



Original Article

Efficacy of a group-based 8-week multicomponent cognitive training on cognition, mood and activities of daily living among healthy older adults: A two-year follow-up of a randomized controlled trial



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ABSTRACT

Background: Cognitive training (CT) has been one of the important non-pharmaceutical interventions that could delay cognitive decline. Currently, no definite CT methods are available. Furthermore, little attention has been paid to the effect of CT on mood and instrumental activities of daily living (IADL).

Objectives: To assess the effectiveness of a multicomponent CT using a training program of executive functions, attention, memory and visuospatial functions (TEAM-V Program) on cognition, mood and instrumental ADL.

Design: A randomized, single-blinded, treatment-as-usual controlled trial.

Setting: Geriatric clinic in Bangkok, Thailand.

Participants: 80 nondemented community-dwelling older adults (mean age 65.7 ± 4.3 years).

Intervention: The CT (TEAM-V) Program or the treatment-as-usual controlled group. The TEAM-V intervention was conducted over 5 sessions, with a 2-week interval between each session. A total of 80 participants were randomized ($n = 40$ the TEAM-V Program; $n = 40$ the control group).

Measurements: The Thai version of Montreal Cognitive Assessment (MoCA), The Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-cog), Thai version of Hospital Anxiety and Depression Scale (HADS) and The Chula ADL were used to assess at baseline, 6 months, 1 year and 2 years.

Results: Compared with the control arm ($n = 36$), the TEAM-V Program ($n = 39$) was associated with significantly improved general cognition (MoCA, $P = 0.02$) at 2 years. Compared with baseline, participants receiving the TEAM-V Program were associated with significantly improved immediate recall (word recall task, $P < 0.001$), retrieval and retention of memory processes (word recognition task, $P = 0.01$) and attention (number cancellation part A, $P = 0.01$) at 2 years. No training effects on anxiety ($P = 0.94$), depression ($P = 0.093$) and IADL ($P = 0.48$) were detected.

Conclusions: The TEAM-V Program was effective in improving global cognitive function. Even though, the program did not significantly improve anxiety, depression and IADL compared with the control group, memory and attention improved in the intervention group compared with baseline. Further studies incorporating a larger sample size, longitudinal follow-up and higher-intensity CT should be conducted.

1. Introduction

Dementia is a common medical condition among older adults in which the symptoms of cognitive impairment significantly affect daily living and social function [1]. The number of people with dementia would increase from 57.4 million cases in 2019 to 152.8 million cases in 2050 [2]. The clinical trials have focused on nonpharmacologic inter-

ventions to prevent dementia among healthy older adults such as physical activity, social engagement and cognitive training intervention [3]. A large, long-term (2-year follow-up), randomized controlled trial suggested a multidomain intervention including cognitive training could improve or maintain cognitive functioning among older adults [4].

Cognitive training (CT) uses guided practice on a set of tasks related to memory, executive function, attention or other brain functions. The

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goals of training are to improve or maintain ability in specific cognitive domains. This training can take many formats. For example, it can be conducted individually or in group, with either a single, e.g., memory, or multiple, e.g., memory and executive function topics [5]. CT can induce plastic changes at the level of intrinsic activity patterns in older adults without dementia, mainly by modifying neuronal functional connectivity [6].

A recent systematic review showed CT reported improvements in cognitive performance among older participants of CT with or without booster session in long-term studies [7]. In addition, a recent randomized controlled trials revealed multicomponent cognitive training improved logical reasoning compared to the control group up to 12 months [8]. However, the training did not significantly impact global cognition in this study [9].

CT not only improves cognition but also improve instrumental activities of daily living (IADL). For example, the Advanced CT for Independent and Vital Elderly (ACTIVE) study, the first large scale randomized controlled trial, demonstrated significant improvements in cognition such as memory and reasoning, which were sustained for up to 10 years, and showed benefit to IADL [10].

Although several studies proved the beneficial effects of CT among healthy older adults concerning cognition [11], little attention has been paid to the effect of CT on mood, despite depression and anxiety being known to negatively impact cognition and related to early cognitive decline [12]. Interestingly, CT among people at risk of dementia such as depression and/or minor neurocognitive disorder showed improvements in cognitive and mood functions [13]. In addition, a study has revealed CT among older people with minor neurocognitive disorders could protect against a decline in mental abilities such as depression and anxiety [14]. However, some CT Programs used advanced or expensive technology. Furthermore, trainings for healthy older adults in developed countries were mostly computer-based [15] that were difficult to apply to some locations such as rural areas in Thailand.

In Thailand, according from five-year dementia registry data revealed the prevalence of in-patients diagnosed with dementia increased from 15.4 % in 2015 to 21.6 % in 2019. During these 5 years, 59.3 % were dead. Mean cost of expense during admission were 31,52.79 Baht [16]. Therefore, dementia prevention is very importance. However, studies pertaining to CT in Thailand are conducted mostly among older adults with major neurocognitive disorder [17] and for minor neurocognitive disorder [18–21]. CT among healthy older adults were in short-term follow-up [22,23]. A training of executive functions, attention, memory and visuospatial functions (TEAM-V Program) was developed for group-based multicomponent CT. In our related study, at 1 year-follow-up, the program was effective in reducing anxiety. Even though, the program did not significantly improve cognition, depression and IADL compared with the control group, global cognition, memory, attention and executive function improved in the intervention group compared with baseline [24]. Therefore, longitudinal follow-ups could be extended to strengthen the study findings.

The aim of the present study was to assess the effectiveness of a group-based 8-week multicomponent CT using the TEAM-V Program concerning cognition, mood and IADL among healthy older adults over 2 years. The hypothesis was individuals receiving the program would demonstrate improved cognitive function, mood and IADL outcomes or delay their impairment compared with those not receiving the program at 6-months follow-up, 1-year follow-up and up to 2 years.

