, we defined CS as "an engagement in a range of activities and discussions aimed at general enhancement of cognitive and social functioning" proposed by Clare et al.[11,17,18]

METHODS

We followed the meta-analysis guidelines corroborated by the National Evidence-based Health Care Collaborating Agency (NECA), Korea.[19]

Inclusion criteria of the studies

The study flow chart is presented in Figure 1. This meta-analysis focused on RCTs that provided relevant statistical information. Only studies published in English were considered for inclusion. The following criteria were considered: 1) participants had a diagnosis of dementia; 2) all levels of dementia severity that were indicated through group mean scores, range of scores, or individual scores using standardized scales, such as the Mini-Mental State Examination (MMSE)[20] and Clinical Dementia Rating (CDR),[21] were included; 3) data from family

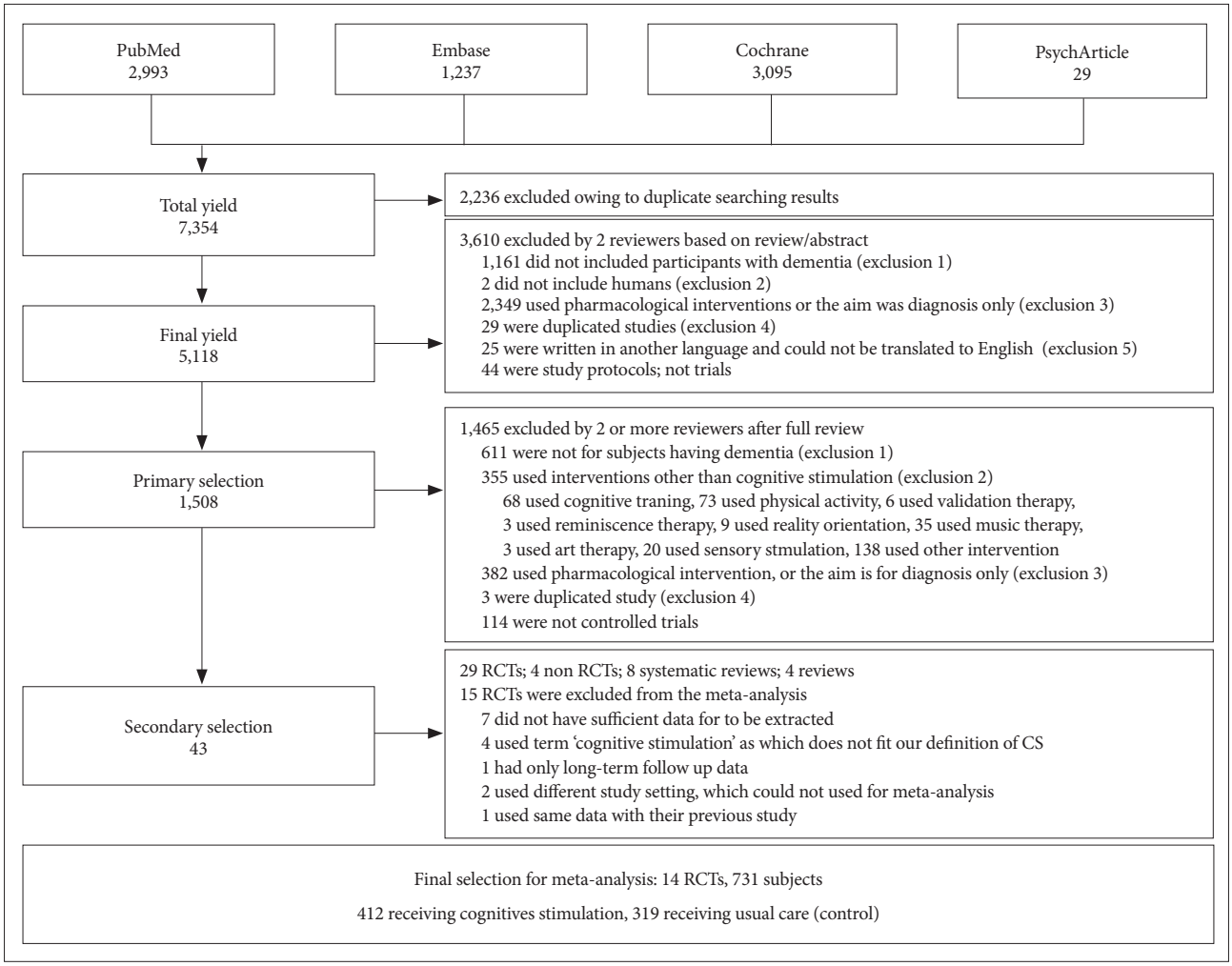

Figure 1. Flowchart of the study selection procedure in this meta-analysis.

members or caregivers were not included; 4) age of the participants and type of dementia were not limited; and 5) the number of participants taking cognitive enhancers was mentioned if necessary.

We considered CS as "an engagement in various activities and discussions (usually in a group) aimed at general enhancement of cognitive and social functioning," according to the definition proposed by Clare et al.[11] We regarded "no treatment," "usual care," and "standard treatment" as controls. The term 'no treatment' was cognitive enhancer, clinic consultations, or contact with mental health team without any structured intervention that could be normally provided in usual treatment settings. There were no restrictions on the duration of interventions or the number of sessions. However, these values were noted.

The following variables were considered as outcome measures for the analyses: 1) the MMSE, Alzheimer's Disease Assessment Scale-Cognition (ADAS-Cog),[22] Montreal Cognitive Assessment (MoCA),[23] or other cognition assessment measures for cognitive impairment associated with global cognitive function; 2) self-reported function, clinically rated function, or caregiver-reported function measures for mood; 3) caregiver-reported function or clinically-rated function measures for behavioral and psychological symptoms; 4) self-reported function or caregiver-reported function measures for QoL, such as the QoL scale in Alzheimer's disease (QoL-AD)[24]; and 5) self-reported function or caregiver-reported function measures for ADL.

