The Effectiveness of Cognitive Flexibility Training Program on Cognitive Functions and Activities of Daily Living in Patients with Ischemic Stroke

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ABSTRACT

Objective: To evaluate the effectiveness of a cognitive flexibility training program on cognitive functions and activities of daily living (ADLs) in patients with ischemic stroke.

Methods: A single blind randomized controlled trial study was conducted in a stroke unit of a tertiary hospital in a Bangkok setting. The sample size was 80 participants of both genders, aged 18 – 80 years. The sample size was stratified by age. Randomization was generated by a computer program dividing 40 participants into the experiment and 40 into the control group. Eleven participants dropped out during data collection. Therefore, 34 participants in the experimental group received cognitive flexibility training four days a week for 30-40 minutes per day over a period of 4 weeks in addition to usual care. There were 35 participants in the control group who received diary recording and usual care. The study used various instruments for data collection, including a Thai version of the Montreal Cognitive Assessment and Barthel's Index of Activities of Daily Living. Data were analyzed by multivariate analysis of covariance (MANCOVA).

Results: The experimental group had higher cognitive functions and abilities in performing activities of daily living than the control group with statistical significance ($p < .05$).

Conclusion: The study suggested that the program can be used to increase both cognitive functions and activities of daily living. Nurses and healthcare staff should apply this program in patients with acute ischemic stroke for nervous system recovery.

Keywords: Ischemic stroke; cognitive flexibility training program; cognitive functions; activities of daily living (Siriraj Med J 2021; 73: 236-244)

INTRODUCTION

Stroke, or cerebrovascular disease, is a severe neurological disease that affects many aspects involving patients, families, economics and society. Stroke is also commonly found in adults and elderly around the world. According to a 2019 World Stroke Organization report, stroke is a major public health problem and the second leading cause of death in the world. There are 80 million stroke patients worldwide; an average of 13.7 million new patients are found per year and there are 5.5 million

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stroke-related deaths annually.[1] In Thailand, stroke is a disease with the second highest mortality rate and second leading burden of disease. In addition, stroke can cause disability-adjusted life years (DALYs) from death and premature deaths at higher rates than the burden of illness.[2]

Stroke is a leading cause of cognitive impairment due to decreased blood supply to the brain and oxygen deficiency resulting in degeneration of neurons in the brain. The incidence of cognitive impairment in stroke patients is between 20-60% from the first 24 hours to 6 months after the stroke occurs.[3] Approximately 50 - 70% of patients have mild to moderate cognitive impairment with significant impact on advanced cognitive skills, executive function and cognitive flexibility. Furthermore, 15 to 30% of stroke survivors live with disabilities including impaired physical and cognitive functions. Patients, therefore, require assistance in their daily activities and dependency within one year post-stroke.[4]

Cognitive flexibility is considered a hallmark of human cognition and intelligent behavior.[5] It is also considered a core executive function and can be conceptualized as a well-delimited ability of the cognitive system, namely, set-shifting and higher-order ability such as cognitive control, a measure for divergent thinking and planning and flexibility in problem-solving. The focus is on the introduction of nerve impulses and network connections in the brain working together as a dynamic.[6] Cognitive flexibility produces thinking processes and skills in a systematic way and connects basic concepts and skills in daily activities through the coordination of two hemispheres of the brain, modifying the structure and function of the brain and signalling the transmission of nerve impulses that are more effective, thereby resulting in rapid recovery of the nervous system. The optimal recovery period for the nervous system occurs within two to four weeks.[7] The recovery of the nervous system is evident within the first 30 days, and there is still another 90 days of recovery. From 90 days to 6 months, recovery continues to take place, but is not as noticeable as in the initial phase.[8] Therefore, cognitive flexibility training in the acute phase can help restore the cognitive skills and basic daily activities of stroke patients more efficiently.[9]

According to a literature review related to cognitive flexibility training abroad, most of them mainly focused on chronic phase after stroke to improve performance of several daily routines and cognitive recovery in memory and communication. The VR-based intervention involving a virtual simulation of a city tasks in the performance of daily routines in stroke patients underwent a twelve-session intervention over a period of 4-6 weeks, results showed statistical significance in global cognitive functioning, executive functions and ADL performance.[10] The findings correspond with the computer-based cognitive flexibility training consisting of 9 tasks in the domains of shifting ability, cognitive control, adaptation, memory and reasoning over a period of 12 weeks, all groups showed improvements in cognitive and executive functioning. Furthermore, these improvements remained stable at 4 weeks after training completion.[11] In addition, the PC-cognitive training consisting of the fives specific cognitive domains for 8 weeks may be a useful method for accelerating post-stroke cognitive recovery, particularly in memory and language communication.[12]

