Effectiveness of a Brain Training Program on the Cognitive Function of Sepsis Survivors: A Randomized Controlled Trial Study

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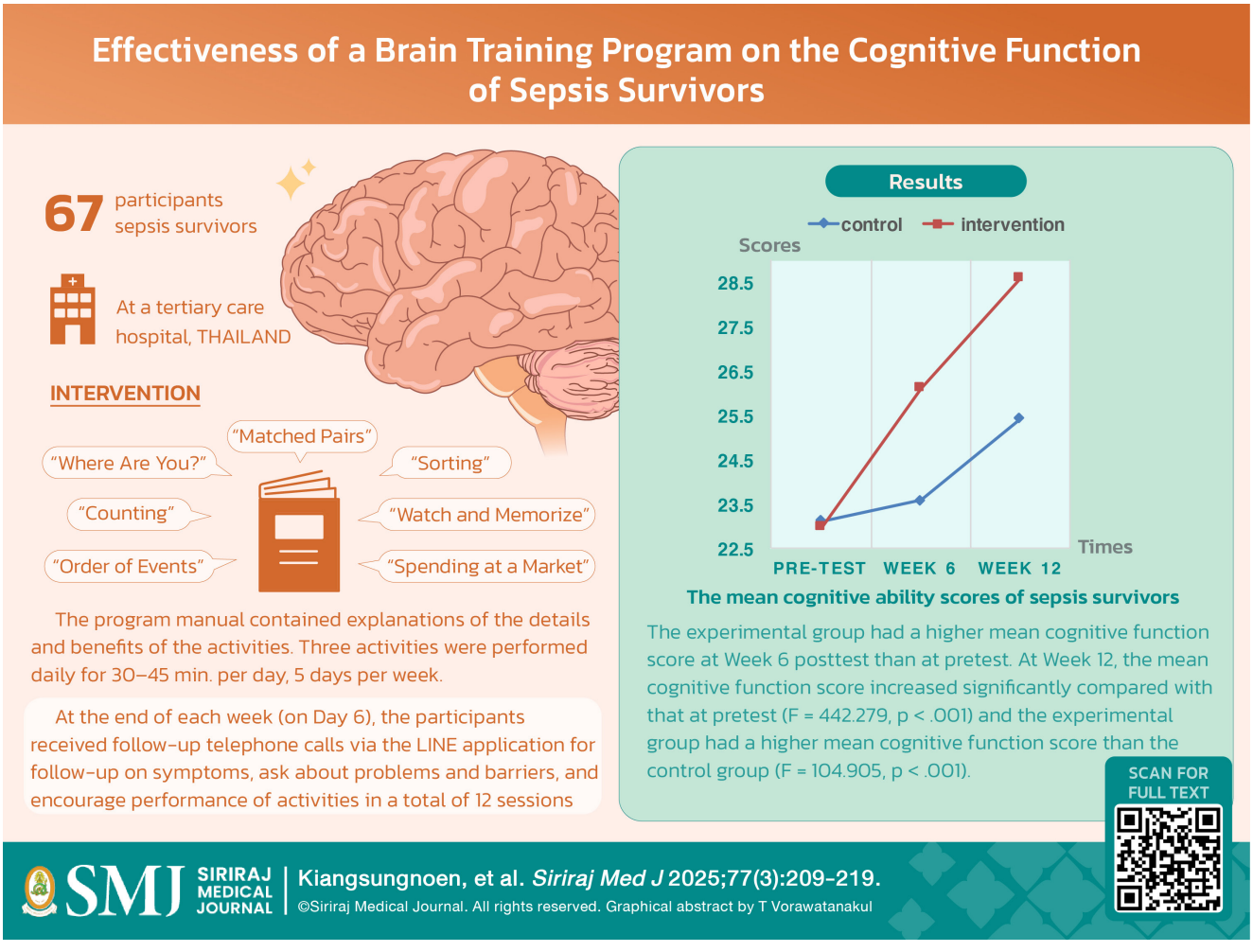

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ABSTRACT

Objective: This study aimed to evaluate the effectiveness of a brain training program designed to enhance the cognitive function of sepsis survivors.

Materials and Methods: We conducted a single-blind randomized controlled trial at a tertiary care hospital involving 67 participants aged over 18 years with participants randomly assigned to two groups, an experimental group (n=33) receiving the brain training program, and a control group (n=34) receiving standard care only. We measured cognitive function at three different time points: Baseline, Week 6, and Week 12, using the Thai Mental State Examination for testing and repeated measure ANOVA for statistical analysis.