Search methods for the identification of studies

We searched the electronic medical databases PubMed, MEDLINE (1966 to April 2015), Embase (1980 to April 2015), psychINFO (1887 to April 2015), and Cochrane Reviews Library (1982 to April 2015) for all relevant English articles. Because of the ambiguity regarding interventions, we selected multiple keywords to improve sensitivity. First, medical subject heading (MeSH) terms were used for literature search, including CS, cognitive rehabilitation, cognitive training, cognitive rehabilitation program, cognitive therapy, nonpharmacological, memory training, exercise, physical activity, music therapy, art therapy, horticulture therapy, occupational therapy, validation therapy, reality orientation, and reminiscence. We then used the Boolean operation (OR) for sensitive search. The search strategies were as follows:

#1 Search (dementia) OR mild cognitive impairment

#2 Search ((((((((((((((cognitive rehabilitation) OR (cognitive stimulation) OR cognitive training) OR cognitive rehabilitation program) OR cognitive therapy) OR nonpharmacological) OR memory training) OR exercise) OR physical

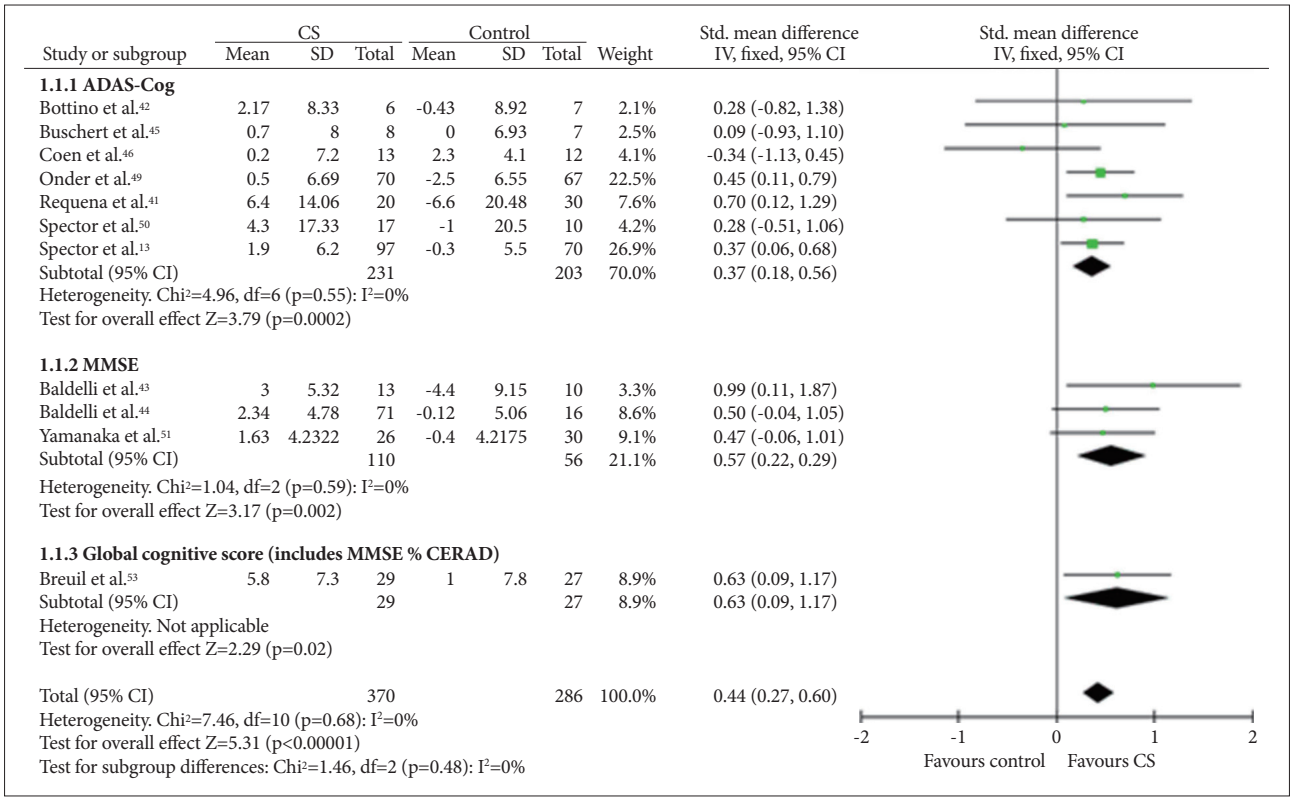

Figure 2. Cognitive stimulation versus no cognitive stimulation. Outcome: global cognition (overall). SD: standard deviation, Std. mean difference: standardized mean difference, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

Table 1. Main characteristics of the included studies

Study	Type of intervention	Control setting	Frequency (session/ week)	Duration	Note	Diagnosis	Total (N)	Active therapy (N)	Control (N)	Nationality	Mean age (standard deviation/ range)	Education (standard deviation)	Baseline MMSE score
Baines et al.[64]	Reality orientation reminiscence	Treatment as usual	5 sessions/ week	4 weeks	30 minutes	"Moderate to severe impairment of cognitive functioning"	15 (M 1, F 14)	5	5	UK	81.5 (range 72–90)		
Baldelli et al.[43]*	Reality orientation therapy	Treatment as usual		3 months		AD	23 (M 0, F 23)	13	10	Italy	84.5 (6.4)		20.6 (4.9)
Baldelli et al.[44]*	Reality orientation therapy	Physical rehabilitation				Dementia	87	71	16	Italy	79.6		
Ballard et al.[34]	Donepezil+ Brief psychosocial therapy	Placebo+brief psychosocial therapy	1 session/ week	4 weeks	week 1: 1 hour week 2, 3: 15 minutes week 4: 30 minutes	AD	198			UK			
Bottino et al.[42]*	"Cognitive rehabilitation"+ rivastigmine	Treatment as usual	1 session/ week	5 months	2	Mild probable AD	13 (M 4, F 9)	6	7		73.7 (range 62–83)		22.31
Breuil et al.[53]*	Cognitive stimulation	Treatment as usual	2 sessions/ week	5 weeks	1 hour per session	Dementia	61 (M 24, F 37)	32	29	France	77.1 (7.1)		
Buettner et al.[27]	Classroom-style mentally stimulating activities	Structured early-stage social support				Dementia	77 (M 15, F 61)	48	29	America	81.5	14.6 (3.6)	25.3 (3.1)
Buschert et al.[45]*	Multi-component cognitive group intervention	Pencil and paper exercises (self-study)	1 session/ week	6 months (20 sessions)	2 hours per session	24 amnestic MCI; 15 mild AD	39				75.9 (8.1)		24.9 (1.6)
Chapman et al.[38]	Cognitive-communication stimulation program plus donepezil	Donepezil only	1 session/ week	8 weeks	90 minutes per session	Mild to moderate AD	54 (M 25, F 29)	26	29	America			