Most of the literature reviewed in relation to cognitive flexibility training in Thailand, involved cognitive training combined with executive function. Most programs included memory attention and diary recording for 4 weeks. The programs could be used to recover brain function and increase attention, memory and basic cognitive skills, not including advanced cognitive skills.[13] Moreover, executive training programs including games and calculations 3 times a week for 25 minutes/session for 6 weeks can be used to improve memory attention and executive functions in chronic phase after stroke.[14] Furthermore, comprehensive rehabilitation programs continued for 30 days could be used to increase both cognitive functions and ADLs in patients with traumatic brain injuries, but did not include cognitive flexibility skills.[15] Thus, the specialized practice of cognitive flexibility training in acute phase after stroke remains limited and may not be enough to create brain connections and adjust perceptions or adaptations in various different situations and effective problem-solving.[11] Training in initial phase would be benefits in promoting of neuroplasticity and resulting in rapid recovery of the nervous system than general training.[24]

For these reasons, the researcher gained an interest in the development of a cognitive flexibility training program in acute ischemic stroke patients, mainly focused on promoting both cognitive functions and ADLs abilities through learning a variety of cognitive flexibility skills over a period of 4 weeks. The program including diary recording, memorization, shopping at the market and bank scenarios, categorization, prioritization, divergent thinking, planning and flexibility problem-solving with activities to recover nervous system function through the mechanism of modifying the neurological structure and physiology of cognitive processes. Stimulating brain learning with a variety of activities allows the brain to send nerve impulses easily and promotes greater efficiency in neurological recovery.[16]

MATERIALS AND METHODS

Research design

The present study was a single blind randomized controlled study. It was a randomized controlled evaluator-blinded trial in a pre-test - post-test design which assessed by the research assistant who did not know which groups of participants (experimental or control group) to reduce detection bias. The study conducted at a stroke unit of a tertiary hospital in Bangkok, Thailand, from June 2019 to February 2020.

Participants

This study consisted of male and female patients aged between 18 - 80 years and first diagnosed with acute ischemic stroke who had passed the critical phase at least 24 hrs.

Inclusion Criteria

1. Moderate stroke severity or higher as determined by a physician.
2. No vision problems, blindness and visual field defects.
3. No hearing problems or hearing loss confirmed by medical records.
4. Presence of a caregiver with a smartphone, ability to use an application to send messages and availability to participate in the program for four weeks.

Exclusion Criteria

1. Patients diagnosed with aphasia and impaired language comprehension.
2. Patients diagnosed with severe diseases such as ESRD and cancer.
3. Patients with a history of psychiatric illnesses and Alzheimer's disease.
4. Patients with severe cognitive impairment (TMSE < 20 points).
5. Patients with depression (PHQ-9 ≥ 7 points).

Sample size calculation

The researchers used the effect size of a previous study based on cognitive function outcomes.[12] The calculation showed that "f" is 0.4, which is a good effect size. The sample size for the present study was derived though power analysis (alpha = 0.05 with 80% power). The G power program (version 3.1) determined that the total sample size should be 64 people. In this study, the researchers increased the sample size by 20% to account for the drop-out rate. Thus, 80 participants were subsequently and evenly divided into the experimental and control groups by random sampling and stratified by age (≤ 60, > 60 years). A computer-randomized block design randomized 40 participants each into the experimental and control groups.

Ethics

This study was approved by the Human Research Protection Unit, Faculty of Medicine Siriraj Hospital at Mahidol University, Bangkok, Thailand (Si 240/2019). The protocol number is 032/2019(EC3), and all participants signed informed consent forms.

Recruitment

Patients were invited to participate in the study after the researcher gained access to the samples by enlisting the research assistants as research publicists. Then the objectives, durations and risks involved in the study were explained. Confidentiality issues were also addressed. The subjects who agreed to participate then voluntarily completed and signed the informed consent forms (Fig 1).

