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Original Article

Effects of neurobic exercise on cognitive function and serum brain-derived neurotrophic factor in the normal to mild cognitive impaired older people: A randomized control trial

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Abstract

The purpose of this study was to examine the effects of neurobic exercise on cognitive function and serum brain-derived neurotrophic factor (BDNF) in the normal to mild cognitive impaired elderly. Fifty-one participants were simple randomized into two groups. The intervention group received one hour neurobic exercise training per session for two sessions a week for 24 weeks and the control group engaged in their routine activities twice a week at a senior club. All subjects were assessed using a battery of neuropsychological tests and serum BDNF. The results showed that the experimental group had significantly improved cognitive scores compared to the control group ($P<0.05$). Only in the experimental group was there a significant increase in serum BDNF after completing the neurobic exercise session. The study indicated that neurobic exercise has an effect on cognitive function in aging. Moreover, the increased serum level of BDNF might be an indicator for the enhancement of brain function.

Keywords: neurobic exercise, cognitive function, serum brain-derived neurotrophic factor, normal to mild cognitive impairment, older people

1. Introduction

The prevalence of dementia is increasing and it is estimated to have 46.8 million people suffering with dementia worldwide in 2015. This number is expected to almost double every 20 years, reaching 74.7 million in 2030 and 131.5 million in 2050 (Alzheimer's Disease International, 2015). Dementia is a broad category of brain diseases where memory, thinking, behavior, and the ability to perform daily activities severely deteriorates (World Health Organization [WHO], 2017). The proportionate increase in prevalence is expected to be much steeper in low and middle income countries, where half of new dementia cases are in Asia. According to the World Health Organization (WHO), development of preventative strategies for dementia is one of the research priorities to reduce the global burden of dementia by 2025 (WHO, 2016). One approach to reduce the prevalence of dementia is to develop strategies to delay its onset in healthy individuals or in those at risk of developing

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dementia (Gates, Sachdev, Fiatarone-Singh, & Valenzuela, 2011). Cognitive stimulation and cognitive training intervention using a structured practice of complex mental activity in order to enhance cognitive function have been investigated and consistently show benefit in the cognitive function in people with mild to moderate dementia (Aguirre, Woods, Spector, & Orrell, 2013). Recent studies have explored the potential benefit of cognitive intervention in older people with mild cognitive impairment and subjective cognitive decline (Suzuki *et al*., 2013; Szuhany, Bugatti, & Otto, 2015; Tyler, Alonso, Bramham, & Pozzo-Miller, 2002). The findings demonstrated that cognitive enhancement is possible even when the subjects appear cognitively normal on standardized neuropsychological testing. People with mild cognitive impairment could learn new information and memory strategies. However, the limitations of previous studies were small sample size, limited details of randomization, lack of adequate controlled studies, heterogeneity of intervention and outcome measurements, and a lack of standardized measurement instruments (Legault *et al.*, 2011; Nouchi *et al.*, 2012). Furthermore, studies of biomarkers to prove the improvement of neuropsychological tests by cognitive intervention are still limited.

Neurobic exercise is performed via the five physical senses of sight, hearing, smell, taste, and touch. Moreover, neurobic exercise can enhance the nerve impulses and interconnections among different data within the brain. In addition, neurobic exercise can stimulate neurons to create brain nutrients called neurotrophins which have a chemical effect on the growth of nerve cells and also have the effect of increasing the branching of nerve fibers and slowing the degeneration of nerve cells (Katz & Rubin, 1999). Neurobic exercise is generally an activity to do in everyday life but can be modified through a new experience such as blindness activities to modify the information from the senses (Katz & Rubin, 1999). A previous study was performed in 22 female dementia patients that demonstrated a better score in memory testing after the neurobic exercise. However, there was no control group and it was studied only in female subjects with dementia (Kanthamalee & Sripankaew, 2013). Generalizing to the general population needs further investigation to confirm this result in other groups of the population.

Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophin family of growth factors. It is expressed throughout the brain, particularly in the hippocampus, basal forebrain, and prefrontal cortex which are essential for learning, memory, and other cognitive functions (Pezawas *et al*., 2004). It has an effect on neurite outgrowth, synaptic plasticity (Rossi *et al*., 2006), neuronal survival (Husson *et al*., 2005), and neuronal differentiation (Lu, Pang, & Woo, 2005). The BDNF has benefits in long-term memory and overall brain function (Alonso *et al*., 2002). It has tropomyosin-related kinase B (TrkB) as a signaling receptor. Several studies revealed its association with certain psychiatric and neurologic disorders. BDNF/TrkB signaling may be involved in Alzheimer's disease (AD), and associated with amyloid β and tau which are neuropathological hallmarks of AD (Zhang, Kang, Li, Xiao, & Zhou, 2012). Although platelets are a major source of peripheral BDNF, no significant difference was found between serum and plasma. Serum levels are influenced by platelets and plasma level results are inconsistent. Thus, serum measurements seem to be more reliable than plasma measurements (Serra-Millàs, 2016). Peripheral BDNF has been proposed as a biomarker for the successful treatment of major depressive disorder (Polyakova *et al*., 2015). It could be a possible biomarker of cognitive function in AD as well. Previous research has demonstrated the increase of BDNF with a varied physical exercise program. However, the magnitude of this effect was lower in females compared to males (Szuhany *et al*., 2015).

With the increasing incidence of dementia, strategies to slow down the degeneration of the brain are vital. Neurobic exercise might stimulate different parts of the brain and can be done in daily practice at home. Thus, establishing a new brain fitness program, which uses the five physical senses, is particularly interesting. Therefore, the researchers took daily activities that can be considered a new form of neurobic exercise. This research is a randomized controlled trial (RCT) that aimed to study the effect of neurobic exercise on both cognitive function and BDNF in older people who were cognitively normal or had mild cognitive impairment. The aim was to find an alternative way to prevent cognitive decline or help reduce the risk of dementia that may develop in the future. However, since evidence of the effects of a neurobic exercise program is lacking, this research will be a supporting reference for further studies on neurobic exercise.

2. Materials and Methods

2.1 Participants

A single-blind (assessors blinded) RCT was conducted. The participants were 51 local community-dwelling non-demented older adults and adults with mild cognitive impairment who attended an elderly club or local center for older people in Pathum Thani Province near Bangkok. The inclusion criteria were 1) between 60 and 80 years old, 2) the Barthel Activities of Daily Living (ADL) score was more than 12 points, 3) no history of psychiatric disorder or neurological condition, e.g., epilepsy, stroke, dementia, or head injury, 4) no history of functional decline and independent in social and occupational activities, 5) had normal physical senses, and 6) was fluent in the Thai language in both speaking and writing. The exclusion criteria were 1) significant visual or hearing impairment, 2) previous neurological disorders, 3) current smoker or alcohol drinker or 4) medical problems that could interfere with the attendance of the study session. The participants were withdrawn from the study if 1) they were not willing to continue the study, 2) they missed the program for more than 20% of the sessions or 4 consecutive sessions, or 3) they could not comply with the study protocol, such as having acute medical illness or injury. Every participant was informed of the study objectives and process before the intervention. Informed consent was then given by the participants. The study was approved by the ethics review committee for research involving human research subjects, Health Science Group, Chulalongkorn University.

The two groups were matched on age and the global cognitive status was measured by the Montreal Cognitive Assessment (MoCA) Thai version, and the Barthel ADL score. The participants were randomly assigned to either the neurobic exercise program group (NG) or usual care as the control group (CG).