Table 1. Main characteristics of the included studies (continued)

Study	Type of intervention	Control setting	Frequency (session/ week)	Duration	Note	Diagnosis	Total (N)	Active therapy (N)	Control (N)	Nationality	Mean age (standard deviation/ range)	Education (standard deviation)	Baseline MMSE score
Cheng et al.[33]	Cognitive stimulation (Mahjong)	Treatment as usual	3 sessions/ week	12 weeks	1 hour per session	Dementia	71	36	35	China	Active 81.9 (6.2); control 80.9 (7.2)		Active 19.0 (3.2); control 18.9 (4.1)
Cohen-Mansfield[28]	Nonpharmacological treatment: treatment routes for exploring agitation	Placebo intervention		10 days	4 hours per session	Dementia	167 (M 33, F 134)	89	78	America	Active 88.0 (6.4); control 85.0 (8.6)		Active 7.26 (6.0); control 6.88 (6.5)
Ferrario et al.[52]*	Reality orientation therapy	Treatment as usual	5 sessions/ week	21 weeks	60 minutes per session	Dementia	19 (M 8, F 11)	13	6		82.5 (5.2)		Range 18–25
Coen et al.[46]*	Cognitive stimulation therapy	Treatment as usual	2 sessions/ week	7 weeks	45 minutes per session	Dementia	27 (M 13, F 14)	14	11	Ireland	79.8 (5.6)		16.9 (5.0)
Garland et al.[35]	Simulated family presence	Preferred music; placebo (neutral audiotape)				Dementia				Australia			
Ishizaki et al.[47]*	RO, reminiscence therapy, group therapy, brief systemic therapy	Treatment as usual	1 session/ week	6 months		Dementia	25 (M 10, F 15)	14	11	Japan	75.9 (6.9)	8.4 (1.8)	26.4 (2.8)
Kolanowski et al.[29]	Cognitive stimulation	Treatment as usual				Mild to moderate dementia	16	11	5	America	88.4 (4.9)		
Lam et al.[30]	Case management; home visit, phone calls	One home visit for home safety (usual care)				Mild dementia	102 (M 43, F 59)	59	43	Hong Kong	Active 78.6 (6.4); control 78.2 (5.4)		Active 17.6 (5.2); control 18.0 (5.1)

Table 1. Main characteristics of the included studies (continued)

Study	Type of intervention	Control setting	Frequency (session/ week)	Duration	Note	Diagnosis	Total (N)	Active therapy (N)	Control (N)	Nationality	Mean age (standard deviation/ range)	Education (standard deviation)	Baseline MMSE score
Niu et al.[48]*	Cognitive stimulation therapy	Communication exercise				AD	32 (M 25, F 7)	16	16	China	Active 80.56 (4.23); control 79.13 (4.38)	Active 10.56 (1.90); control 10.81 (1.87)	Active 16.93 (3.02); control 17.31 (3.24)
Onder et al.[49]*	Reality orientation therapy combined with cholinesterase inhibitors	Treatment as usual				AD	156 (M 43, F 113)	79	77	Italy	Total 75.8 (7.1) Active 75.7 (7.8); control 75.8 (6.3)	7.3 (3.8)	Active 20.2 (3.3); control 19.9 (3.0)
Poon et al.[39]	Cognitive intervention using a video-conferencing system	Cognitive intervention using a face-to-face system				AD	22	11	11	Hong Kong			
Quayhagen et al.[37]	Active cognitive stimulation	Placebo (passive cognitive stimulation); wait-list control	6 sessions/ week	12 weeks	Total 72 sessions	Probable AD	78 (M 51, F 27)	25	28 (wait-list control: 25)	America			
Quayhagen and Quayhagen[36]	Study 1: active cognitive stimulation:	Study 1: Placebo treatment (passive activities)				AD	56 (M 44, F 12)			America			
Quayhagen and Quayhagen[36]	Study 2: active cognitive stimulation	Study 2: waiting list				AD	30 (M 19, F 11)			America			
Requena et al.[41]*													
Quayhagen and Quayhagen[36]	Combined drug and cognitive stimulation treatment	Only drug				AD	36	14	20	Spain	Active 74.20 (7.81); control 78.80 (6.62)		Active 22.95 (5.01); control 21.17 (7.56)

Table 1. Main characteristics of the included studies (continued)

Study	Type of intervention	Control setting	Frequency (session/ week)	Duration	Note	Diagnosis	Total (N)	Active therapy (N)	Control (N)	Nationality	Mean age (standard deviation/ range)	Education (standard deviation)	Baseline MMSE score
Requena et al.[41]*	Combined drug and cognitive stimulation treatment	Only drug				AD	36	14	20	Spain	Active 74.20 (7.81); control 78.80 (6.62)		Active 22.95 (5.01); control 21.17 (7.56)
	A.G.E. program (Activity program, guidelines for psychotropic medications, and educational rounds)	Treatment as usual				Dementia	81	42	39	America	Active 82.0 (8.0); control 81.2 (7.2)		Active 9.1 (7.4); control 8.9 (6.1)
Spector et al.[50]*	Cognition-based therapies	Usual care				Dementia	27	17	10	UK			
Spector et al.[13]*	Cognitive stimulation therapy	Treatment as usual				Dementia	201	115	86	UK	85.3 (6.9)		14.5 (3.9)
Spector et al.[12]	Cognitive stimulation therapy	Usual activities				Dementia	201	115	86	UK	85.3 (6.9)	11.5	14.5 (3.9)
Wallis et al.[32]	Reality orientation therapy	A variety of group and individual activities	5 sessions/ week	3 months	30 minutes per session	Dementia	38	18	20	UK	71.8 (16.6)		
Woods[40]	Reality orientation	Social therapy groups (usual care)	5 sessions/ week	20 weeks	30 minutes per session	Dementia	18	5	5		76.6 (range 61−90)		
Woods et al.[14]	Cognitive stimulation therapy	Treatment as usual	2 sessions/ week	7 weeks	45 minutes per session	Moderate to severe dementia	201			UK	85.3		14.4 (3,8)
Yamanaka et al.[51]*	Japanese version of group cognitive stimulation therapy (CST-J)	Treatment as usual	2 sessions/ week	7 weeks	45 minutes per session	Moderate to severe dementia	56 (M 12, F 44)	26 (M 6, F 20)	30 (M 6, F 24)	Japan	83.91 (5.98) Active 84.12 (5.52); control 83.73 (6.44)		Active 17.00 (0.83); control 16.87 (0.77)