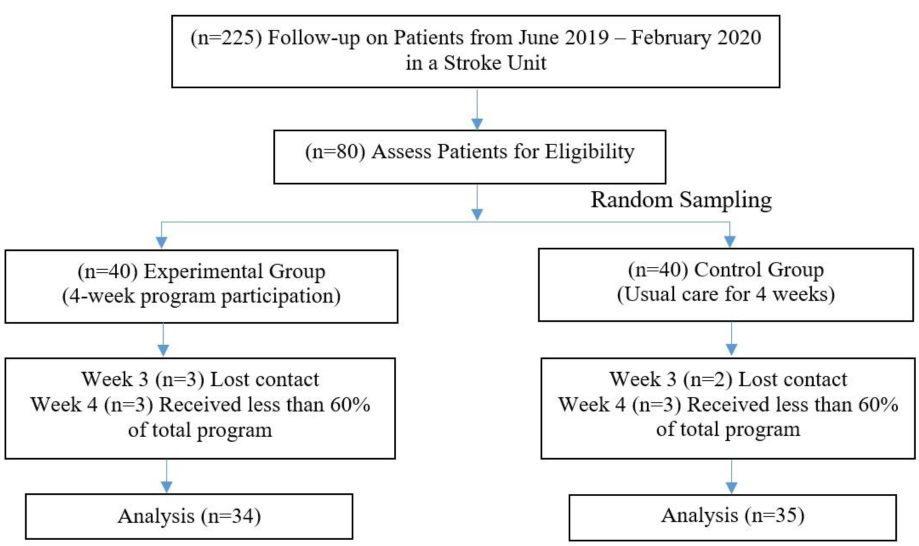

Fig 1. Flow Chart of the Research Process.

Intervention

Experimental Group

The cognitive flexibility training program, which was a set of activities developed by the literature review, included diary recording, memorization, shopping at the market, bank scenarios, categorization, prioritization, divergent thinking, planning and flexibility in problem-solving activities, which took 30 - 45 minutes/session for a total of 4 daily sessions, 4-week periods. The program required patients to do the exercises in the book handed out as a guide for patients to use in cognitive training while in the hospital and after discharge from hospital (Table 1).

Control Group

During the 4-week periods, patients received diary writing training which took 15 - 20 minutes a day and usual nursing care at a stroke unit of a tertiary hospital. The researcher telephoned to evaluate the problems and obstacles encountered in diary writing once a week, asked about general health conditions and encouraged continuous use of diary writing.

TABLE 1. Program activities.

Time period	Sessions	Activities
Week 1 Day 1	1. Pretest assessment by research assistant. (15 minutes)	- Research assistant assessed cognitive function by using the MoCA-Thai and Barthel ADL Index to assess ADL performances before the experiment.
Day 2 – 5	2. Cognitive flexibility training program by the researcher. (45 minutes)	**Pre-training activities (15 minutes)** - Orientation time, place, person - Self-awareness training and brain exercises - Diary writing **Training activities (30 minutes)** - Working and recall memory training: spell the name, surname, months backwards, proverb telling activities - Set shifting training: 5 step sequences activities - Cognitive control training: beads sorting, magic character games, pattern block and categorization practice activities - Divergent thinking training: magic matchstick games, calculation activities, reasoning and decision-making activities - Planning and flexibility problem-solving training: shopping at the market and bank scenarios activities
Week 2-4	1. Cognitive flexibility training program by the researcher. (30 – 40 minutes) 2. Telephone follow-up calls by the researcher. (10 minutes)	- The researcher provided the guidelines and handbook for the cognitive flexibility training program to the subjects for training continuously at home. - Caregivers sent the exams' pictures to the researcher via an applications on smartphone. **Personal Follow-Up Telephone Calls (10 minutes)** - Evaluate the problems and obstacles encountered in training at home - Asked about general health conditions - Encouraged continuous use of the program
End of week 4	1. Post-test assessment by research assistant. (15 minutes)	- The research assistant assessed cognitive function by using the MoCA-Thai and Barthel ADL Index to assess ADL performance after the experiment. - To reduce detection bias, the research assistant was blind to which patients were in the control and experimental groups.

Measurements

1. Part 1: Demographic and Clinical Characteristic Data

Demographic information on age, gender, marital status, family role, occupation, education years and clinical characteristics including underlying diseases, lesions, stroke symptoms, interventions, severity of stroke, length of stay and onset of stroke in minutes were obtained from all of the participants.