From previous studies, the cognitive change after the intervention between the groups varied from 23 to 98% (Gates *et al.*, 2011; Suzuki *et al*., 2013). The sample size for this study was determined to compare cognitive measures based on the expected effect size of 40% and the standard deviation of the observations in each of the two groups at 70%. A sample size of 25 per group was required to detect a change on the neuropsychological test with 80% power and type I error at 5%. As there were 48 sessions of the study program, the researcher allowed a 30% dropout; therefore, 36 participants per group were required.

2.2 Neuropsychological examination

Neuropsychological testing was performed twice: once at baseline and once within 1–3 days after the last training session at the 24th week. Cognitive assessment was performed to measure global cognitive function, attention, auditory, visual memory, and executive function. The authors used the MoCA (Nasreddine *et al*., 2005) in the Thai version to measure general cognitive function. The Trail Making Test (Part A and Part B) was used to measure attention (Reitan & Wolfson, 1985). The memory function was tested by Verbal Paired Associates I and II in Wechsler Memory Scale third edition: WMS-III to measure the auditory memory (Wechsler, 1997) and Rey-Osterrieth Complex Figure test to measure the visual memory (Osterrieth, 1945). The executive function was measured by the Wisconsin Card Sorting Test (Heaton, Chelune, Talley, Kay, & Curtiss, 1993). All tests were performed by an experienced neuropsychologist who was blinded to the study group.

2.3 Neurobic exercise group (NG)

Neurobic exercise applies five physical senses, i.e., sight, hearing, smelling, tasting, touching, and feeling the emotion in the training exercise. Neurobic exercise comes from the scientific basis where the cerebral cortex consists of an unexpectedly vast number of different areas, and each area specializes in different functions to receive, render, and store information from the physical senses. Therefore, the cognition through the senses does not conclude in one place in the brain because there are hundreds of different neural pathways and a lot of connecting areas in the cerebral cortex. Neurobic exercise encourages the use of the vast unused areas in the brain to induce more interconnections and possible combinations of the brain (Katz & Rubin, 1999).

The developed neurobic training program consisted of nine exercises with stimuli of the five physical senses. The program was reviewed by senior clinicians and university lecturers that included 1 psychiatrist, 2 psychologists, 1 neuropsychologist, and 1 neurophysiologist. The Item Objective Congruence was 0.82. The nine neurobic exercises were as follows:

1) Draw and paint on the paper as instructed by the researcher within the time set,

2) Touch items inside a box and allow the subjects to guess what they have touched. Ten minutes later, the participants were asked to write the answer on the paper with a non-dominant hand,

3) Play the word dumb game by using only gestures and speech,

4) Close eyes with a blindfold, smell an object (food, herb or flavoring) and guess what it was. Ten minutes later, the participants were asked to write the answer on the paper with a non-dominant hand,

5) Close eyes with a blindfold, listen to a sound and guess what it was. Ten minutes later, the participants were asked to write the answer on the paper with a non-dominant hand,

6) Close eyes with a blindfold, taste juice or food and guess what they ate or drank. Ten minutes later, the participants were asked to write the answer on the paper with a non-dominant hand,

7) Write based on a proposition with a non-dominant hand,

8) Mold clay within a set time,

9) Play a word guessing game by using a finger to write a word on the back of the other participant.

These training activities affected a widespread network of thalamic and bihemispheric structures in the frontal lobe which control attention (Filley, 2002) and also stimulate the hippocampus which is a part of the limbic system affecting memory function. In addition, the training program also stimulated the prefrontal lobe affecting high brain resolution, planning, and reasoning in decision making (Manchester, Priestley, & Jackson, 2004; Serino *et al*., 2006).

Each individual session consisted of three out of nine exercises, and lasted for one hour. The whole training protocol included one hour of cognitive training per day for two days per week during a period of 24 weeks (48 sessions). The minimum frequency of cognitive training was 2 days per week which was shown to improve cognitive function, while 24 weeks of intervention was an appropriate duration reported to have a significant improvement of cognitive function. (Bugos *et al*., 2007; Noice & Noice, 2009; Klusmann *et al*., 2010; Slegers, Boxtel, & Jolles, 2009).