2. Methods

2.1. Eligibility criteria and recruitment methods

This experimental study is a part of the CT Program among older adults without neurocognitive impairment project, conducted by the research team from The Institute of Geriatrics Medicine, Department of Psychiatry and Geriatrics Medicine Unit at Ramathibodi Hospital and

Outpatients and Family Medicine Department at Phramongkutklao Hospital, Bangkok, Thailand. The required sample size of participants to be included in the study was set at 217, including a drop out of 30 %. This was determined by power calculation with a power of 0.8 and an alpha error of 0.05, based on cognition as the primary outcome and an estimated overall effect size of $f = 0.13$, which also corresponds to the Thai National Dementia Survey [25]. The participants were enrolled from across the four regions of the country. Research sites in each region were led by medical professionals such as geriatrics nurses, receiving training during a 4-day workshop, held in February 2017, by the main research team. The workshop covered both clinical and instrumental assessment of cognitive function and method of delivering the CT Program.

Participants in this study were from the central region of Thailand; we recruited 98 participants who visited the Geriatric Clinic, Outpatient Department, Phramongkutklao Hospital, Bangkok, Thailand between April and May 2017. The enrolled participants were aged > 60 years and willing to participate in all 5 activities. The exclusion criteria were: Thai version of Hospital Anxiety and Depression Scale (HADS) higher than 11 on anxiety or depression [26], Thai version of Montreal Cognitive Assessment (MoCA) less than 26 [27], presenting any conditions affecting participation in program activities, e.g. balancing problems, hearing impairment as well as any psychiatric diseases and neurologic problems such as stroke. This study was approved by the Institutional Review Board of the Royal Thai Army Medical Department Ethics Committee as instituted (IRBRTA 599/60) by the Declaration of Helsinki, and all participants were required to provide written informed consent before enrollment. The study was registered under the Thai Clinical Trials Registry (TCTR20190709003).

2.2. Study design

This involved a single-blinded randomized controlled trial. Fig. 1 illustrates the timeline of the study enrollment. Our reporting in the manuscript adheres to the CONSORT 2010 Guideline [28]. After providing informed consent, participants were randomly allocated to either: the intervention group; or control group on a 1:1 basic using simple randomization methods. Randomization was carried out employing a Clinical Trials Manager who was blinded to patient status throughout the study. Independent teams conducted the administration of the cognitive measures and the training sessions. The participants were blinded to the treatment assignment. All subjects were explained about the protocol of their allocated group. Those who refused to fully attend all required activities were excluded from the study. Recruitment was continuously performed until the number of participants reached 40 for each group. The cognitive functions, moods, and IADL were assessed by a neuropsychologist at baseline, 6 months, 1 year and 2 years. The neuropsychologist was blinded to patient status throughout the study.

2.3. Description of the intervention

The control group received standard clinical care from their usual health-care professionals such as information on physical exercise, smoking cessation and nutrition as recommended by the existing guideline [29]. The intervention group received CT using the TEAM-V Program that comprised a multidomain CT program consisting of training of executive function, attention, memory and visuospatial function. The training was held from May to July 2017, 5 sessions, with a 2-week interval between each session and 120 min per session. All of 39 participants were included per group session. Each session involved training of different domains of cognition. Participants were encouraged to practice their homework during the intervention period, and the details of each session are shown in Table 1. After the intervention, participants were encouraged to continue practicing CT as much as possible.