2. Part 2: Cognitive Functions Measurement

The MoCA-Thai (Montreal Cognitive Assessment) was developed by Solaphat Hemrungrojn and the Faculty (2011).[22] The examination was used to assess various skills of cognition before and after receiving the training program and contained eight question categories including executive, naming, memory, attention, language, abstraction, delayed recall and orientation with a total score of 0 – 30 points. The results of test-retest reliability equalled 0.95.

3. Part 3: Activities of Daily Living (ADLs) Performance Measurement

Barthel's ADL index (Barthel's Index of Activities of Daily Living) was developed by Piyapata Detphratham and colleagues (2006).[23] The scoring criteria was 0, 5, 10 and 15 points. A full score of 0 – 100 points was assessed by observing the behaviour of the patients in 10 activities: feeding, transfer, grooming, toilet use, bathing, mobility, stairs, dressing, bowel movements and bladder continence. The results of inter-rater reliability equalled 0.99.

Statistical analysis

SPSS statistics software (Version 22) was used for data analysis. The significance level was set at .05. Demographic data and clinical characteristics were analyzed by distribution of frequency and percentage while comparisons of the differences in demographic characteristics were made by using chi-square, Fisher's exact test and independent t-test statistics.

Differences in the average pre-post test scores of cognitive function and ADLs in ischemic stroke patients in the experimental and control groups were analyzed by using mean, standard deviation, minimum-maximum and paired t-test statistics. Moreover, differences in the average post-test scores for cognitive function and ADLs between experimental and control groups were analyzed by using multivariate analysis of covariance (MANCOVA) statistics. The pre-test scores for cognitive function and ADLs were used as covariates.

RESULTS

Part 1: Demographic and Clinical Characteristic Data

Thirty-four subjects remained in the experimental group at the end of the study (attrition rate = 15%). Contact was lost with three persons, while three other persons received less than 60% of the total program. Thirty-five subjects remained in the control group (attrition rate = 12.5%). Contact was lost with two persons and three other persons received less than 60% of the total program. Overall, the total attrition rate was 13.75%.

The demographic information of both groups included 53.6% of the subjects who were aged over 60 years, an average age of 60.4 years (±13.72) for stroke survivors and an average age of 45.9 years (±11.93) for caregivers. Most of the samples were males (62.3%), married (75.4%), family members (58%), had average education for 9.4 years (±5.06) and were unemployed (34.8%). However, when personal characteristics were compared between the experimental and control groups, there were no statistically significant difference (Table 2).

According to the clinical characteristics of the research, the most common diseases found in both groups were hypertension at 66.7%, dyslipidemia at 36.2%, diabetes mellitus at 31.9% and atrial fibrillation at 21.7%. Approximately half of the patients presented with pathological lesions in the left brain at 52.2%, which resulted in right-side weakness. The symptoms of stroke included limb weakness at 52.2%, difficulty speaking at 78.3% and facial palsy at 72.5%. Moderate or greater severity of stroke was determined by average scores of 12.3 points (±5.77), while the time to hospital since the onset of stroke in minutes was 146.2 minutes (±94.14) and the average of length of stay was 7.7 days (±5.04). Furthermore, the majority of treatments were rt-PA 37.7% and rt-PA combined with mechanical thrombectomy (MT) 27.5%. However, when the clinical characteristics were compared between the two groups by using chi-square, Fisher's exact test and independent t–test were not significantly different (Table 3).

Part 2

The experimental group had cognitive function after training equal to 24.71 points (S.D. 2.11), which was higher than that of the control group with a score 22.40 points (S.D. 2.44). Furthermore, when tested with paired t-test statistics, the cognitive functions within the experimental group before and after training were significantly different (p-value < 0.05). In addition, the average ADLs abilities in the experimental group before training was 60.00 points (S.D. 13.93), while the control group had 65.29 points (S.D. 15.76). After training, the experimental group had a score of 83.38 points (S.D =

TABLE 2. Demographic data of the experimental and control groups.