2.4 Control group (CG)

The control group was asked to attend a seminar in weeks 6, 12, and 18. The seminar content was about health promotion for older people. The control group engaged in their routine activities as usual twice a week at their senior club.

2.5 Serum BDNF measurement

Blood samples were collected twice, once at baseline and once within 1–3 days after the last training session at the 24th week. Blood samples were collected between 8:00 and 9:00 a.m. into a free-anticoagulant vacuum tube. The samples were allowed to clot and then centrifuged at 1500 × *g* for 15 min. The serum samples were stored at −80 °C until they were assayed and thawed immediately prior to the measurement of the biochemical parameters. Serum levels of BDNF were determined using enzyme-linked immunosorbent assay kits (Quantikine ELISA Human Free BDNF Kit, R&D Systems, Inc., Minneapolis, MN, USA).

2.6 Statistical analysis

The statistical analysis was performed using SPSS version 19 software for Windows. Baseline characteristics and

characteristics of factors were analyzed using descriptive statistics. Categorical variables of sex, education, physical activity, and medical illness were analyzed using the Chi-squared test. The Fisher exact test was used in a count of less than 5. MoCA and Barthel ADL scores were determined using the independent sample t-test. Within the group, cognitive function score and serum BDNF levels were determined using the paired sample t-test and between two groups the independent sample t-test was used.

3. Results

3.1 Demographic and clinical characteristics

Seventy-two participants were included in the study. Twenty-one participants withdrew from the study: 8 in the NG group and 13 in the CG group. In the NG group, the reasons for withdrawal were: (1) duration of study was too long (4 cases); (2) acute medical illness (1 case); and (3) transportation problem (3 cases). In the CG group, all 13 cases dropped out because the duration of study was too long. The demographic characteristics of the 51 participants who completed the study are summarized in Table 1. The two groups were not significantly different in age, sex, medical illness, engagement in physical activities, psychotropic drug use, MoCA score or Barthel ADL score.

Table 1. Baseline demographic and clinical characteristics of participants in the control and neurobic exercise groups.

Data	Control (n=23)	Neurobic exercise (n=28)	P-value
Age, years (mean±SD)	69.35±5.74	70.36±5.17	0.513
Female	11 (47.8)	15 (53.6)	0.683
Education (secondary school and lower)	11 (47.8)	13 (46.4)	0.994
Physical activity (exercise less than once a week)	10 (43.5)	13 (46.4)	0.833
Medical illness			
Hypertension	8 (34.8)	11 (39.3)	0.741
Diabetes mellitus	5 (21.7)	7 (25)	0.785
Dyslipidemia	4 (17.4)	4 (14.3)	0.990
Cardiovascular diseases	1 (4.3)	1 (3.6)	0.990
No known underlying disease	12 (52.2)	13 (46.4)	0.683
% psychotropic drug used	0	0	NA
MoCA (mean±SD)	18.09±5.03	20.54±4.57	0.075
Barthel ADL score (mean±SD)	19.78±1.04	19.43±1.50	0.344

Data are presented as n (%) unless indicated otherwise.

3.2 Cognitive scores and serum BDNF levels

The cognitive scores of neuropsychological evaluations and serum BDNF levels in the control and neurobic exercise groups before and after intervention are shown in Table 2. All parameters between the CG and NG groups at baseline were not significantly different (P>0.05).

A comparison between the NG and CG groups for the Rey-Osterrieth Complex Figure Test T score and the Wisconsin Card Sorting Test-Preservative response (T-score and Standard-score) were significantly higher in the NG group than in the CG group (P<0.05). Regarding the Trail Making Test Part B, the NG group had a significantly lower score than the CG group (P<0.05). In the CG group, the post-test score of the Wisconsin Card Sorting Test- Preservative response was significantly lower than the pretest score (P<0.05). The post-test scores of the Verbal Paired Associates I and the Rey-Osterrieth Complex Figure Test were both immediate and the Delayed T score and the Wisconsin Card Sorting Test-Error response in the NG group were significantly higher than the pretest (P<0.05) (Table 2) and the Trail Making Test Part B were significantly lower than the pretest (P<0.05).