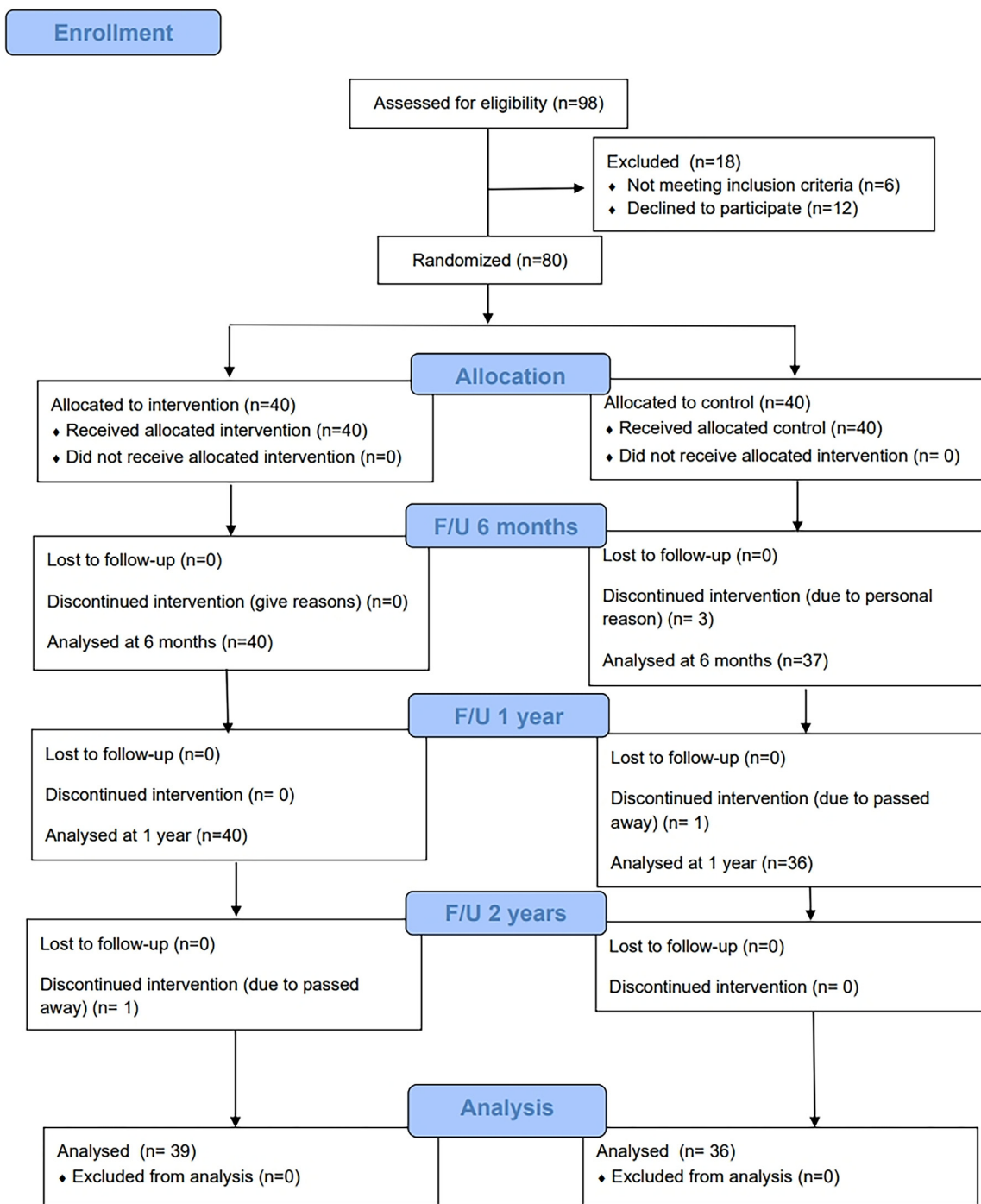


Fig. 1. CONSORT diagram of study enrollment flow.

Table 1
The TEAM-V Program cognitive training activities.

Sessions	Type/main domain training	Contents of training	Example of activities in class	Example of homework
1	Attention	Switching, selective and sustained attentions	Listening carefully a story and a song as a distractor, answers the detail of the story	Identifying internal and external distracters in daily living
2	Attention and memory	Attention and short-term memory	Practicing mental visualization techniques to memorize information such as names and objects	Memory techniques using in real life such techniques to remember of shopping lists
3	Memory	Short and long-term memory	Listening a story and practicing strategies such as mnemonics, mind map and picture to improve memory	Short-term memory: summarized news with mnemonics, mind map and picture Long-term memory: autobiography
4	Visuospatial	Spatial-temporal reasoning	Identify number of overlap descriptions, analyze a figure and reproduce it	Drawing a map from home to hospital
5	Executive function	Management skills	Planning and doing sandwich with limited resources	-

2.4. Neuropsychological testing for baseline assessment and outcome measures

The primary outcome was change of cognitive function of participants. To identify changes of global cognitive function, we applied the Thai version of MoCA to assess various domains of cognition including attention, executive function, memory, language, visuospatial skills, conceptualization, calculation and orientation. The sensitivity and specificity were 81 % and 86 %, respectively [27]. To identify changes of different domains of cognitive function, we applied main sub-tests of Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-cog) [30,31].

- Word recall task was administered to measure immediate recall memory. The participants were given 3 trials to remember a list of 10 words in block letter on white cards. Scoring was 1 point for each word if the participant did not remember it. Average total learning over 3 trials was examined.
- Constructional praxis was used to assess visuospatial function. The participants were asked to copy a cube on a piece of paper. Scoring was 1 point for each error including not 3-dimensional, the front face in the incorrect orientation, internal lines drawn incorrectly between corners and opposite sides of face not parallel or not equal size.
- Number cancellation part A was considered to be a general measure of attention. The participants were asked to cross off as many target as possible in 45 s. Scoring for part A was total of correct numbers crossed off.
- Delayed recall was administered to measure delayed recall memory. The participants were asked to recall as many words as possible from the 10 words presented during the Word recall task.
- Maze test was used to assess executive function. The participants were asked to find the route from the start to the exit of the 7 mazes in the paper. Times of completion were records.
- Word recognition task was considered to be a general measure of retrieval and retention of memory process. The participants were given 3 trials to remember a list of 12 words in block letter on white cards. Then, the participants were given another set of words, some of the words were on the cards, but some of the words were not on the cards. Scoring was 1 point for each word if the participant did not remember it. Average total learning over 3 trials was examined.

Interpretation of sub-tests of ADAS-cog, a higher score indicates worse cognitive performance, while a lower score indicates better cognitive performance, except number cancellation part A and delayed recall, in which a higher score indicates better cognitive performance, while a lower score indicates worse cognitive performance.

Secondary outcomes were:

1. Thai version of HADS comprised an anxiety and depression assessment tool. It consists of 14 question; 7 questions for anxiety and 7 questions for depression. Each item had been answered by the patient on a four point (0-[3]) response category. Score range from 0 to 21 for anxiety and 0-21 for depression. A score of 11 or more are generally considered to have anxiety or depression. The sensitivity of anxiety and depression was 100 % and 85.7 %, respectively, and the specificity of anxiety and depression was 86.0 % and 91.3 %, respectively [26].
2. The Chula ADL Index is the Thai version and was used in this study under the term IADL, which assess the ability to perform complex tasks such as shopping and house keeping. The IADL indicates the ability to exist in the community independently, including the ability to perform daily tasks. Score range from 0 to 9. The coefficient of reproducibility and scalability were 0.96 and 0.67, respectively [32].

2.5. Statistic analysis

Statistic analyses were performed using Statistical Package for the Social Sciences version 23.0 for Window (SPSS, Chicago, IL, USA). Un-

less otherwise stated, all values were presented as the mean \pm SD. Demographic comparisons between the intervention and control groups used the Fisher's exact test, Independent *t*-test and Mann-Whitney U test. Participants in the intervention group who attended less than 80 % of the sessions (4 sessions) were not included in the analysis. A value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Demographic analysis and baseline characteristic

A detailed flow chart of the present study is shown in Fig. 1. Of the 98 participants referred to the trial, 80 participants met eligibility criteria and completed baseline assessment. Totally, 76 (95 %) participants performed the 1-year follow-up and 75 (93.8 %) participants completed the 2-year follow-up. Adverse events were not reported from either group.

Patients' characteristics at baseline for each group are shown in Table 2. The mean age of participants was 65.7 years. Most participants were women (79.5 % in the intervention group vs. 72.2 % in the control group), most had a bachelor's degree (64.1 vs. 61.1 %), had a chronic medical condition (84.6 vs. 91.7 %), exercised regularly (97.4 % vs. 83.3 %), and enjoyed leisure activities (87.1 vs. 97.2 %). No significant intergroup differences were noted between age, gender, marital status, level of education, existing medical conditions, lifestyle such as exercise, leisure activities and participation in social activities, body mass index and the scores of MoCA, HADS and IADL at baseline.