Results: The experimental group had a higher mean cognitive function score at Week 6 posttest than at pretest. At Week 12, the mean cognitive function score increased significantly compared with that at pretest ($F = 442.279$, $p < .001$) and the experimental group had a higher mean cognitive function score than the control group ($F = 104.905$, $p < .001$).

Conclusion: The brain training program significantly increased the cognitive function levels of sepsis survivors in 6–12 weeks. The result of this study shows the benefits of a brain training program in increasing cognitive functions. Therefore, such a brain training program should be implemented among sepsis survivors to improve their cognitive functions.

Keywords: Sepsis survivors; brain training program; cognitive functions (Siriraj Med J 2025; 77: 209-219)

INTRODUCTION

Sepsis is a major current public health problem worldwide. A report on the analysis of the global sepsis situation in 2017 revealed that 48.9 million patients have had sepsis and approximately 38 million survive sepsis.[1] According to estimates on sepsis incidence and deaths from 15 countries from 1979 to 2015, 19.4 million patients experience sepsis annually. Although the mortality rate is lower, the number of sepsis survivors increased to 14.1 million patients annually (72.68%).[2] This finding is consistent with a report showing that medical advances in the treatment of sepsis have enabled patients with sepsis and those with severe cases to gain greater access to treatment and care in the intensive care unit, thereby doubling their survival rates.[3,4]

Currently, reports of sepsis survivors are increasing due to rapid access to treatment and increased quality of related clinical treatments; specifically, more stringent screening, concise diagnosis criteria, fast diagnosis, and clearer treatment guidelines have led to an increase in the number of survivors by 40%. After hospital discharge survivors have a mortality rate of 30-50% in 2 years, whereas 60% recover normal function within 1 year.[5-7] Moreover, sepsis survivors usually contract post-infection illnesses called post-sepsis syndrome with similarly increasing incidence and effects causing impaired psychological and physical balance.[8]

Psychological effects usually cause reduced cognitive function, attention deficiency, incoherence, reduced speaking ability and poor executive functions in the long term.[9,10] After hospital discharge, patients experience anxiety and abnormal psychological symptoms. Consequently, depression manifests with physically fatigue, appetite loss, and exhaustion, all of which weaken the immune system and increase the likelihood of severe recurrent infections affecting return to work, quality of life, and family relationships.[6] In these patients, common physical effects include the inability to work independently, reduced ability to perform the activities of daily living such as toileting or bathing and financial management due to muscle fatigue and damaged peripheral nerves. Cognitive impairment is a frequently encountered and significant starting point of psychological and physical effects in patients with post-sepsis syndrome.

The evidence shows that long-term cognitive impairments are commonly observed among sepsis survivors, with up to 50% experiencing neurocognitive impairment.[6,11] Around one in six patients, particularly those recovering from severe sepsis, may develop significant cognitive and physical impairments within the first 72 hours of recovery.[11] These impairments result from systemic inflammation that affects brain function.[6] Additionally, these patients are at higher risk of cognitive deficits such as memory and executive function impairments, which can significantly reduce quality of life and increase the need for rehabilitation.[6,11] Moreover, 6.1% of patients had cognitive impairment before hospitalization compared with 16.7% who had it after hospital discharge. One year after hospital discharge, 25%–45% of patients experience cognitive impairment. Among patients treated in an

intensive care unit because of sepsis, the incidence of cognitive impairment was 79% in the first 3 months and persisted for at least 8 years after hospital discharge.[12]

Sepsis triggers immune system cells to release more high-mobility group box 1 (HMGB1) protein, causing permanent inflammation and neurocognitive impairment, affecting the neuroendocrine system and causing impairments in memory, attention, verbal fluency, and executive functions.[8,13] Although natural recovery from cognitive impairment to normal conditions within 1 year is possible, patients cannot fully recover alone. In the long term, sepsis survivors encounter difficulties in returning to work. Memory, attention, and executive function impairment continue to affect quality of life and family burden.[6] However, despite the lack of direct treatment, patients can recover from cognitive impairment when the brain recovers; otherwise, patients require a long time to recover.