In addition, the serum BDNF level in the NG group was significantly higher than the pretest (P<0.05) (Table 2 and Figure 1). In the NG group, the positive percent changes of the serum BDNF, TMT-B, VPA I, ROCFD, WCSTEts, ROCF I, and WCSTEss were 29.73%, 22.84%, 12.38%, 11.40%, 10.29%, 10.23%, and 6.82% respectively. In the CG group, the negative percent changes of the WCSTPts and WCSTPss were 10.11 and 6.69% (Table 2).

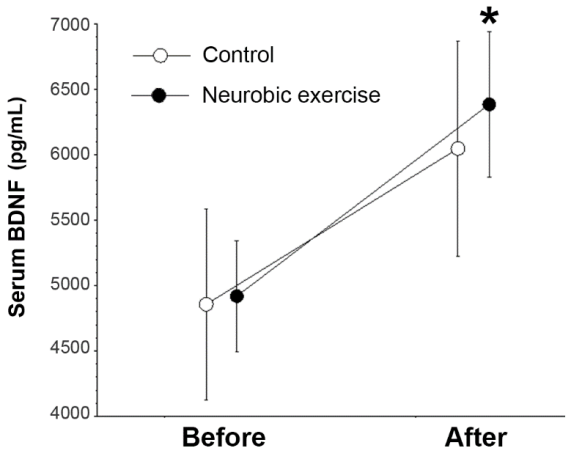

Figure 1. Serum BDNF levels before and after the neurobic exercise compared with those of the control group. The plots are shown as mean±SEM. An asterisk indicates a significant difference at P-value <0.05 using paired t-test.

4. Discussion and Conclusions

In this study, we aimed to examine the effects of neurobic exercise on cognitive function and serum BDNF in cognitively normal to mild cognitive impaired elderly subjects. We found that neurobic exercise improved cognitive function in older adults. The participants who trained in the neurobic exercise program showed a significant increase in the score of the Rey-Osterrieth Complex Figure test in both the immediate and delayed T score more than the untrained subjects in the CG group, which reflected better visual memory. Kanthamalee and Sripankaew (2013) found that neurobic exercise improved 23% higher from baseline and that the results were concordant to this study. Neurobic exercise may help activate the prefrontal association cortex

Table 2. Cognitive tests and serum BDNF levels between the control and neurobic exercise groups, before and after intervention.