Each asterisks represents included studies. For Requena 2006, the no treatment group was excluded owing to non-randomization; therefore, comparisons were only performed for CS+drug

activity) OR music therapy) OR art therapy) OR horticulture therapy) OR occupational therapy) OR validation therapy) OR reality orientation) OR reminiscence))))))))))))))

#3 Search #1 and #2 filters: Clinical trial; Controlled clinical trial; Randomized controlled trial; Systematic reviews; Humans

To identify additional studies, reviews were hand-searched for both published and unpublished trials, and the authors were contacted if required.

Data collection and analysis

Primary selection was performed by reviewers independently based on the abstract. Then, secondary selection was performed by all researchers after full review. Regular consensus meetings were held to select studies according to the inclusion criteria. Studies were excluded if 1) the subjects were cognitively normal or had other neurological disorders that did not meet the criteria of dementia (DSM-IV-TR)[25]; 2) subjects were not human; 3) interventions were non-pharmacological methods that did not involve CS or were pharmacological methods; 4) the study was a duplicate publication; and 5) we could not find the original abstract or article, or we could not translate the study to English. The reviewers used a standardized abstracted form adapted from the Korean National Evidence-based Health Care Collaborating Agency (NECA) 19. All included studies were reviewed and graded according to the risk of bias checklist, using the Cochrane approach (risk of bias table) (Figure 2).

The meta-analysis was performed using the software RevMan (Review Manager) Version 5.2. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012). In most cases, summary effects were computed using a fixed-effects model, because the studies had similar settings and methodologies, and this approach provides more conservative result than a random-effects model. However, the random-effects model was used when statistical heterogeneity was proven by a Higgins' I-squared value of over 50% between studies.[19,26] We did not consider the long-term effects of interventions. Effect sizes were analyzed as standardized mean differences (SMDs), and Cohen's d was used with 95% confidence intervals (CIs) for comparisons between the active treatment (CS) and control (usual care) groups.

RESULTS

We identified a total of 7,354 articles in the literature search, and after deleting duplicate publications, 5,118 articles remained. After performing the processes of elimination, we identified 29 RCTs involving CS that met our inclusion criteria. Among these studies, 15 studies were excluded; seven studies did not have sufficient data for extraction,[27-33] four studies employed different definition of CS,[34-37] one study provided long-term follow-up data only,[38] two studies compared the efficacy between two different types of CS,[39,40] and one study[14] shared the same dataset with their previous study.[13] For Requena 2006,[41] the 'no treatment' group was excluded owing to non-randomization; therefore, comparisons were only performed for CS+drug. Finally, 14 studies were included in this meta-analysis.[13,41-53] From these studies, we identified 731 participants [412 re-

Table 2. Excluded studies

Study	Reason for exclusion
Ballard et al.[34]	Open trial, pre-post evaluation; not a randomized case-control study
Buettner et al.[27]	Controls used structured intervention
Chapman et al.[38]	Follow-up study only; did not fit our study setting
Cheng et al.[33]	Eligible, but extractable data were limited
Cohen-Mansfield[28]	Eligible, but extractable data were limited
Garland et al.[35]	Intervention did not meet the definition of cognitive stimulation; mainly used music as a therapeutic modality
Kolanowski et al.[29]	Review only; no extractable data
Lam et al.[30]	Eligible, but extractable data were limited
Poon et al.[39]	Active group and control group used cognitive stimulation
Quayhagen et al.[37]	Intervention did not meet the definition of cognitive stimulation; more suitable for cognitive training than cognitive stimulation
Quayhagen and Quayhagen[36]	Intervention did not meet the definition of cognitive stimulation; more suitable for cognitive training than cognitive stimulation
Rovner et al.[31]	Extractable data were limited; statistics were not fully presented for the control group
Walllis et al.[32]	Eligible, but extractable data were limited
Woods[40]	Active group and control group used cognitive stimulation
Woods et al.[14]	Reported on Spector 2003 study results

ceived CS and 319 used usual care (control)]. Further information on the included and excluded studies is presented in Table 1 and 2.

Efficacy for cognition

Data on cognition were available in 12 studies,[12,13,41-46,49-51,53] which included 370 participants who received CS and 286 who received usual care. The SMD between the CS and control groups was 0.44 [95% CI (0.27, 0.60)], and this value was statistically significant (fixed effect, Z=5.31, p<0.00001, I-square=0%) (Figure 2). As most of the studies used more than one outcome measure, analysis was performed on the most comprehensive measure. In seven studies that used the ADAS-Cog (Figure 3), the mean difference between the CS and control groups was 2.21 [95% CI (0.93, 3.49)], and this value was statistically significant (fixed effect, Z=3.38, p=0.00007, I-square=33%). In 11 studies that used the MMSE (Figure 4), the mean difference between the CS and control groups was 1.41 [95% CI (0.98, 1.84)], and this value was statistically significant (fixed effect, Z=6.39, p<0.00001, I-square=9%). However, we could not confirm the effectiveness of CS for specific cognitive domains as only one study reported on such effectiveness of CS.[12] In that study, the improvement in language subscale (commands and spoken language items) was significantly better in the CS group than in the control group.