In the literature, cognitive function recovery has become possible through brain training programs focused on cognitive impairment in various areas, particularly attention, memory, and executive functions to treat patients with other brain injuries such as stroke. Currently, research has focused on the effects of cognitive rehabilitation programs for survivors of critical care, with sepsis survivors being a subgroup in some studies. However, there is a lack of research specifically on cognitive rehabilitation programs targeted at patients who have survived sepsis. Brain training programs have been proven to be effective and beneficial for patients. Therefore, to recover brain function, specific methods are needed. By organizing activities for practicing cognitive skills, nurses can help patients recover cognitive function by encouraging and promoting neurological recovery through brain training, which can begin immediately after patients are out of crisis from sepsis and have stable neurological symptoms. Activity models must be clear and repetitive until patients learn how to trigger nerve cell connections and cognitive recovery. Early cognitive function recovery after a crisis from sepsis can, therefore, result in the recovery of more cognitive function.[7,13]

MATERIALS AND METHODS

Study design and participants

This study was a single-blind randomized controlled trial with repeated-measures. Measurements were taken at 3 time points: Baseline, Week 6, and Week 12. This randomized trial was conducted from September 2022 to April 2023. The study was approved by Mahidol University Multi-faculty Cooperative IRB Review COA No. IRB-NS2022/691.2705.

The study population included male and female patients aged ≥18 years who had been diagnosed with sepsis, treated until they were out of crisis, and met the following inclusion criteria: survival after >72 hrs. of sepsis, no 2 of 4 symptoms, presenting symptoms based on the SIRS criteria 2021[14,15]; good consciousness, a TMSE score of 20–25 points (mild to moderate level), no depression (2Q), and co-habiting caregivers who possess a smartphone with internet or Wi-Fi access and ability to participate in the brain training program with patients.

The researcher calculated the sample size using power analysis. The required sample size calculation for repeated measures analysis of variance (ANOVA) tests is a sample of 68 participants (34 per group), with a power (p) of 0.80, a significance level (α) of 0.05, a medium effect size (f) of 0.25, and an attrition rate of 20%. The researcher prepared for the sampling process with the assistance of a research assistant who was not involved in the research project. The research assistant generated numbers 1–68 by using a computer program to randomize assignments. The researcher then used these numbers to designate participants as part of either Group 1 or Group 2. The numbers were then placed in sealed brown envelopes. Group 1 served as the control group and Group 2 as the experimental group. The researcher asked the participants to randomly select an envelope. The researcher then opened each sealed envelope to reveal the assigned number and grouped the participants into either the control group or the experimental group based on the numbers inside the envelope. To prevent dissemination of the program from the experimental group to the control group, the researcher conducted individual teaching sessions in designated rooms to train participants in the experimental group on brain training program usage. Participants in the control group were instructed to maintain a daily journal as part of their activities. Additionally, the researcher explicitly advised participants and their caregivers in both groups to avoid sharing any information or activities received during the study, beyond the standard nursing care provided by ward nurses, with other research participants.

Intervention

Both groups received routine care consisting of collection of demographic data, assessment of consciousness with the Glasgow coma scale, assessment of perception of dates, times, places, and persons, personal hygiene care, and consultation with a physical therapist to assess physical impairment. In patients who had impaired physical function, physical therapists began therapy immediately once vital signs and symptoms were stable.

The experimental group participated in the brain training program based on the literature review.[8,16,17] Before activities, the program stimulated patients' perception by having them meditate and count backward (30, 29, 28, 27…1), The program consisted of the following eight activities: "Where Are You?" "Matched Pairs", "Sorting", "Counting", "Watch and Memorize", "Order of Events", "Spending at a Market", and "Record of Emotions". The program emphasized the development of memory, recall, attention, and executive functional capacity. The program manual contained explanations of the details and benefits of the activities. Three activities were performed daily for 30–45 min. per day, 5 days per week. At the end of each week (on Day 6), the participants received follow-up telephone calls via the LINE application for follow-up on symptoms, ask about problems and barriers, and encourage performance of activities in a total of 12 sessions. The participants were granted 24-hour. access to the researchers for consultation throughout the study period.

The control group used the daily record form prepared by the researcher for the participants to plan activities and follow plans to increase cognitive function over 12 weeks.

The clinical trial protocol was registered with the Thai Clinical Trial Registry No. TCTR20240824003 on 19 September 2022 before enrollment of the first case.

Data collection and outcome

For data collection, the participants completed a demographic data questionnaire consisting of items on gender, age, weight, height, body mass index, marital status, education level, religion, occupation, mean monthly income, treatment rights, caregivers, alcohol consumption, use of the brain recovery program, and activities of daily living. Data on illness and treatment consisted of records of personal illnesses or concomitant diseases and blood test results. The researcher collected data from medical records in person by asking for permission from the participants. The depression level was assessed first. For participants who met the criteria, the TMSE was administered. The researcher evaluated the content validity and reliability of the instruments by consulting a total of five experts. The content validity was 0.85 in a sample of five patients. Using Cronbach's alpha coefficient, the reliability of the TMSE was 0.90 in a sample of 30 patients with similar characteristics. The researcher considered a reliability threshold of 0.80 acceptable. In the present study, the reliability in the sample of 68 participants was 0.90

Statistical analysis

The researchers performed all data analyses by using SPSS Statistics 25, using descriptive statistics to analyze demographic characteristics, as well as the history of illness and treatment. The researchers compared the differences between the experimental and control groups at Baseline by using chi-square tests, Fisher's exact tests, or independent t-tests. The researchers then compared the differences in mean cognitive function scores at Baseline, Week 6, and Week 12 between the experimental and control groups by using repeated measures ANOVA.