Characteristics	Experimental Group n (%)	Control Group n (%)	*P*-value
Age			0.81[a]
≤ 60 years	15 (44.1)	17 (48.6)	
> 60 years	19 (55.9)	18 (51.4)	
Patients	$\bar{x}$ = 59.9, SD = 15.14	$\bar{x}$ = 61.0, SD = 12.30	0.75[c]
Caregivers	$\bar{x}$ = 43.9, SD = 12.47	$\bar{x}$ = 47.9, SD = 11.38	0.17[c]
Gender			1.0[a]
Male	21 (61.8)	22 (62.9)	
Female	13 (38.2)	13 (37.1)	
Marital Status			0.27[b]
Single/Widowed/Divorced	10 (29.4)	7 (20.0)	
Married	24 (70.6)	28 (80.0)	
Family Roles			1.0[a]
Family Head	14 (41.2)	15 (42.9)	
Family Member	20 (58.8)	20 (57.1)	
Occupations			0.90[b]
Unemployed	11 (32.4)	13 (37.1)	
Employed	8 (23.5)	5 (14.3)	
Business Owner	5 (14.7)	5 (14.3)	
Retirement/Civil Servant	10 (29.4)	12 (34.3)	
Education (years)	$\bar{x}$ = 9.5, SD = 5.29	$\bar{x}$ = 9.2, SD = 4.82	0.81[c]

[a] = Chi-square test, [b] = Fisher's exact test, [c] = Independent t-test

11.85), which was higher than the control group with an average of 67.86 points (S.D. 14.72). And when tested with paired t-test, the activities of daily living within the experimental group before and after training were significantly different (p-value < 0.05) (Table 4).

Part 3

When using the pre-test scores of cognitive function and ADLs as covariates with multivariate analysis of covariance (MANCOVA) statistics, the effectiveness of the cognitive flexibility training program on cognitive functions after the experiment was less than 0.05 (p-value < 0.05), and the ability to perform ADLs after the experiment was also less than .05 (p-value < 0.05). It has been stated that the cognitive function and ADLs of the experimental group who received the training program were different with statistical significance at .05. The findings demonstrate the effectiveness of the cognitive flexibility training program on increasing cognitive function and ADLs performance (Table 5).

DISCUSSION

According to the research findings on the effectiveness of the cognitive flexibility training program, the patients with ischemic stroke who received the training program had higher levels of cognitive functions and ADLs than who received usual nursing care only with statistical significance. Furthermore, the patients who received the program had higher levels of cognitive functions and ADLs than pre-training with statistical significance.

The above findings can be described as follows: The patients with acute ischemic stroke who received the cognitive flexibility training program had higher levels of cognitive function and ADLs. These may cause by the patients received longer intervention time in the experimental group. Furthermore, in developing

TABLE 3. Clinical characteristics of the experimental and control groups.

Characteristics	Experimental Group n (%)	Control Group n (%)	*P*-value
Underlying Diseases			0.43[b]
Hypertension	21 (61.8)	25 (71.4)	
Dyslipidemia	12 (35.3)	13 (37.1)	
Diabetes mellitus	11 (32.4)	11 (31.4)	
Atrial fibrillation	4 (11.8)	11 (31.4)	
Lesions			0.81[a]
Left side brain	17 (50.0)	19 (54.3)	
Right side brain	17 (50.0)	16 (45.7)	
Stroke symptoms			
Left side weakness	17 (50.0)	16 (45.7)	0.81[a]
Right side weakness	17 (50.0)	19 (54.3)	0.81[a]
Dysarthria	26 (76.5)	28 (80.0)	0.77[a]
Facial palsy	22 (64.7)	28 (80.0)	0.19[a]
Intervention			0.98[b]
None	10 (29.4)	10 (28.6)	
rt-PA	12 (35.3)	14 (40.0)	
MT	2 (5.9)	2 (5.7)	
rt-PA with MT	10 (29.4)	9 (25.7)	
Severity of Stroke	$\underline{\chi}$ = 12.9, SD = 5.12	$\underline{\chi}$ = 11.7, SD = 6.41	0.40[c]
Length of Stay (days)	$\underline{\chi}$ = 6.8, SD = 4.68	$\underline{\chi}$ = 8.6, SD = 5.40	0.14[c]
Onset of Stroke (minutes)	$\underline{\chi}$ = 156.4, SD = 104.0	$\underline{\chi}$ = 135.9, SD = 83.4	0.37[c]

[a] = Chi-square test, [b] = Fisher's exact test, [c] = Independent t-test

TABLE 4. The results on cognitive functions and activities of daily living (ADLs) abilities between the experimental and control groups at pre- and post-test.