3.2. Effects of intervention on cognitive function

Table 3 illustrates the mean differences in neuropsychological test scores between the intervention and control groups at 6-month, 1-year and 2-year follow-up. At 2-year follow-up, the intervention group showed significantly greater improvement than the control group in global cognitive function (MoCA, $P = 0.017$) in Fig. 2. Moreover, the intervention group showed significant improvement from baseline in immediate recall (word recall task, $P < 0.001$), retrieval and retention of memory process (word recognition task, $P = 0.008$) and attention (number cancellation part A, $P = 0.012$). However, the control group showed significantly greater improvement than the intervention group in executive function (maze test, $P = 0.019$) at 2-year follow-up. Furthermore, the control group showed significant improvement from baseline in executive function (maze test, $P = 0.003$) and retrieval and retention of memory processes (word recognition task, $P = 0.015$). However, attention showed significant deterioration (number cancellation part A, $P < 0.001$).

3.3. Effects of intervention on mood and IADL

Table 3 illustrates the mean differences in HADS and IADL scores between the intervention and control groups at 6-month, 1-year and 2-year follow-up. No training effects on anxiety ($P = 0.940$), depression ($P = 0.927$) and IADL ($P = 0.482$) were detected at 2 years.

4. Discussion

The aim of this study was to compare the effectiveness of a group-based 8-week multicomponent CT using the TEAM-V Program with the treatment-as-usual control among healthy older adults. The participants in the intervention group showed significant improvement in global cognitive function compared with that of the control group. Moreover, the intervention group also showed significant improvement from baseline in memory and attention at 2-year follow-up.

Regarding the improvement of global cognitive function, in the intervention group receiving CT using the TEAM-V multidomain CT

Table 2
Participant characteristics at baseline.

Characteristic	Intervention group (n = 39) mean ± SD	Control group (n = 36) mean ± SD	P-value
Age (years)	66.2 ± 4.6	65.1 ± 4.0	0.267 ^c
Females, n (%)	31(79.5 %)	26(72.2 %)	0.648 ^a
Marital status			0.351 ^b
Single, n (%)	8(20.5 %)	6(16.7 %)	
Married, n (%)	24(61.5 %)	24(66.6 %)	
Other (Widowed, separated, divorced), n (%)	7(18 %)	6(16.7 %)	
Highest level of education			0.966 ^b
7–12 years, n (%)	1(2.6 %)	1(2.8 %)	
Associate's degree, n (%)	2(5.1 %)	3(8.3 %)	
Bachelor's degree, n (%)	25(64.1 %)	22(61.1 %)	
Graduate degree, n (%)	11(28.2 %)	10(27.8 %)	
Chronic medical conditions, n (%)	33(84.6 %)	33(91.7 %)	0.402 ^a
Diabetes, n (%)	4(10.3 %)	0 (0 %)	0.116 ^b
Hypertension, n (%)	12(30.8 %)	17(47.2 %)	0.149 ^a
Dyslipidemia, n (%)	21(53.8 %)	18(50 %)	0.736 ^a
Regular exercise, n (%)	38(97.4 %)	30(83.3 %)	0.079 ^b
Smoking			0.051 ^b
Never, n (%)	39(100 %)	33(91.7 %)	
Former, n (%)	0(0 %)	3(8.3 %)	
Alcohol consumption			0.508 ^b
Never, n (%)	33(84.6 %)	28(77.8 %)	
Former, n (%)	0(0 %)	1(2.8 %)	
Social drinking	1(2.6 %)	0(0 %)	
Daily drinking	5(12.8 %)	7(19.4 %)	
Having leisure activities, n (%)	34(87.1 %)	35(97.2 %)	0.266 ^b
Participation in social activities, n (%)	26(66.7 %)	28(77.8 %)	0.306 ^a
Body mass index (kg/m ²)	24.0 ± 3.4	24.5 ± 3.5	0.526 ^c
MoCA	27.8 ± 1.3	27.6 ± 1.5	0.536 ^c
Immediate recall memory	3.0 ± 1.3	2.7 ± 1.0	0.265 ^c
Retrieval and retention of memory process	5.3 ± 2.2	5.0 ± 1.8	0.474 ^c
Delayed recall memory	2.5 ± 1.4	2.3 ± 1.5	0.710 ^d
Attention	25.6 ± 6.5	27.3 ± 6.5	0.253 ^d
Visuospatial function	0.3 ± 0.7	0.3 ± 0.8	0.925 ^d
Executive function	58.7 ± 26.4	64.32±36.4	0.862 ^d
HADS: Anxiety	3.5 ± 2.2	4.6 ± 2.5	0.057 ^d
HADS: Depression	2.8 ± 2.3	0.695 ^d	
IADL	2.9 ± 2.1	8.0 ± 0.2	0.160 ^d
	7.8 ± 0.6		

Notes:

^a Chi-square test.

^b Fisher's exact test.

^c Independent *t*-test.

^d Mann-Whitney U test. Abbreviations: MoCA, the Thai version of Montreal Cognitive Assessment; HADS, the Thai version of Hospital Anxiety and Depression Scale; IADL, instrumental activities of daily living; SD, standard deviation.