RESULTS

Overall, 68 participants completed the baseline assessment. One participant from the control group withdrew from the study. Since including this case did not meet the study's assumptions, the researchers excluded it as an outlier. Therefore, a total of 67 participants completed the study with an experimental group of 34 persons and a control group of 33 persons (Fig 1) The experimental group was composed of 44.1% males and 55.9% females, whereas while the control group was composed of 54.5% males and 45.5% females. The overall mean age was 54.52 years (SD = 9.001) with mean ages of 55.50 (SD = 8.969) and 53.52 (SD = 9.059) years in the experimental and control groups, respectively. Most participants had an elementary level of education (73.5% in the experimental group; 57.6% in the control group). The experimental and control groups had mean BMI of 23.56 (SD = 3.566) and 23.40 (SD = 3.465) Kg/m^2, respectively. Most of the participants in both groups had concomitant diseases (overall = 86.8%; experimental group = 91.2%; control group = 82.4%). The top three concomitant diseases found in the experimental and control groups were hypertension (50% and 32.4%), diabetes (20.6% and 38.2%), and kidney disease (17.6% and 20.6%), respectively. When the researcher compared the two groups by demographics, illness, and treatment data using chi-square statistics or Fisher's exact test and independent t-test, there were no significant differences ($p > .05$) (Table 1).

At Pretest, Week 6 posttest, and Week 12 posttest, in the control group, the researcher analyzed the variability in mean cognitive ability scores across repeated measurements at different time points using one-way repeated measures ANOVA. Preliminary tests for compound symmetry revealed that a failure to meet the assumption. Consequently, the researcher applied the Huynh-Feldt correction method ($p > .75$). The analysis showed significant differences in mean cognitive ability scores across at 3 time points: before the intervention at Week 6, at the conclusion of the study and at Week 12 ($F = 132.048$, $p < .001$). The experimental group met the assumption of compound symmetry, allowing for the use of the Sphericity Assumed method for data interpretation. The results also demonstrated