Behavior and psychological symptoms (BPSD)

Six studies[13,46,48-50,52] that included a total of 409 participants provided data on BPSD. Among these studies, three studies[13,46,50] used the Clifton Assessment Procedures for the Elderly (CAPE),[54] two[48,49] used Neuropsychiatric Inventory (NPI),[55] and one[52] used the irritability and withdrawal subscales of the Multidimensional Observation Scale for Elderly Subjects (MOSES)[56] (Figure 5). Quantitative analysis did not show any benefit of CS for the BPSD measures [random effect, SMD=0.32, 95% CI (-0.06, 0.70), Z=1.67, p=0.10].

Mood

Six studies[41,43-46,52] that included a total of 220 participants provided data on mood, and all described depression as a

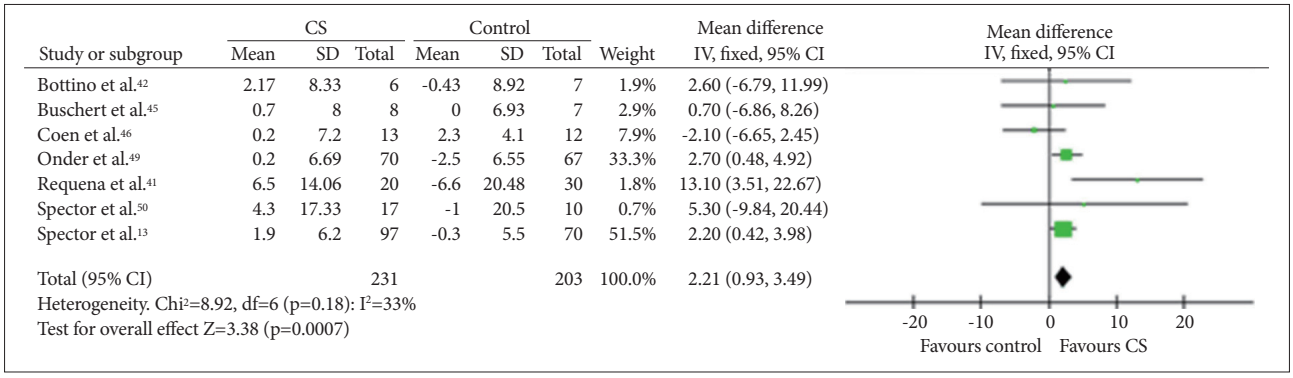

Figure 3. Cognitive stimulation versus no cognitive stimulation. Outcome: Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog). SD: standard deviation, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

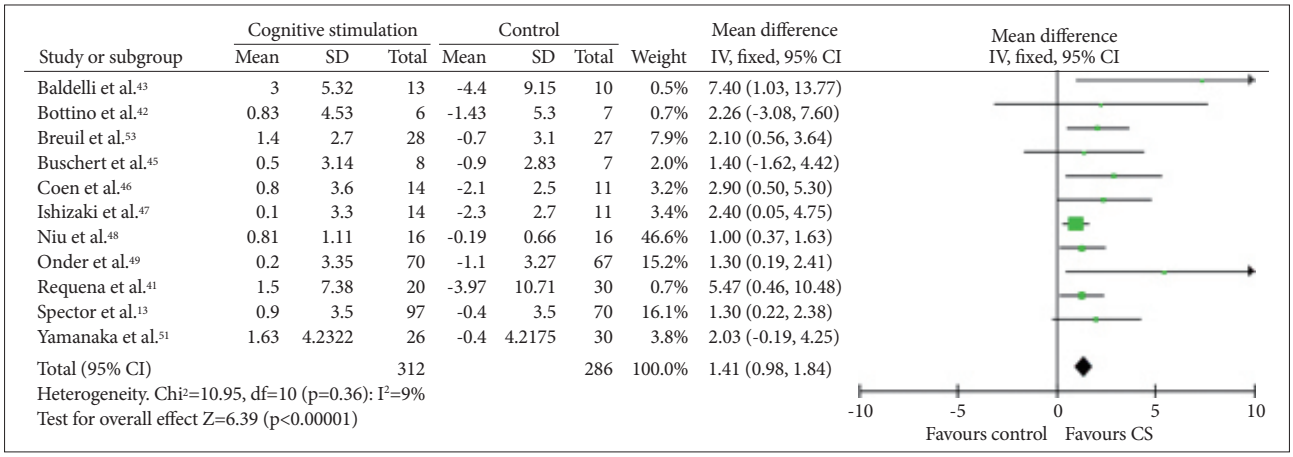

Figure 4. Cognitive stimulation versus no cognitive stimulation. Outcome: MMSE. SD: standard deviation, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