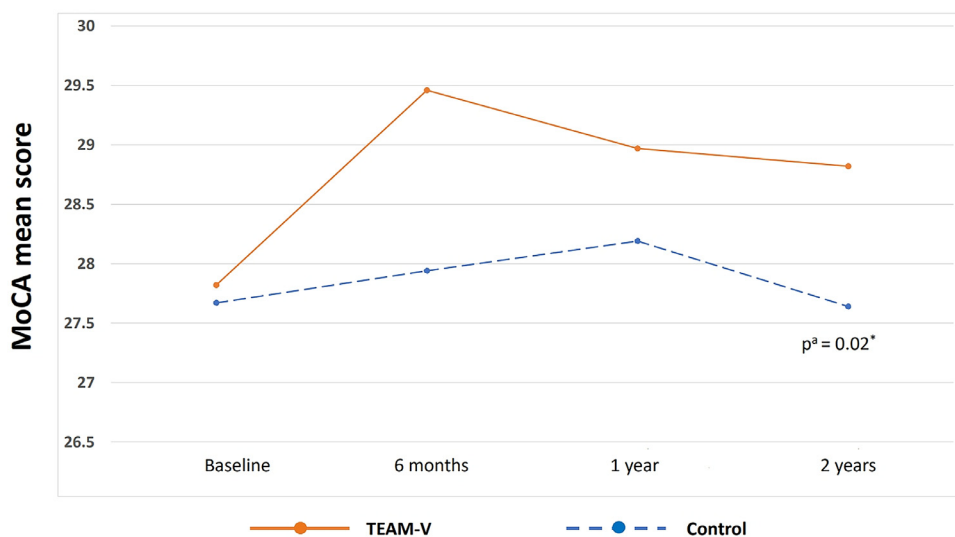


Fig. 2. MoCA mean scores at baseline, 6-months, 1-year and 2-year follow-up . Note: ^aIndependent *t*-test. **P* < 0.05. Abbreviations: MoCA, the Thai version of Montreal Cognitive Assessment.

Table 3

Mean differences in cognitive function, moods and IADL scores between intervention group and control group at 6-month, 1-year and 2- year follow-up.

		Intervention group (n = 39) mean difference ± SD	Control group (n = 36) mean difference ± SD	P-value
Global cognitive function				
MoCA	6 Months	0.6 ± 1.7	0.3 ± 1.6	0.486 ^a
	1 Year	1.1 ± 1.7	0.5 ± 1.9	0.186 ^a
	2 Years	1.0 ± 1.8	-0.03 ± 1.9	0.017 ^{a,*}
	Intragroup P-value	0.001 ^c	0.930 ^c	
Cognitive function in each domain				
Immediate recall memory	6 Months	-0.6 ± 1.4	-0.3 ± 1.3	0.332 ^a
	1 Year	-0.4 ± 1.2	0.1 ± 1.3	0.115 ^a
	2 Years	-0.7 ± 1.0	-0.15 ± 1.2	0.051 ^a
	Intragroup P-value	<0.001 ^c	0.486 ^c	
Retrieval and retention of memory process	6 Months	-1.0 ± 2.3	-0.6 ± 2.1	0.464 ^a
	1 Year	-0.4 ± 2.0	0.0 ± 2.1	0.372 ^b
	2 Years	-0.9 ± 1.9	-0.8 ± 2.0	0.934 ^a
	Intragroup P-value	0.008 ^c	0.015 ^c	
Delayed recall memory	6 Months	-0.4 ± 1.8	-0.0 ± 2.1	0.241 ^b
	1 Year	-0.4 ± 1.6	-0.1 ± 1.6	0.387 ^b
	2 Years	-0.5 ± 1.5	0.2 ± 2.2	0.242 ^b
	Intragroup P-value	0.064 ^d	0.903 ^d	
Attention	6 Months	-0.3 ± 5.2	-1.5 ± 5.3	0.304 ^a
	1 Year	2.5 ± 4.7	0.1 ± 4.6	0.028 ^a
	2 Years	-2.3 ± 5.3	-3.9 ± 5.2	0.169 ^a
	Intragroup P-value	0.012 ^c	<0.001 ^c	
Visuospatial function	6 Months	-0.1 ± 0.8	0.2 ± 0.9	0.143 ^b
	1 Year	-0.1 ± 0.7	-0.1 ± 0.6	0.983 ^b
	2 Years	-0.2 ± 0.7	0.11 ± 0.7	0.191 ^b
	Intragroup P-value	0.206 ^d	0.366 ^d	
Executive function	6 Months	-0.9 ± 27.1	-11.2 ± 27.2	0.155 ^b
	1 Year	10.0 ± 30.1	-5.3 ± 30.3	0.051 ^b
	2 Years	2.6 ± 29.5	-14.8 ± 25.0	0.019 ^{b,*}
	Intragroup P-value	0.645 ^d	0.003 ^d	
Mood				
Anxiety	6 Months	-0.2 ± 2.15	0.6 ± 1.98	0.065 ^b
	1 Year	-0.1 ± 2.16	0.7 ± 2.01	0.065 ^b
	2 Years	-0.2 ± 2.26	-0.5 ± 1.65	0.940 ^b
	Intragroup P-value	0.583 ^d	0.107 ^d	
Depression	6 Months	-0.43 ± 2.17	0.76 ± 2.17	0.055 ^b
	1 Year	-0.15 ± 2.21	0.47 ± 1.93	0.201 ^b
	2 Years	-0.03 ± 1.97	-0.06 ± 2.08	0.927 ^b
	Intragroup P-value	0.834 ^d	0.919 ^d	
IADL				
IADL	6 Months	0.13 ± 0.61	-0.05 ± 0.33	0.133 ^b
	1 Year	0.08 ± 0.47	-0.03 ± 0.29	0.321 ^b
	2 Years	0.08 ± 0.48	0.00 ± 0.24	0.482 ^b
	Intragroup P-value	0.317 ^d	1.000 ^d	

Notes:

^a Independent t-test.

^b Mann-Whitney U test.

^c Paired t-test.

^d Wilcoxon Signed Ranks Test.

* P < 0.05. Intragroup P-value: compare the means at baseline and 2-year follow-up. Abbreviations: MoCA, the Thai version of Montreal Cognitive Assessment; IADL, instrumental activities of daily living; SD, standard deviation.

Program consisting of training of executive function, attention, memory and visuospatial function, the beneficial effects of parallel training in different domains of a multidomain cognitive program could have additive effects versus a cognitive program focusing on a single restricted area. One study in mice, using a multi-domain cognitive training (spatial navigation task, object recognition, and fear conditioning) compared with a single-domain cognitive training (spatial navigation task) showed the multi-domain cognitive training exhibited an improvement in cognitive functions, reductions in amyloid load and microgliosis, and a preservation of cholinergic function. These findings provide causal evidence for the potential of CT to mitigate the cognitive deficits in Alzheimer disease [33]. Moreover, this may be explained by the fact that CT enhances functional connectivity within cognitive brain networks [34].