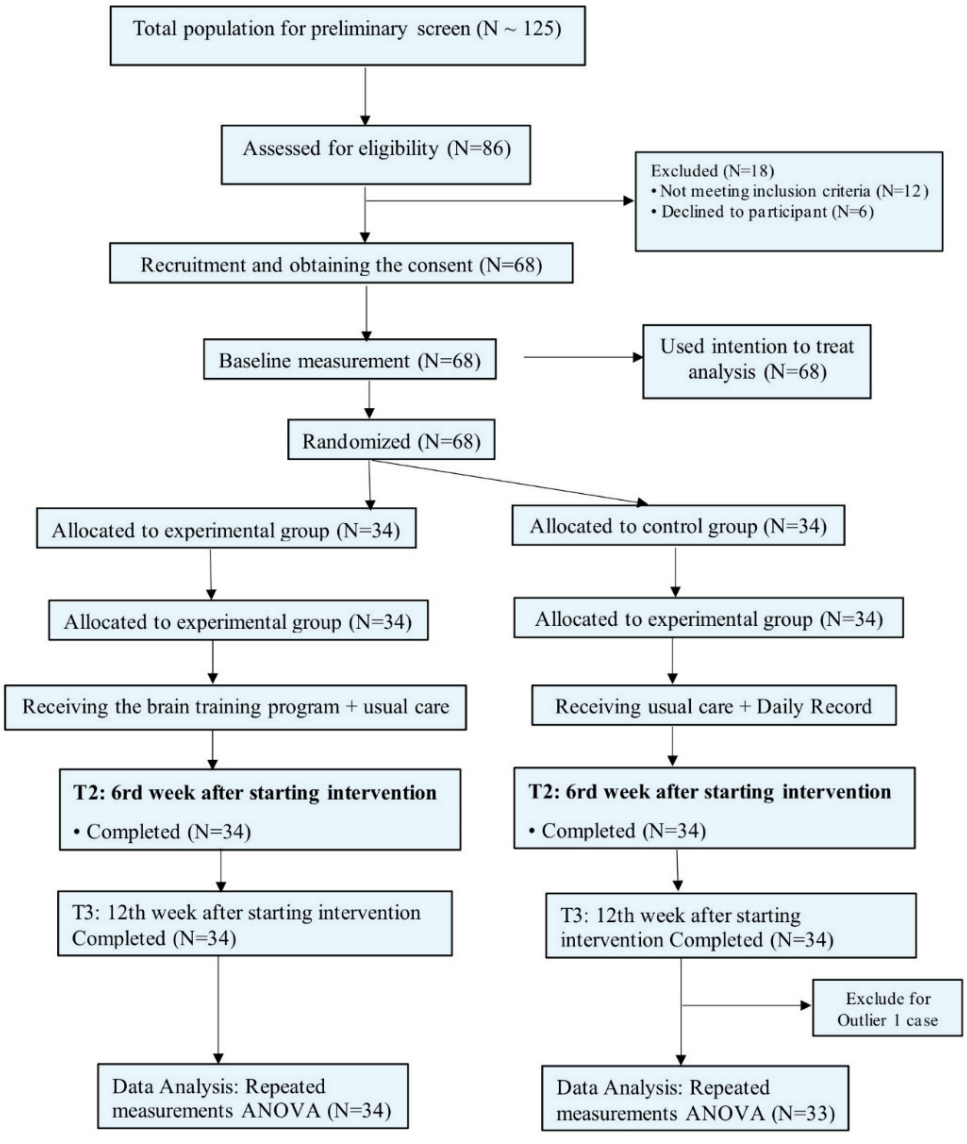

Fig 1. The flow diagram of the study

significant differences in mean cognitive ability scores across at 3 times ($F = 442.279$, $p < .001$).

In comparing the differences between pairs at each time point within the experimental group, the mean scores for cognitive functions differed in the following three pairs: 1) the mean score for cognitive function at Week 6 posttest had a higher score than that at pretest (a differences of 3.14 points); 2) the mean scores for cognitive functions at Week 12 posttest was higher than that at Week 6 (a difference of 2.47 points) 3) and the mean scores for cognitive functions at Week 12 posttest were higher than that at pretest (a difference of 5.61 points), showing a significant difference ($p < .001$) every time. (Table 2) The graph slope for the experimental group was higher than that for the control group. (Fig 2)

In comparing the differences in the mean scores of cognitive functions at each time point between the groups at pretest, Week 6 posttest, and Week 12 posttest, the time effect from Period 1 (pretest) to Period 3 (Week 12 posttest) in the experimental group showed a significant increase the mean scores for cognitive functions ($F = 534.702$, $p < .001$). Furthermore, the time * group interaction was significantly different ($F= 104.905$, $p < .001$). The control group had the same mean scores for cognitive functions, whereas the experimental group had consistently higher mean scores for cognitive functions. (Table 3)

DISCUSSION

Effects of the brain training program on the cognitive functions of sepsis survivors

The findings from this study support its hypothesis. After the brain training program, the experimental group had higher cognitive function levels at Week 6 and

TABLE 1. Demographic characteristics and history of illness and treatment in sepsis survivors (N = 67).

Demographic Characteristics	Experimental (n=34)		Control (n= 33)		$\chi 2$ / *t*-test	P - value
	Number	Percentage	Number	Percentage		
Gender					0.729	0.393
Male	15	44.1	18	54.5		
Female	19	55.9	15	45.5		
Education					-	0.587[F]
Uneducated/						
Primary Level	25	73.5	19	57.6		
High School	7	20.6	10	30.3		
Graduate Diploma	1	2.9	2	6.1		
Bachelor Degrees	1	2.9	2	6.1		
Age (years)					-	0.311[F]
≤ 45	4	11.8	7	21.2		
46-64	29	85.3	23	69.7		
≥ 65	1	2.9	3	9.1		
Mean (SD)	55.50 (8.969)		53.52 (9.059)			
MIN-MAX	33-69		32-66			
BMI (Kg/m^2)					-	0.901[F]
< 18.5	1	2.9	1	3.0		
18.5-22.9	16	47.1	17	51.5		
≥ 23	17	50.0	15	45.5		
Mean (SD)	23.56 (3.566)		23.40 (3.465)			
MIN-MAX	18.07-33.69		18.36-31.11			
Comorbidity					-	0.476[F]
No	3	8.8	6	17.6		
Yes (more than one)	31	91.2	28	82.4		
Hypertension	17	50.0	11	32.4	2.186	0.139
Diabetes	7	20.6	13	38.2	2.550	0.110
Kidney Disease	6	17.6	7	20.6	0.095	0.758
Dyslipidemia	4	11.8	4	11.8		1.000[F]
Cancer	6	17.6	2	5.9		0.259[F]
Gout	1	2.9	1	2.9		1.000[F]
Other	16	47.1	15	44.1	0.059	0.808
Severity of Sepsis						
Mild	17	50	17	51.5	0.901	0.015
Moderate	17	50	16	48.5		

F = Fisher's exact test

TABLE 2. Within-group comparisons of the mean cognitive ability scores of sepsis. Survivors at Pretest and Posttest (Weeks 6 and 12).