Variables	Control (n=23)				Percent difference	Neurobic exercise (n=28)				Percent difference
	Pre-test Mean± SD	Post-test Mean± SD	Difference Mean (95% CI)	p-value (paired t-test)		Pre-test Mean± SD	Post-test Mean± SD	Difference Mean (95% CI)	p-value (paired t-test)	
MoCA	18.09± 5.03	18.26± 6.58	0.17 (-1.78, 1.43)	0.825	0.93	20.54± 4.57	20.64± 5.15	0.10 (-1.15, 0.94)	0.836	0.48
VPA I	8.30± 2.49	8.91± 3.10	0.60 (-1.51, 0.30)	0.179	7.34	8.96± 2.82	10.07± 3.23	1.10 (-1.95, -0.25)	**0.013***	12.38
VPA II	8.57± 2.66	8.78± 2.62	0.21 (-1.08, 0.64)	0.607	2.45	9.39± 2.98	10.14± 3.52	0.75 (-1.59, 0.92)	0.079	7.98
ROCFI	38.78± 14.47	39.70± 15.94	0.91 (-6.00, 4.18)	0.714	2.37	46.04± 16.44	50.75± 17.91	4.71 (-7.76, -1.66)	**0.004*@**	10.23
ROCFD	37.17± 14.62	37.52± 16.36	0.34 (-6.31, 5.62)	0.905	0.94	43.57± 16.01	48.54± 19.24	4.96 (-8.96, -0.96)	**0.017*@**	11.40
TMT-A	126.13± 65.17	116.78± 56.54	9.34 (-23.87, 42.56)	0.565	7.41	111.96± 51.30	95.29± 43.39	16.67 (-2.40, 35.76)	0.084	14.88
TMT-B	284.33± 140.75	280.48± 145.73	3.85 (-34.37, 42.09)	0.835	1.35	254.48± 99.82	183.63± 100.36	70.85 (38.98, 102.71)	**0.000*@**	27.84
WCSTEts	34.30± 8.32	34.17± 7.27	0.13 (-2.66, 2.92)	0.924	0.38	32.25± 5.73	35.57± 8.28	3.32 (-5.92, -0.71)	**0.014***	10.29
WCSTEss	76.48± 12.41	76.30± 10.96	0.17 (-3.99, 4.33)	0.932	0.23	73.29± 8.54	78.29± 12.64	5.00 (-8.94, -1.05)	**0.015***	6.82
WCSTPts	37.39± 8.14	33.61± 8.20	3.78 (0.70, 6.86)	**0.018***	10.11	35.18± 10.66	39.75± 10.61	4.57 (-9.28, 0.14)	0.057@	12.99
WCSTPss	80.96± 11.98	75.54± 12.15	5.39 (0.80, 9.98)	**0.023***	6.69	77.57± 16.04	84.50± 16.00	6.92 (-13.95, 0.10)	0.053@	8.93
WCSTCts	34.35± 7. 56	35.17± 6.46	0.82 (-3.25, 1.60)	0.488	2.38	35.32± 8.07	33.32± 5.13	2.00 (-0.50, 5.50)	0.099	5.66
WCSTCss	77.04± 11.21	77.87± 9.83	0.73 (-4.03, 2.55)	0.646	1.07	77.82± 12.19	74.86± 7.48	2.96 (-1.71, 7.63)	0.204	3.80
Serum BDNF	4853 ± 3266	6045 ± 3669	1193 (-352, 2737)	0.123	24.56	4914 ± 2101	6375 ± 2765	1462 (75, 2848)	**0.034***	29.73

MoCA = Montreal Cognitive Assessment (score); VPA I = Verbal Paired Associates I (scale score); VPA II = Verbal Paired Associates II (scale score), ROCFI = Rey-Osterrieth Complex Figure Immediate (T-score); ROCFD = Rey-Osterrieth Complex Figure Delayed (T-score); TMT-A = Trail making test A (second); TMT-B = Trail making test B (second); WCSTEts = the Wisconsin Card Sorting Test Error response (T-score); WCSTEss = the Wisconsin Card Sorting Test Error response (Standard-score), WCSTPts = the Wisconsin Card Sorting Test-Preservative response (T-score); WCSTPss = the Wisconsin Card Sorting Test-Preservative response (Standard-score); WCSTCts = the Wisconsin Card Sorting Test-Conceptual response (T-score); WCSTCss = the Wisconsin Card Sorting Test-Conceptual response (Standard-score); Serum BDNF = Serum Brain-Derived Neurotrophic factor (pg/mL); CI= confidence interval.
* P<0.05 (within group); @ P<0.05 (between two groups).

part of the brain which is responsible for creating memory (working memory) and stimulating the hippocampus and limbic system to improve memory function. The findings supported recent research that indicated that memory improved from cognitive training in older people (Gumther, Schafer, Holzner, & Kemmle, 2003; Klusmann *et al.*, 2010; O'Dwyer, Burton, Pachana, & Brown, 2007).