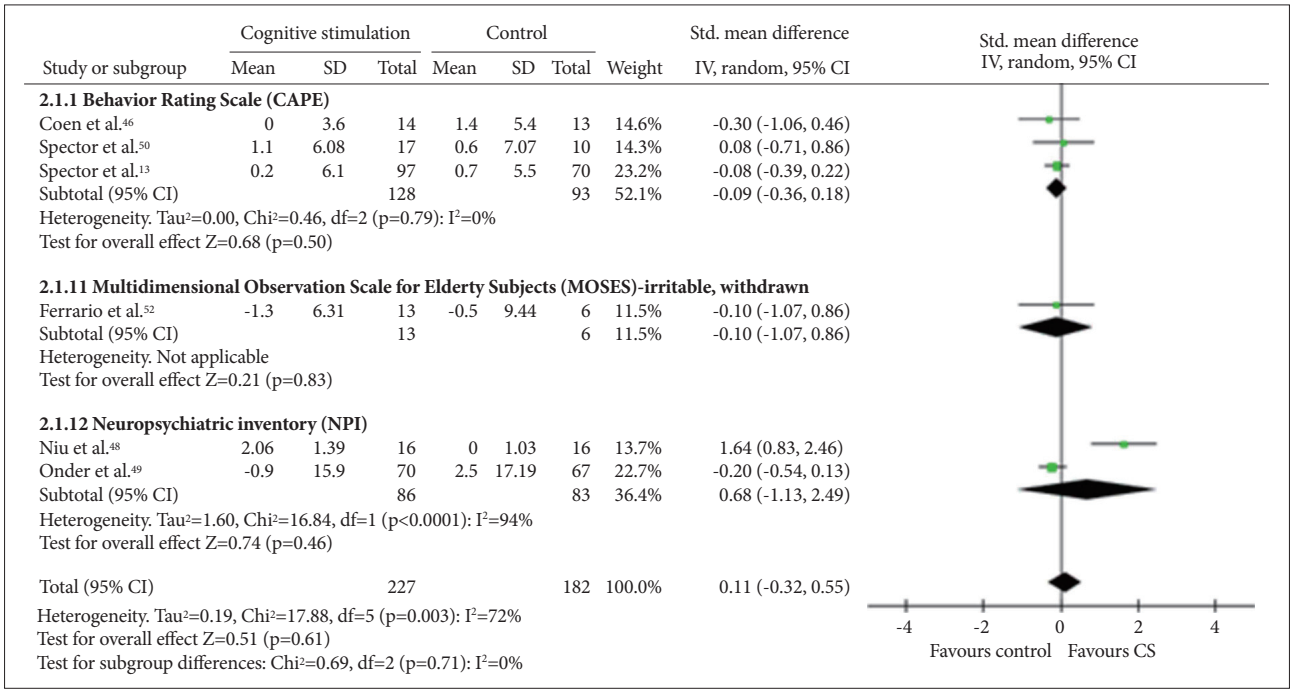

Figure 5. Cognitive stimulation versus no cognitive stimulation. Outcome: behavioral and psychological symptoms. SD: standard deviation, Std. mean difference: standardized mean difference, IV, random: a ramdom-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

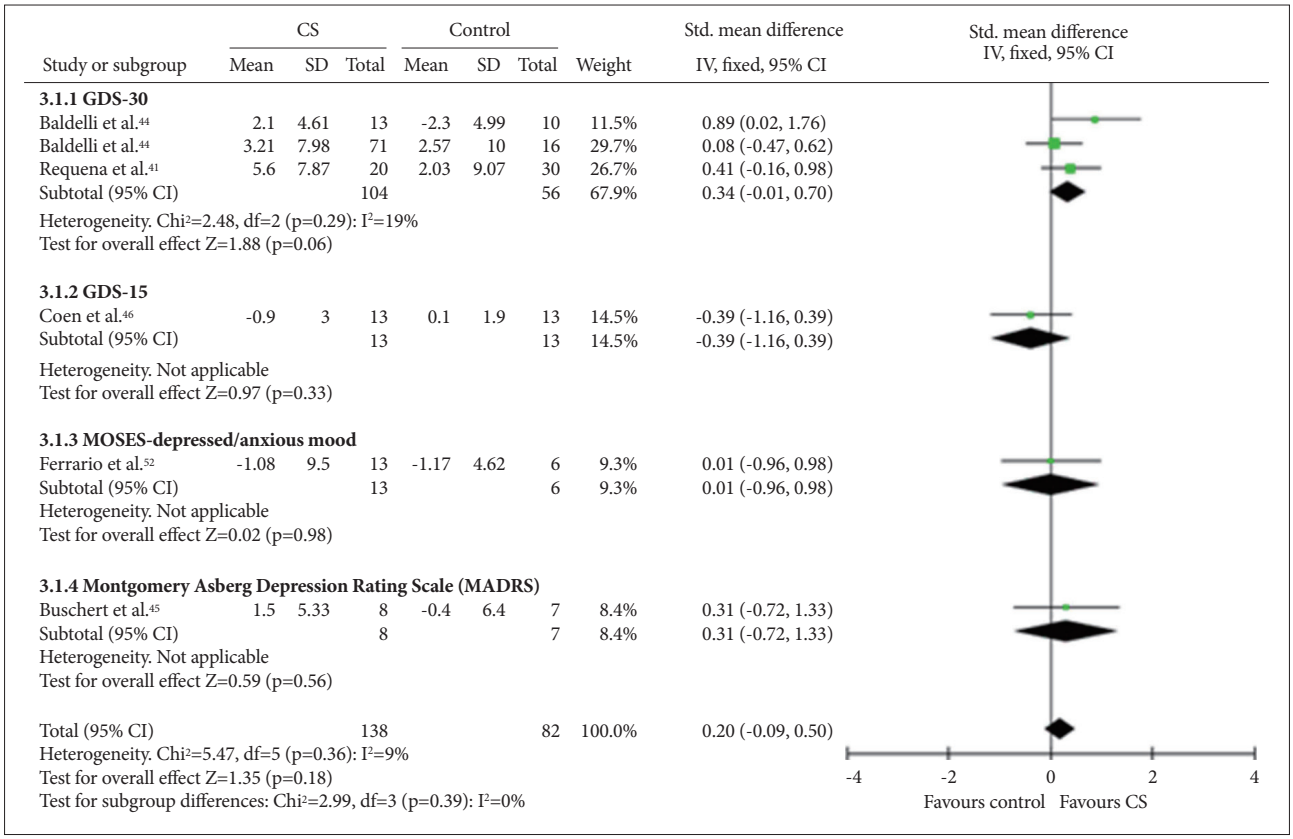

Figure 6. Cognitive stimulation versus no cognitive stimulation. Outcome: mood. SD: standard deviation, Std. mean difference: standardized mean difference, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

mood symptom. Among these studies, three studies[41,43,44] used the 30-item Geriatric Depression Scale (GDS-30),[57] one 46 used the 15-item GDS (GDS-15),[58] one 45 used the Montgomery-Asberg Depression Rating Scale (MADRS), and one[52] used the depressed/anxious mood subscales of the MOSES (Figure 6). Quantitative analysis did not show any benefit of CS for the mood measures [fixed effect, SMD=0.20, 95% CI (-0.09, 0.50), Z=1.35, p=0.39].