Source		Time			F[a]	P-value	Post-hoc[b]
		Pretest	Week 6	Week 12			
Mean Cognitive Ability Scores							
Control	Mean	23.12	23.58	25.42	132.048	<.001*	Pre> wk 6> wk 12
(N=33)	SD	1.408	1.119	1.119			
Experimental	Mean	22.98	26.12	28.59	442.279	<.001*	
(N=34)	SD	1.138	1.149	1.048			

* *p-value* < .001, Pre = Mean cognitive function at Baseline, Week 6 = Mean cognitive at Week 6, Week 12 = Mean cognitive at Week 12, [a] = Huynh-Feldt and Sphericity Assumed method, [b] = Bonferroni

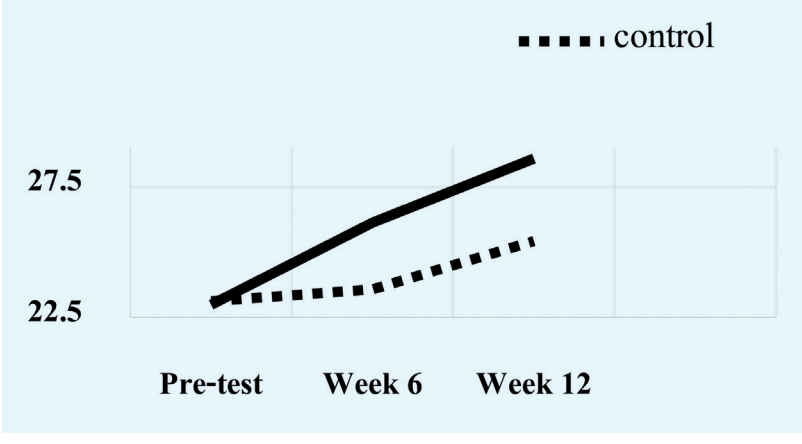

Fig 2. The graph slope for between-group comparisons of the mean cognitive ability scores of sepsis survivors at pretest and posttest (Weeks 6 and 12)

TABLE 3. Between-group comparisons of the mean cognitive ability scores of sepsis survivors at pretest and posttest (Weeks 6 and 12).

Source	SS	df	MS	F[a]	P-value	Partial Eta Squared
Time	524.854	2	262.427	534.702	< .001***	0.892
Error	63.803	130	.491			
Group	173.182	1	173.182	55.633	< .001***	0.461
Error	202341	65	3.113			
Time* Group	102.973	2	51.487	104.905	< .001***	0.617
Error	63.803	130	.491			

*** *p-value* < .001, [a] = Huynh-Feldt method.

Week 12 posttest than at pretest levels; these scores were significantly higher than those of the control group ($p < .01$). The brain training program in the experimental group consisted of meditation training and activities such as "Where Are You?", "Matched Pairs", "Sorting", "Counting", "Watch and Memorize", "Order of Events", "Spending at a Market", and "Record of Emotion", which helped stimulate cognitive function.

Brain training programs for cognitive awareness have not been directly studied in relation to sepsis survivors. However, critically ill patients in ICUs include a significant subgroup of sepsis survivors. Post-ICU cognitive impairment (Post-ICU CD) is a neurological disorder caused by conditions leading to the degeneration of the central nervous system. Memory, logical thinking, attention, visual perception, and overall cognitive functions are commonly impaired in ICU survivors.[18] Epidemiological data suggest that Post-ICU CD occurs at high rates among ICU survivors. A study from China reported an incidence of cognitive dysfunction ranging from 18.2% to 61.6% based on evaluations conducted from 7 days to 24 months after ICU discharge.[18-22] Systematic reviews also highlight the association of Post-ICU CD, particularly in elderly patients with reduced physical functioning.[23] Memory impairment has been identified as the most prominent issue, followed by deficits in processing and attention, and these impairments can persist for up to six years or longer after hospital discharge.[24] A full recovery of pre-ICU cognitive function levels has been achieved by few patients, leaving Post-ICU CD as a lasting challenge affecting daily life.