Memory and attention problems are a common concern for older adults. Therefore, the TEAM-V Program provided 2 sessions for mem-

ory and attention training, but other domains received 1 session per domain. In the intervention group, our findings demonstrated significant improvements in attention, immediate recall memory, retrieval and retention of memory processes at 2-year follow-up. However, no improvements were found for delayed recall, possibly because delayed recall needs more rehearsal and refreshing than other types of memories [35].

In addition, visuospatial functions were not improved in the intervention group because visuospatial processing involves a very dynamic and complex brain network such as interconnection with dorsal and ventral pathways [36]. Therefore, the visuospatial training in the TEAM-V Program provided only 1 session, and only a simple homework assignment such as drawing a map from home to hospital that may have been insufficient to improve visuospatial function. Training using various methods and high intensity such as navigation tasks, visuomotor trainings and visuoconstruction procedures would further improve this

function [37]. For example, a novel visuospatial exercise using cubes with six colored patterns 90 min/week for 12 weeks could improve visuospatial ability [38].

For the executive function, the participants in the control group showed significantly improvement in executive function compared with that of the intervention group at 2-year follow-up. It may be the control group had worse baseline scores compared with the intervention group. Many parts of brain were involved such as the frontal junction and pre-cuneus controlled executive function. It comprises many domains such as working memory, inhibitory control and cognitive flexibility [39]. Therefore, CT must involve complex tasks in many sessions. For the TEAM-V Program, the executive function training had only 1 session of planning and involved creating sandwiches with limited resources. Compared with a CT of executive function by 12-week cooking program, the training session lasted for about 90-min once a week among older adults with dementia. The cooking training task could maintain executive function [40]. Moreover, a meta-analysis of the combined cognitive and physical interventions effectively delayed the decrease of executive functions among older adults and this effect was influenced by the length and frequency of the intervention [41]. Therefore, the difficulty and duration of activities in TEAM-V Program may not have been sufficient to improve executive function. In addition, the Compensation-Related Utilization of Neural Circuits Hypothesis suggested individual's cognitive capacity affects the response of cognitive training [42]. Therefore, evaluation of the individual's cognitive capacity will help organize activities and task demands appropriately. Moreover, combined physical exercise with CT may be more effective. For example, a recent meta-analysis of randomized controlled trials showed aerobic exercise and dual-task training were effective to improve cognitive frailty [43].

No significant improvement was observed of anxiety and depression between the intervention group and the control group at 2-year follow-up. However, a trend indicating difference between groups was observed in anxiety and depression between the two groups at 6 months and 1 year (for anxiety). Accordingly the China Health and Retirement Longitudinal Survey (CHARLS) study revealed social engagement not only significantly improved self-rated health but also reduced mental distress [44]. Moreover, the most recent longitudinal studies have demonstrated high social engagement and benefits on depression and anxiety [45]. Therefore, interaction with others during group activities in the TEAM-V Program could have helped participants to improve their self-esteem and to enjoy activities that helped them to achieve a better mental health in short term follow-up. However, 5 sessions in the 8-weeks TEAM-V Program were insufficient to improve mental health in long-term follow-up. The results were the same as the randomized controlled trial of computerized cognitive training with 10 h of initial training and followed by 2 booster sessions at 5 and 11 months; no significant difference in mood was found at 52-week follow-up [46]. Therefore, more training and frequent booster sessions will help to improve mood in long-term follow-up.

In the present study, no statistically significant changes were found in IADL scores in both intervention and control groups. Quite possibly successful completion of IADL depends upon having cognitive skills, e.g., memory, executive function, necessary to accomplish the tasks [47]. However, because of minimal functional decline across healthy older adults, longer follow-up is likely required to observe training effects on IADL. For example, the ACTIVE study, an experimental study among 2832 healthy older adults with 10-years follow-up found that in 3 intervention groups of CT by memory training, reasoning training or speed training was reportedly less difficulty in IADL compared with that of the no-contact control group [48]. In addition, IADL might not be impacted by cognitive performance but rather by other factors that may not be responsive to the CT. Moreover, CT may improve IADL among people with dementia more than among healthy older adults. An experimental study of CT conducted among healthy older adults, healthy older adults with minor neurocognitive disorders and Alzheimer's disease also found IADL significant improved in the intervention group of

Alzheimer's disease, but not among those with minor neurocognitive disorders and healthy older adults [49].

To our knowledge, the present study is the first to report a multi-component CT with RCT design among healthy older adults with 2-year follow-up in Thailand. The TEAM-V Program consisted of many simple activities that are convenient to apply in remote areas in Thailand or in other countries. For example, the program could easily train volunteers to conduct stimulating cognition activities for healthy older adults in elderly clubs. In addition, although some older adults would be unfamiliar with high technology such as computer or online program, they could still join. In addition, a very high adherence was noted in the intervention group (only 3 individuals discontinued intervention due to personal reasons and 1 person passed away) during 2-year follow-up. It would be possible that participants felt the program was useful and practical to apply in their daily life. However, the program still needed to be tested compared other group activities and other settings as well as to be corrected for some limitations.

However, limitations were encountered in the present study. First, participants were recruited from a hospital in the central region in Thailand. Therefore, the results may be unable to generalize to other regions of Thailand or other countries. It should also be noted that in both groups, the percentage of females was greater than that of males. The sample size of 80 participants may limit the generalizability of the findings. A larger sample could provide more robust data and validate the results. Moreover, the use of treatment-as-usual control limited the interpretation of the training effects found. An improved design incorporating active control may better clarify the nature of the training effects found. Quite possibly the improvements in cognition and mood could have been attributed to nonspecific effects and from factors such as other interventions that may have formed part of a patient's routine management or CT undertaken by participants of their own accord. Another limitation of this study is that the authors did not check how long and to what extent the participants conducted their homework. For future studies, a homework-diary should be implemented to control intensity and determine total time spent on the cognitive homework. In addition, sample size, longitudinal follow-up (at least 7 to 14 years especially to assess the improvement of IADL and higher intensity CT should be implemented. A meta-analysis suggested that the CT showed better effectiveness with weekly training sessions ≥ 3 times weekly, totaling training weeks ≥ 8 weeks, and total training session ≥ 24 sessions among healthy older adults [50], could be extended in future studies to strengthen outcomes. Moreover, future research should include other potential modifiable and non-modifiable risk factors that might interfere with cognitive function such as metabolic diseases, atrial fibrillation, current medication and supplement use, family history of neurocognitive disorder and ApoE4 genetic [51], brain imagery techniques and biomarkers to identify the specific aspects related to cognitive improvement in CT.