Quality of life (QoL)

Four studies[45,46,50,51] that included a total of 265 participants provided data on QoL. All these studies used the QoL-AD (Figure 7). Quantitative analysis showed that CS was beneficial for QoL in people with dementia [fixed effect, SMD=2.05, 95%

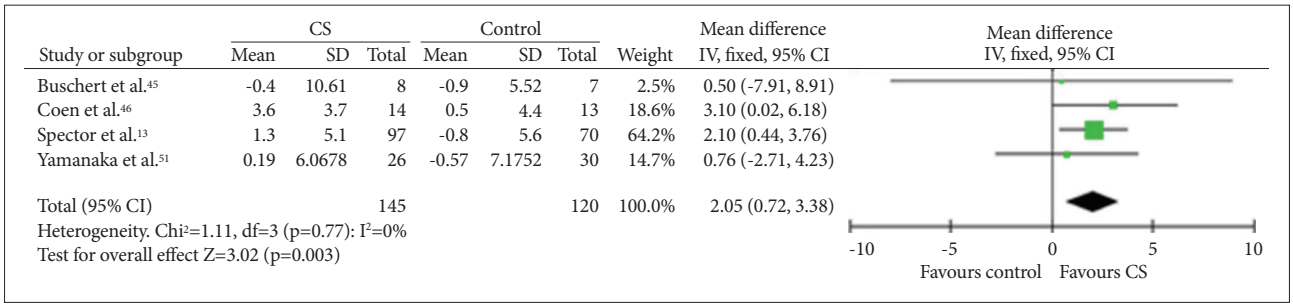

Figure 7. Cognitive stimulation versus no cognitive stimulation. Outcome: Quality of life. SD: standard deviation, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

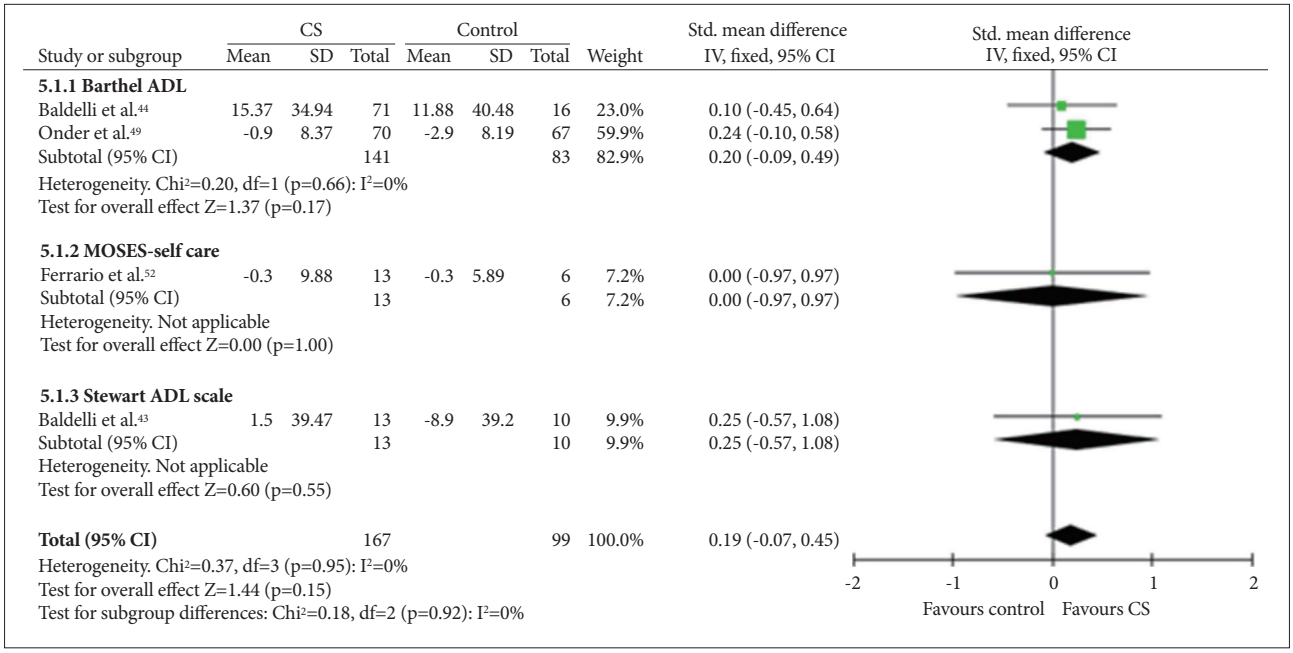

Figure 8. Cognitive stimulation versus no cognitive stimulation. Outcome: ADL. SD: standard deviation, Std. mean difference: standardized mean difference, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

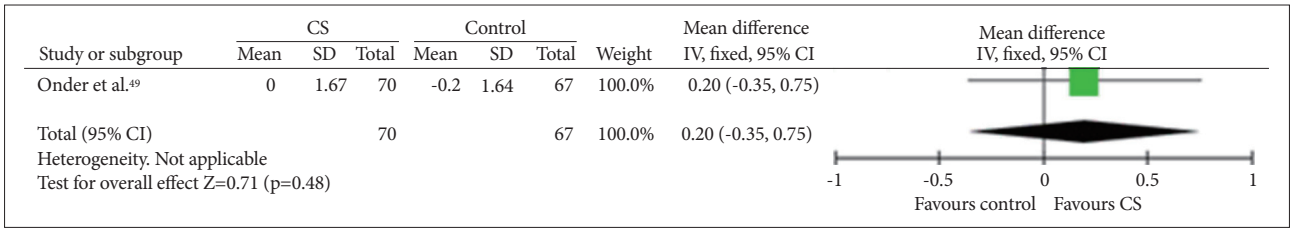

Figure 9. Cognitive stimulation versus no cognitive stimulation. Outcome: Instrumental ADL. SD: standard deviation, IV, fixed: a fixed-effects meta-analysis with inverse variances weights, CI: confidence interval, df: degrees of freedom, tau² and I²: heterogeneity values, Chi²: Chi-square test value, Z: Z-value as the overall effect, p: p-value.

CI (0.72, 3.38), Z=3.02, p=0.003].