Zhao et al. implemented a brain intervention plan proposed by Brummel et al. to examine its effects on Post-ICU CD, observing significantly lower rates of cognitive impairment in the intervention group compared to the control group after three months.[25,26] Patients with severe symptoms demonstrated prevention of further decline in cognitive domains such as processing, language, orientation, memory, and vision. Similarly, the RETURN (Returning to Everyday Tasks Utilizing Rehabilitation Networks) reported significant improvements in planning, decision-making, and cognitive processing functions in a study through goal-oriented brain rehabilitation training in general and surgical ICU survivors.[27] Despite these advancements, no standardized rehabilitation protocol has been established for improving cognitive function in sepsis survivors with severe symptoms and cognitive impairment.[28]

The researchers included eight components in the brain interventions designed for this study. It has been shown that brain training improves brain function by promoting the expression of neurotrophic factors in the hippocampus, which supports neuronal recovery and enhances memory and cognitive functions. Improvements in different areas of cognition have been attributed to each intervention component. Following brain intervention training, the intervention group demonstrated significant improvements in cognitive functions such as awareness, processing, memory, attention, language, abstract thinking, and orientation when compared to the control group. These findings suggest that brain rehabilitation training can result in significant improvements in brain function for sepsis survivors.

In the study, the TMSE scores in both groups improved at varying levels after ICU discharge, though cognitive functions such as processing, memory, attention, and abstract thinking initially showed the most significant decline. The researchers observed substantial improvements in brain function and quality of life in the intervention group compared to the control group after three months of brain training. The intervention group had a mean TMSE score of 28.59, which was significantly higher than the score of 25.49 recorded in the control group. These results underscore the therapeutic benefits of early brain training in mitigating cognitive impairment and enhancing quality of life for patients discharged from the ICU.

However, some patients did not fully recover normal brain function after three months of rehabilitation. Consistent with previous findings, the researchers identified older age and multiple underlying conditions as common factors in these patients, noting that older patients with more comorbidities face greater challenges in recovering from Post-ICU CD compared to younger, healthier individuals.

Over the past few decades, psychological and neurobiological studies have demonstrated that mental health profoundly affects brain functions such as memory, attention, language, and cognitive processing. Positive emotions coordinate and optimize brain activity, while negative emotions disrupt and impair it. Since the hospital is designated as the mental health center for Sichuan Province and specializes in psychiatric care, the researchers incorporated mental health evaluations and treatments into the brain rehabilitation protocol to ensure maintenance of a positive outlook by patients. After completing the brain training program, the intervention group demonstrated better quality of life compared to the control group in various aspects, including physical functioning, physical roles, emotional roles, and mental health.[29,30]

Reinforcement from healthcare personnel such

as nurses through the LINE application, which enables monitoring and assessment of performance of activities and communication with the participants, provides social support based on feedback from messages and stickers praising and encouraging the participants to improve activity outcomes. After the researchers saw the participants' performance, the participants were encouraged and supported to keep performing activities. Furthermore, the follow-up telephone calls via the LINE application once weekly throughout the study to inquire in real time about problems and barriers in activities, including general symptoms, encouraged health behavior modification, which is similar to many studies that monitored patients by telephone and found that periodical follow-up telephone calls about activities and consultations improved cooperation among participants and encouraged them to continue the program[26], which further helped make the brain training program more effective.

In this study, the researcher used the concepts of pathophysiology[8] and brain plasticity by Hebb[16] consisting of three mechanisms: (1) Loss of balance in endothelial functions and blood pressure changes resulting in insufficient brain circulation and cerebral ischemia; (2) Increases in acetylcholinesterase activity and reductions in receptor density in the hippocampus causing cholinergic dysfunction, which results in impaired neurotransmission, neurocognitive impairment, and partial memory loss; (3) Microglia and astroglia stimulation worsening inflammation (Interleukins 6 and 12) leading to intrusion to the blood–brain barrier and function loss, which dangerously allows the passage of toxins and thus causes nervous system injury and inflammation. The brain training program emphasizes stimulating the brain to return to activity. The immediate restructuring process of neurons in the brain takes only 1 second. Neurons change shape and coordinate to replace the damaged parts of the brain continuously, which is a unique self-repair characteristic of the brain. Changes to brain structure with neuron connections can occur at all times. Interactions with the environment, including past experiences and new learning, results in the creation of new circuits and nerve connections. According to Hebb,[16] repetitive learning or practice of any activity stimulates dendrites to grow and branch in the cerebral cortex, thereby improving coordination effectiveness among the neurons in the brain, which can restore lost functions.

Among sepsis survivors, brain cell death causes cognitive impairment due to ischemia, causing brain injuries at the cerebral cortex and disrupting nerve cells containing monoamines such as dopamine, norepinephrine, and serotonin. Neurotransmitters communicate and exchange information with the prefrontal cortex. The disruption of such functions reduces neurotransmitter production and signal and information exchange with the prefrontal cortex. Increased acetylcholinesterase activity in the hippocampus causes loss of function and cognitive impairment in the areas of memory, recall, and executive function among sepsis survivors.