5. Conclusion

To summarize, the current randomized controlled trial provided evidence that the TEAM-V Program was effective in improving global cognition. Although the program did not show significantly improved anxiety, depression and IADL compared with that of the control group, memory and attention in the intervention group tended to improve compared with baseline. Further studies incorporating a larger sample size, longitudinal follow-up and higher-intensity CT should be conducted. Interestingly, the program could be easily implemented across a variety of settings, and may even enable healthy older adults to continue engagement in inexpensive and practical CT.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- Arvanitakis Z, Shah RC, Bennett DA. Diagnosis and management of dementia: review. *JAMA* 2019;322:1589–99.
- Nichols E, Steinmetz JD, Vollset SE, Fukutaki K, Chalek J, Abd-Allah F, et al. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the global burden of disease study 2019. *Lancet Public Health* 2022;7:e105–25.
- Ballesteros S, Kraft E, Santana S, Tziraki C. Maintaining older brain functionality: a targeted review. *Neurosci Biobehav Rev* 2015;55:453–77.
- Ngandu T, Lehtisalo J, Solomon A, Levalähti E, Ahtiluoto S, Antikainen R, et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomized controlled trial. *Lancet* 2015;385:2255–63.
- Lenze EJ, Bowie CR. Cognitive training for older adults: what works? *J Am Geriatr Soc* 2018;66:645–7.
- Li T, Yao Y, Cheng Y, Xu B, Cao X, Waxman D, et al. Cognitive training can reduce the rate of cognitive aging: a neuroimaging cohort study. *BMC Geriatr* 2016;16:12.
- da Silva TB, Bratkauskas JS, Barbosa MEC, da Silva GAR, Zunkeller MG, de Moraes LC, et al. Long-term studies in cognitive training for older adults: a systematic review. *Dement Neuropsychol* 2022;16:135–52.
- Kunkler MC, Falkenreck JM, Ophay A, Dencker K, Friese A, Jahr P, et al. Long-term effects of the multicomponent program BrainProtect® on cognitive function: one-year follow-up in healthy adults. *J Alzheimers Dis Rep* 2024;8:1069–87.
- Falkenreck JM, Kunkler MC, Ophay A, Weigert H, Friese A, Jahr P, et al. Effects of the multicomponent cognitive training Program BrainProtect in cognitively healthy adults: a randomized controlled trial. *J Alzheimers Dis* 2023;94:1013–34.
- Rebok GW, Ball K, Guey LT, Jones RN, Kim HY, King JW, et al. Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *J Am Geriatr Soc* 2014;62:16–24.
- Gross AL, Parisi JM, Spira AP, Kueider AM, Ko JY, Saczynski JS, et al. Memory training interventions for older adults: a meta-analysis. *Aging Ment Health* 2012;16:722–34.
- Mah L, Szabuniewicz C, Fiocco AJ. Can anxiety damage the brain? *Curr Opin Psychiatry* 2016;29:56–63.
- Diamond K, Mowszowski L, Cockayne N, Norrie L, Paradise M, Hermens DF, et al. Randomized controlled trial of a healthy brain ageing cognitive training program: effects on memory, mood, and sleep. *J Alzheimers Dis* 2015;44:1181–91.
- Belleville S, Hudon C, Bier N, Brodeur C, Gilbert B, Grenier S, et al. MEMO+: efficacy, durability and effect of cognitive training and psychosocial intervention in individuals with mild cognitive impairment. *J Am Geriatr Soc* 2018;66:655–63.
- Gates NJ, Vernooij RW, Di Nisio M, Karim S, March E, Martinez G, et al. Computerised cognitive training for preventing dementia in people with mild cognitive impairment. *Cochrane Database Syst Rev* 2019;3:CD012279.
- Senanarong V, Rattanabannakit C, Hunnangkul S, Wongkom N, Likitjaroen Y, Witoonpanich P, et al. Five year dementia registry in Thailand: regional distribution, etiologies, and outcome of dementia. *Alzheimer's Dement* 2023;19(Suppl.4):e061560.
- Chaiwong P, Rattakorn P, Mumkhetvit P. Effect of cognitive training program on cognitive abilities and quality of life in elderly with suspected dementia. *Bull Chiang Mai Assoc Med Sci* 2015;48:182–91.
- Chaikham A, Putthinoi S, Lersilp S, Bunpun A, Chakpitak N. Cognitive training program for Thai older people with mild cognitive impairment. *Procedia Environ Sci* 2016;36:42–5.
- Nakawiro D, Chansirikarnjana S, Srisuwan P, Aebthaisong O, Sudsakorn P, Vidhyachak C, et al. Group-based training of executive function, attention, memory and visuospatial function (Team-V) in patient with mild neurocognitive disorder. *J Psychiatr Assoc Thailand* 2017;62:337–48.
- Sukontapol C, Kemsan S, Chansirikarn S, Nakawiro D, Kuha O, Taameeyapradit U. The effectiveness of a cognitive training program in people with mild cognitive impairment: a study in urban community. *Asian J Psychiatr* 2018;35:18–23.
- Jirayucharoensak S, Israsena P, Pan-Ngum S, Hemrungronj S, Maes M. A game-based neurofeedback training system to enhance cognitive performance in healthy elderly subjects and in patients with amnesic mild cognitive impairment. *Clin Interv Aging* 2019;14:347–60.
- Phanasathit M, Nimnuan C, Lohsoonthorn V. The effects of cognitive training in healthy community residing Thai elderly: a randomized controlled trial. *Psychol Res Behav Manag* 2022;15:3709–20.
- Phrom K, Kamnardsiri T, Sungkarat S. Beneficial effects of interactive physical-cognitive game-based training on fall risk and cognitive performance of older adults. *Int J Environ Res Public Health* 2020;17:6079.