ADL and instrumental ADL

Three studies[43,44,52] measured only basic ADL, and one study[49] measured both basic and instrumental ADL (Figures 8 and 9). Quantitative analysis did not show any benefit of CS for basic ADL measures [fixed effect, SMD=0.19, 95% CI (-0.07, 0.45), Z=1.44, p=0.92]. Quantitative analysis for instrumental ADL was not possible because only one study assessed instrumental ADL and there was no significant difference in improvement between the study groups.

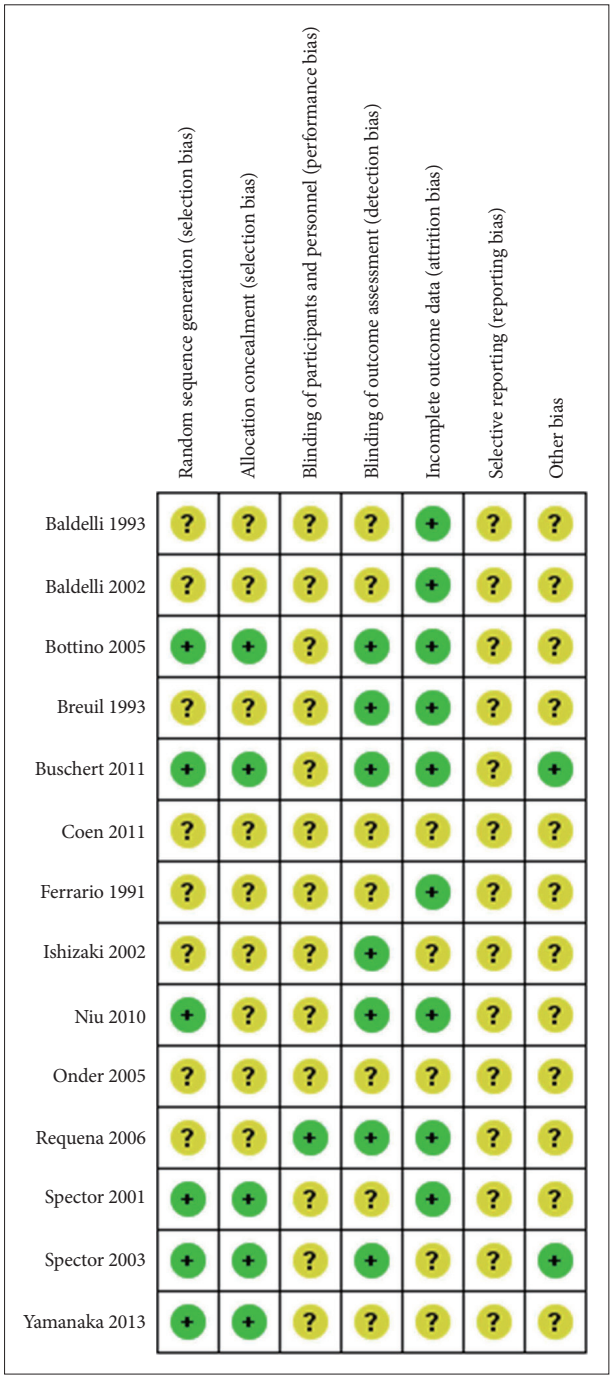

Figure 10. Risk of bias summary: Review of authors' judgments about each risk of bias item for each included study.

DISCUSSION

In this meta-analysis, CS was found to be effective for improving global cognition (1.80 points in the ADAS-Cog and 2.60 in the MMSE). The MMSE score has been reported to decline by 2–4 points annually in mild and moderate dementia patients.[17] Although the improvement in global cognition with CS was not associated with a significant improvement in ADL, the findings portrayed an optimistic view of CS as a standard non-pharmacological therapy for dementia. Although it is yet not fully understood how CS preserves cognitive function in people with dementia, maintaining mental activities may protect against cognitive decline[59,60] by facilitating brain plasticity, proliferation and survival of hippocampal neurons,[61] and the enlargement of the brain and/or cognitive reserve.[62] In the present study, we could not perform a meta-analysis on the effectiveness of CS for each specific cognitive domain owing to the insufficient number of studies. However, in some previous studies,[47,50] CS was effective in improving commands and spoken language.

Maximizing QoL in people with dementia is one of the major goals in the management of dementia. As QoL in people with dementia is important to family caregivers and health service providers, as well as the people with dementia themselves, QoL is often included as an outcome measure in clinical trials on dementia.[63] In the present study, although the effect size was small to moderate, we found that CS significantly improved the QoL-AD scores in people with dementia. Interventions that can enhance cognition have been reported to improve the sense of well-being and the QoL in people with dementia.[30]

In this study, CS was not beneficial for improving mood and BPSD, as in a previous Cochrane review.[17] However, these results do not necessarily indicate that CS may not be helpful at all for improving mood and/or BPSD. The lack of efficacy of CS for mood, and BPSD in the present study may be attributed, at least in part, to the fact that people with dementia having severe mood symptoms or BPSD were excluded from most clinical trials on the efficacy of CS.[53] In addition, some open-label studies have shown the efficacy of CS for mood and/or BPSD in people with dementia. For example, Ballard et al.[34] reported that CS improved the Cohen-Mansfield Agitation Inventory score in people with dementia.

Current study has several limitations. First, most studies included in this meta-analysis had unclear risk of bias (Figure 10). We failed to find truly double-blinded studies in this analysis. The participants and staffs might have been aware of

their treatment condition, which could lead to biased results. Second, there was broad heterogeneity in the study settings and the actual elements of the CS program. Third, the "sham" type of activities that were employed as control or placebo therapy had some components of CS according to the definition of Clare et al.[11] Actually, unorthodox group activities have also been reported to be effective in people with dementia.[17,40,41] Fourth, the studies included in the present meta-analysis did not provide the efficacy of CS according to the type of dementia. The efficacy of CS may not be uniform across different types of dementia. Furthermore, the efficacy of CS has never been studied in rare types of dementia. Fifth, the analyses were insufficient to prove the quantitative therapeutic correlation of CS. Some studies in this analysis did not clearly present the duration and frequency of the intervention. Further research is warranted on the relationship between the intervention and the dose effect.

In conclusion, CS is more effective than usual activities for improving global cognition and QoL in people with dementia.

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