The brain training program using the cognitive exercise manual consists of eight activities focused on the development of memory, attention, and executive functions, requiring 30–45 min. per activity, 3 activities per day, 5 days per week over 12 weeks. The program promotes changes in body shape and nervous system coordination to replace the damaged parts of the brain. Brain training programs and cognitive stimulation activities are effective for enhancing cognitive functions by promoting dendritic growth in the prefrontal cortex and strengthening neural connections in the hippocampus, critical for memory and decision-making. Engaging in cognitively demanding tasks, such as solving problems or learning new skills, supports dendritic branching in the prefrontal cortex, which governs executive functions like decision-making and emotional regulation[9] Structured programs like Brain HQ and Lumosity have demonstrated their ability to improve neural connectivity and cognitive performance while slowing cognitive decline, particularly in older adults.[30] These findings highlight the potential of brain training to enhance cognitive resilience and mitigate age-related or disease-related cognitive impairments.

In this study, the control group demonstrated significantly stable cognitive impairment with slight increases in cognitive functions at Week 12 ($p < .05$), possibly because of the natural recovery of neurological and cerebral functions. In other words, in brain injury caused by ischemia and inflammation, connection functions between DNA, molecules, and nerve cells in the brain and electrophysiology triggered the recovery of brain functions by promoting changes in its structure, causing other parts of the brain to develop and function in place of the damaged parts by promoting the growth of new nerve cells, starting from within 3–7 days after injury. The aforementioned processes occur mostly 7–14 days after injury and are nearly complete at 30 days. After an injury, cognitive impairment can persist for up to 6 months. This finding aligns with the results of Qionglan et al.[32] who examined the effects of an early cognitive function recovery program and found that the incidence of cognitive impairment in the experimental group significantly declined after 3 months into the

program ($p < .05$). This study showed that the cognitive function recovery program could prevent loss of executive, language, planning, memory, and attention functions.

One limitation of this study was the lack of a standardized cut-off point for cognitive impairment among sepsis survivors in Thailand. The Thai Mental State Examination (TMSE), a cognitive assessment tool tailored for the Thai population, has been studied across various age groups and educational levels. For example, research on community-dwelling individuals aged 50 and above found median TMSE scores of 27 for literate participants and 23 for illiterate participants. These findings suggest that a TMSE score between 20 and 25 might be considered within the normal range for certain populations.[33] However, this range has not been specifically validated for sepsis survivors, highlighting the need for further investigation in this subgroup. Additionally, the brain training program for cognition in sepsis survivors relied on monitoring participants via the LINE application, which excluded individuals without access to smartphones from participating. Lastly, data collection was limited to sepsis survivors receiving follow-up care at a single urban tertiary hospital in northeastern Thailand. As a result, the findings may not be generalizable to the broader population of sepsis survivors.

Recommendations for implementing the findings

Nursing practice

Nurses and healthcare team members can incorporate the brain training program into the care of sepsis survivors to assess cognitive function and enhance brain stimulation. The program particularly targets cognitive impairments in areas such as attention, memory, and executive function.

Nursing research

Prospective studies on the effectiveness of the brain training program for sepsis survivors across various settings and contexts are recommended. Additionally, studies with follow-up periods of 6 months, 9 months, or over 1 year focusing

CONCLUSIONS

The brain training program improves cognitive function in sepsis survivors over 6 to 12 weeks with focus on attention, memory and executive function. Healthcare teams are encouraged to integrate the program into regular follow-up care to motivate and support behavior adjustments. Further studies in diverse settings and with long-term follow-ups are recommended to comprehensively evaluate the program's effects on brain function, daily activities, and quality of life.

Data Availability Statement

Available for review upon reasonable request.

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DECLARATION

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There are no sources of funding to disclose.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Registration Number of Clinical Trial

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Author Contributions

JK was responsible for study design, review literature, development of methodology, data collection, application of statistical techniques to analyze data and interpretation, writing initial and final drafts, and visualization. WP was responsible for conceptualization, study design, development of methodology, data interpretation, discussion, writing review and editing, and supervision. CR assisted with study design, development of methodology, application of statistical techniques to analyze data, writing review and editing, and supervision. YR assisted with the development of methodology, writing review and editing, and supervision. All authors read and approved the final manuscript.

Use of Artificial Intelligence

We confirm that no artificial intelligence (AI) was used in the writing of this work. All content was created solely by human authors.

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