Variables	Experimental Group mean (SD)	min - max	Control Group mean (SD)	min - max	*P*-value
Cognitive Functions					<0.001
Before Training	21.12 (2.33)	17 – 25	21.89 (2.69)	18 – 27	
After Training	24.71 (2.11)	20 – 28	22.40 (2.44)	18 – 27	
ADLs Performance					<0.001
Before Training	60.0 (13.93)	40 – 90	65.3 (15.76)	40 – 100	
After Training	83.3 (11.85)	60 – 100	67.8 (14.72)	40 – 100	

Paired *t*-test

TABLE 5. The results of the effectiveness of the cognitive flexibility training program on cognitive functions and activities of daily living between the experimental and control groups.

Source	Dependent Variables	Mean Square	F	*P*-value
Covariates				
MoCA (Pretest)	Cognitive Functions	210.35	386.469	<0.001
	Activities of Daily Living	143.80	4.488	.038
Barthel (Pretest)	Cognitive Functions	0.802	1.473	.229
	Activities of Daily Living	5973.4	186.447	<0.001
Effects of the intervention	Cognitive Functions	148.52	272.869	<0.001
	Activities of Daily Living	6659.7	207.869	<0.001

Box's M = 2.608, *P*-value < 0.05
Multivariate analysis of covariance (MANCOVA)

neuroplasticity, which is considered an important mechanism for recovering brain ability, the concept of neuroplasticity is the ability to change structure and function in the central nervous system, which can occur throughout life depending on the experience or activity of the stroke patient. It is an important mechanism for restoring the ability of the nervous system.[18] Neuroplasticity was mostly found to occur during Weeks 3 to 4 after the ischemic events and continued for three months after stroke.[24] This finding was consistent with the conceptual framework of the pathophysiological aspect of brain plasticity[17] and modulation of neural plasticity (experience-dependent plasticity),[18] which states that neuroplasticity is an important mechanism for restoring the ability of the nervous system with changes in the anatomical structure and nerve network in addition to increasing the dendrite branches and stimulated recovery of the nervous system through a cognitive process. Thus, the nerve cells sprout, become elongated or regenerate and, when continuously stimulated, have increased ability of nerve conduction and networking between brain hemispheres working together as a dynamic. As a result, the brain changes its structure and adjusts its function to replace injured nerve cells for increased in cognitive function. Moreover, dynamic linkage allows patients to perform more activities of daily living independently.

The findings correspond with findings of Faria and colleagues (2016)[10] who examined the effectiveness of a VR-based intervention. The results showed statistical significance in global cognitive functions, executive function and ADLs performance. Furthermore, the findings correspond with Van de ven and colleagues (2017)[11] who examined the effectiveness of computer-based cognitive flexibility training, all groups improved on cognitive and executive functioning. In addition, the findings also correspond with De Luca and colleagues (2018)[12] who examined the effectiveness of PC-cognitive flexibility training, the findings suggest that training may be a useful method for accelerating post-stroke cognitive recovery. However, the findings differ from the study of Aulwatthanasiri, P. (2012),[13] Khantee, R. (2016)[14] and Phancham, N. (2010).[15] This study took less training time and improved both cognitive functions and ADLs in patients through the stimulation of cognitive processes by various skills with statistical significance.

In the control group, cognitive functions and ADLs before and after training were significantly different. This finding can be explained in that there was a spontaneous recovery of the nervous system. The recovery is evident within the first 30 days followed by another 90 days. From 90 days to 6 months, recovery continues to take place, but is not as noticeable as in the initial phase.[8] During the first week, there is recovery from local factors, improved blood circulation and partial recovery of the brain cells. Later is the process of neuroplasticity, which requires rehabilitation and training activities. Therefore, cannot yet be concluded that all treatments will enable rapid rehabilitation for patients.

Limitations

The findings of present study show that the 4-week program is compatible with participants who routinely come for follow up appointments at three to four weeks post-stroke. Moreover, this program should be given more training time in control group. In addition, to promote cognitive functions and ADLs performance, this program should be extended to interventions lasting at least 3-month based on the nervous system recovery theory.

CONCLUSION

According to the findings, the cognitive flexibility training program consisting of memory training and 4 domains of cognitive flexibility (set shifting, cognitive control, divergent thinking/planning and flexibility in problem-solving) can increase both cognitive functions and ADLs through the mechanism of modifying neurological structure and the physiology of cognitive processes. Thus, nurses and healthcare staff should apply this program in patients with acute ischemic stroke for nervous system recovery.

Conflicts of Interest: Authors report no conflicts of interest in this work.