- Srisuwan P, Nakawiro D, Chansirikarnjana S, Kuha O, Chaikongthong P, Suwanagot T. Effects of a group-based 8-week multicomponent cognitive training on cognition, mood and activities of daily living among healthy older adults: a one-year follow-up of a randomized controlled trial. *J Prev Alz Dis* 2020;7:112–121.
- Jitapunkul S, Kunanusont C, Phoolcharoen W, Suriyawongpaisal P. Prevalence estimation of dementia among Thai elderly: a national survey. *J Med Assoc Thai* 2001;84:461–7.
- Nilchaikovit T, Lortrakul M, Phisanuthideth U. Development of Thai version of hospital anxiety and depression scale in cancer patients. *J Psychiatr Assoc Thailand* 1996;41:18–30.
- Julayanont P, Tangwongchai S, Hemrungronj S, Tunvirachaisakul C, Panthumchinda K, Hongsawat J, et al. The montreal cognitive assessment-basic; a screening tool for mild cognitive impairment in illiterate and low-educated elderly adults. *J Am Geriatr Soc* 2015;63:2550–4.
- Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c869.
- Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, et al. Dementia prevention, intervention, and care. *Lancet* 2017;390:2673–2734.
- Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry* 1984;141:1356–64.
- Mohs RC, Knopman D, Petersen RC, Ferris SH, Ernesto C, Grundman M, et al. Development of cognitive instruments for use in clinical trials of antidementia drugs: additions to Alzheimer's disease assessment scale that broaden its scope. *Alzheimer Dis Assoc Disord* 1997;11:S13–21.
- Jitapunkul S, Kamolratanakul P, Ebrahim S. The meaning of activities of daily living in a Thai elderly population; development of a new index. *Age Ageing* 1994;23:332–6.
- Mehla J, Deibel SH, Karem H, Hong NS, Hossain SR, Lacoursiere SG, et al. Repeated multi-domain cognitive training prevents cognitive decline, anxiety and amyloid pathology found in a mouse model of Alzheimer disease. *Commun Biol* 2023;6:1145.
- van Balkom TD, van den Heuvel OA, Berendse HW, van der Werf YD, Vriend C. The effects of cognitive training on brain network activity and connectivity in aging and neurodegenerative diseases: a systematic review. *Neuropsychol Rev* 2020;30:267–86.
- Camos V, Portrat S. The impact of cognitive load on delayed recall. *Psychon Bull Rev* 2015;22:1029–34.
- Trés ES, Brucki SM. Visuospatial processing: a review from basic to current concepts. *Dement Neuropsychol* 2014;8:175–81.
- Tippett WJ, Rizkalla MN. Brain training: rationale, methods, and pilot data for a specific visuomotor/visuospatial activity program to change progressive cognitive decline. *Brain Behav* 2014;4:171–9.
- Nemato M, Sasai H, Yabushita N, Tsuchiya K, Hotta K, Fujita Y, et al. A novel exercise for enhancing visuospatial ability in older Adults with frailty: development, feasibility, and effectiveness. *Geriatrics (Basal)* 2020;5:29.
- Heckner MK, Cieslik EC, Eickhoff SB, Camilleri JA, Hoffstaedter F, Langner R. The aging brain and executive functions revisited: implications from meta-analysis and functional-connectivity evidence. *J Cogn Neurosci* 2021;33 1761–52.
- Murai T, Yamaguchi H. Effects of a cooking program based on brain-activating rehabilitation for elderly residents with dementia in a roken facility: a randomized controlled trial. *Prog Rehabil Med* 2017;2:20170004.
- Guo W, Zang M, Klich S, Kawczyński A, Smoter M, Wang B. Effect of combined physical and cognitive interventions on executive functions in older adults: a meta-analysis of outcomes. *Int J Environ Res Public Health* 2020;17:6166.
- Fu L, Kessels RP, Maes JH. The effect of cognitive training in older adults: be aware of CRUNCH. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn* 2020;27:949–962.
- Zhang Y, Zhou J, Zhang X, Liu J, Li M, Liang J, et al. Management of cognitive frailty: a network meta-analysis of randomized controlled trials. *Int J Geriatr Psychiatry* 2023;38:e5994.
- Liu J, Rozelle S, Xu Q, Yu N, Zhou T. Social Engagement and Elderly Health in China: evidence from the China Health and Retirement Longitudinal Survey (CHARLS). *Int J Environ Res Public Health* 2019;16:278.
- Wickramaratne PJ, Yangchen T, Lepow L, Patra BG, Glicksburg B, Talati A, et al. Social connectedness as a determinant of mental health: a scoping review. *PLoS One* 2022;17:e0275004.
- Smith M, Jones MP, Dotson MM, Wolinsky FD. Computerized cognitive training to improve mood in senior living settings: design of a randomized controlled trial. *Open Access J Clin Trials* 2018;10:29–41.

- [47] Jones RN. Cognitive training improves cognitive performances, but what else? *J Am Geriatr Soc* 2018;66:648–9.
- [48] Tennstedt SL, Unverzagt FW. The ACTIVE study: study overview and major findings. *J Aging Health* 2013;25:3S–20S.
- [49] Giuli C, Fattoretti P, Gagliardi C, Mocchegiani E, Venarucci D, Baliotti M, et al. My Mind Project: the effects of cognitive training for elderly—the study protocol of a prospective randomized intervention study. *Aging Clin Exp Res* 2017;29:353–60.
- [50] Chiu HL, Chu H, Tsai JC, Liu D, Chen YR, Yang HL, et al. The effect of cognitive-based training for the healthy older people: a meta-analysis of randomized controlled trials. *PLoS One* 2017;12:e0176742.
- [51] Glans I, Nägga K, Gustavsson A, Stomrud E, Nilsson PM, Melander O, et al. Associations of modifiable and non-modifiable risk factors with cognitive functions – a prospective, population-based, 17 years follow-up study of 3,229 individuals. *Alzheimers Res Ther* 2024;16:135.