In addition, participants in the NG group had significantly lower Trail Making Test Part B scores than the CG group. This result indicated that after a training exercise, the participants could focus on any situation or event for a longer period of time. Mozolic, Long, Morgan, Rawley-Payne and Laurienti (2011) used the modality-specific attention training program to improve the attention score by 25.89%

from baseline which was consistent with our finding where the improvement was found to be 27.84%. Neurobic exercises help stimulate a widespread network of thalamic and bihemispheric structures in which the frontal lobes enhance the attention ability in aging (Filley, 2002). Beneficial changes at structural and functional levels in the aging brain can also occur due to cognitive training (Lustig, Shah, Seidler, & Reuter-Lorenz, 2009). Moreover, previous studies supported our results which indicated that attention ability was enhanced by cognitive exercise (Tusch *et al*., 2016).

We investigated the executive function using the Wisconsin Card Sorting Test and our results showed that both the T score and the standard-score of the Wisconsin Card Sorting Test-Preservative response were significantly higher in the NG group than the CG group which showed 12.99% and 8.93% improvements, respectively. These results indicated that the neurobic exercise helped improve mental flexibility in older adults and implied that the participants could make rational decisions and solve problems better. The neurobic exercises might help stimulate brain activities in part of the prefrontal lobe involving making decisions when solving complex problems and planning (Manchester *et al*., 2004; Mapou, 1992; Serino *et al*., 2006). Our study demonstrated that cognitive training can improve the executive function in older people (Ball *et al*., 2002; O'Dwyer *et al*., 2007). In the CG group, we found that the T score and standard-score of the Wisconsin Card Sorting Test-Preservative response were significantly lower than the pre-test score by 10.11% and 6.69%, respectively. These results indicated that older adults who do not receive the neurobic exercise or any brain training might have a decline in mental flexibility and executive function involving making decisions, solving complex problems, and planning.

Finally, we examined the serum BDNF level between the NG and CG groups. The level of serum BDNF significantly increased after the intervention in the NG group which showed that neurobic exercise induced higher serum BDNF which might reflect the enhancement of brain function. Angelucci *et al*. (2015) found that cognitive training improved the level of serum BDNF by 40% from the baseline which was consistent with our study. Generally, levels of BDNF relate to the health of the brain. Patients who have low levels of BDNF are more likely to have AD, depression, schizophrenia, and Huntington's disease (Ciammola *et al*., 2007; Gama *et al*., 2007; Laske *et al*., 2006; Piccinni *et al*., 2008). Increasing age was associated with smaller hippocampal volumes, reduced levels of serum BDNF, and poorer memory performance. Lower levels of BDNF were associated with smaller hippocampus and poorer memory, even when adjusting for the variation related to age (Erickson *et al*., 2010). Moreover, BDNF is a potential marker of neural integrity. In humans, BDNF is involved in the formation of long-term memory in the hippocampus (Yeh *et al*., 2012). The BDNF is an important molecular mediator of the neuroplasticity of the brain, particularly in survival, differentiation, and neuronal growth (McAllister, Katz, & Lo, 1999) and may influence brain functions, including learning and memory (Tyler, Alonso, Bramham, & Pozzo-Miller, 2002). Thus, an increase of BDNF might contribute to a reduced risk of dementia.

The strength of this study is that it includes older people with normal cognition or mild cognitive impairment who are the main proportion in this age group. Also, the tools and activities used in the intervention are easily integrated into other home-based activities. Successful intervention could be implemented in a large population. Also, with the significant increase of serum BDNF in the intervention group as a biomarker, it is a potential intervention to enhance brain function. In addition, the neuropsychological tests were performed with an interval period of 24 weeks; therefore, the practice effect was unlikely to occur. Another concern regarding the neuropsychological testing is that it takes the elderly a long time to finish the tests which makes them less attractive and the elderly easily lose focus.

In conclusion, this study indicates that neurobic exercise can increase the level of serum BDNF indicating enhancement of brain function. As a result, neurobic exercise can be used as an effective method to create a brain training program to reduce the risk of dementia in the elderly.

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