REFERENCES

1. Lindsay MP, Norrving B, Sacco RL, Brainin M, Hacke W, Martins S, et al. Global Stroke Fact Sheet 2019. Int J Stroke 2019;14:806-17.
2. Strategy and Planning Division Office of the Permanent Secretary. Public Health Statistics A.D.2018. Nonthaburi: WVO Thai Printing; 2018.
3. Turunen KE, Laari SP, Kauranen TV, Uimonen J, Mustanoja S, Tatlisumak T, et al. Domain-specific cognitive recovery after first-ever stroke: a 2-year follow-up. J Int Neuropsychol Soc 2018;24:117-27
4. Pahlman U, Savborg M, Tarkowski E. Cognitive dysfunction and physical activity after stroke: The Gothenburg cognitive stroke study in the elderly. J Stroke Cerebrovasc Dis 2012;21: 652-8.
5. Rende B. Cognitive flexibility: Theory, assessment, and treatment. Semin Speech Lang 2000;21:121-53.
6. Ionescu T. Exploring the nature of cognitive flexibility. New Ideas Psychol 2012; 30:190-200.
7. Ward NS. Restoring brain function after stroke-bridging the gap between animals and humans. Nat Rev Neurol 2017;13:244-55.
8. Stinear CM, Petoe MA, Byblow WD. Primary motor cortex excitability during recovery after stroke. Brain Stimul 2015;8: 1183-90.
9. Zucchella C, Capone A, Codella V, Vecchione C, Buccino G, Sandrini G, et al. Assessing and restoring cognitive functions early after stroke. Funct Neurol 2014; 29:255.
10. Faria AL, Andrade A, Soares L, Badia SB. Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a randomized controlled trial with stroke patients. J Neuroeng Rehabil 2016;13:96.
11. Van de ven RM, Buitenweg JI, Schmand B, Veltman DJ, Aaronson JA, Nijboer TC, et al. Brain training improves recovery after stroke but waiting list improves equally: A multicenter randomized controlled trial of a computer-based cognitive flexibility training. PloS One 2017;12:e0172993.
12. De Luca R, Leonardi S, Spadaro L, Russo M, Aragona B, Torrisi M, et al. Improving cognitive function in patients with stroke: can computerized training be the future? J Stroke Cerebrovasc Dis 2018;27:1055-60.
13. Adulwattanasiri P, Puwarawuttipanit W, Saneha C, Nilanont Y. The effectiveness of brain training program on attention and memory in acute ischemic stroke patients. Proceedings of the 3rd Hatyai National & International Conference; 2012 May 10; Hatyai University.
14. Khanthee R, Dhippayom JP, Munkhetvit P. Effects of cognitive training program on cognitive abilities in stroke patients. J Assoc Med Sci 2016;49:298.
15. Phancham N, Jitpanya C. Effects of comprehensive rehabilitation program and brain exercise on cognitive functions and activities on daily living in patients with traumatic brain injury. JNSCU 2010;22:22-33.
16. Pajaree K. Modern Neurology. Bangkok: October print house; 2019.
17. Hebb DO. The organization of behavior: A neuropsychological theory. New York: Chapman & Hall; 1949.
18. Pekna M, Pekny M, Nilsson M. Modulation of neural plasticity as a basis for stroke rehabilitation. J Stroke 2012;43:2819-28.
19. Glass GV. Primary, secondary & meta-analysis of research. Educ Res 1976;5:3-8.
20. Train the Brain Forum Committee (Thailand). Thai Mental State Examination. Siriraj Hospital Gazette 1993;45:359-74.
21. Lotrakul M, Sumrithe S, Saipanish R. Reliability and validity of the Thai version of the PHQ-9. BMC Psychiatry 2008;8:46-8.
22. Hemrungrojn S. Montreal Cognitive Assessment (MOCA) [Internet]. 2011 [cited 2018 Nov 25]. Available from: http://www.mocatest.org/pdf_files/test/MoCA-Test-Thai.pdf.
23. Dajpratham P, Meenaphant R, Junthon P, Pianmanakij S. The Inter-rater reliability of barthel index in stroke patients. J Rehabil Med 2006;16:1-9.
24. Cho DR, Lee SH. Effects of virtual reality immersive training with computerized cognitive training on cognitive function and activities of daily living performance in patients with acute stage stroke. Medicine 2020; 99:e20598.