

Cognitive Performance after a Transient Ischemic Attack: Attention, Working Memory, and Learning and Memory

Vishuda Charoenkitkarn, Saipin Kasemkitwattana, Barbara Therrien, Orapan Thosingha, Thavatchai Vorapongsathorn

Abstract: This prospective study aimed to explore the three main areas of cognitive function (attention; working memory; and, learning and memory) among individuals who had experienced a transient ischemic attack (TIA). Convenience sampling was used to recruit 52 individuals, who had experienced a TIA, from outpatient and emergency departments in three tertiary hospitals, in Bangkok, and one tertiary hospital in Ayutthaya province, Thailand; as well as 52 persons, who had experienced minor surgery and served as matched control subjects, from the outpatient department at a tertiary hospital in Thailand. Subjects were assessed, 3, 10 and 30 days after experiencing a TIA or having minor surgery, using the Necker Cube Pattern Control Test, Trial Making A Test, Digit Span Forward and Backward Test, Barratt Impulsiveness Scale, Irritability Assessment Scale, Digit Symbol Substitution Test, and Hopkins Verbal Learning Test. A repeated-measures-within-and-across-subjects design was used to analyze the results.

Findings indicate that those who had a TIA continued to experience attention, working memory, and learning and memory changes, but not irritability changes, for over 30 days after symptom occurrence. Three days after symptom occurrence, those who had a TIA showed less ability in the 3 main cognitive performances than did the control group. Their performance ability became worse at day 10, but improved at day 30. All performances among those with a TIA were lower than the control group, at all three time points. Thus, nurses should be concerned about the cognitive ability of those who have had a TIA, as well as their respective families, and provide information to both about the effects of a TIA, particularly 10 days after symptom occurrence.

Thai J Nurs Res 2009; 13(3) 199 - 215

Key Words: attention, cognitive performance, learning and memory, transient ischemic attack, working memory.

Introduction

Individuals who have experienced a transient ischemic attack (TIA) are at risk of a future stroke.^{1,2} One of the most common causes of TIA, or ischemic stroke, is atherosclerosis, which usually occurs in one of the internal carotid arteries.³ Prior studies have suggested that blockage of the internal carotid arteries may be a major risk factor for

Correspondence: Vishuda Charoenkitkarn, RN, PhD candidate, Faculty of Nursing, Mahidol University, Bangkok, Thailand.
E-mail charoenkitkarn@yahoo.com

Saipin Kasemkitwattana, RN, DNSc. Associate Professor, School of Nursing, Mae Fah Luang University, Chiang Rai, Thailand.

Barbara Therrien, RN, PhD, FAAN. Associate Professor, School of Nursing, University of Michigan, Ann Arbor, Michigan, USA.

Orapan Thosingha, RN, DNSc. Assistant Professor, Faculty of Nursing, Mahidol University, Bangkok, Thailand.

Thavatchai Vorapongsathorn, Ph.D. (Research Design & Statistics in Education), Associate Professor, Faculty of Public Health, Mahidol University, Bangkok, Thailand.

cognitive impairment.^{2,4} The carotid arteries supply blood to the anterior two-thirds of the brain (prefrontal cortex, and lateral and temporal lobes).³ These areas control not only motor and sensory function, but also are associated with higher brain functions, such as thoughts and actions. Humans are able to attend to and analyze sensory data, perform memory functions, learn new information, form thoughts, solve problem and make decisions. Therefore, a TIA may produce changes in cognitive functions, which are more difficult to characterize than motor or sensory loss.

Clearly, cognitive difficulties may negatively impact one's learning, understanding, and adoption of new health behaviors. However, previous investigations of cognitive function, among individuals who have experienced a TIA, have found conflicting results.⁵⁻¹⁰ Thus, before developing and implementing presumed effective health education programs to prevent strokes, it is important to identify one's level of cognitive function, including attention, working memory, and learning and memory. Programs may need to be tailored to account for the person's existing cognitive abilities or disabilities. For example, if a person cannot pay attention to the information being transmitted, he/she will not learn and remember.^{11, 12} In other words, if people cannot use the information they receive, they cannot change their behavior.

Literature Review

Despite the short duration of TIA symptoms, and absence of residual disability, those who have experienced a TIA require an active approach, because the risk of future events remains high. The highest risk is within the first 30 days.^{1,2} A study of patients presenting to an emergency department, within 24 hours after a TIA, reported a 5.3% risk of stroke at two days,¹³ a 8 % risk at seven days, and a 12 % risk at one-month.¹ In an attempt to

prevent a recurrent stroke, national stroke guidelines recommend symptom management within the first 48 hours, after the onset of symptoms, and referral to a neurological specialist within 7 to 10 days.^{13,14} Treatment should include 300 mgs of aspirin, along with a 4-week intake of all other medications prescribed by the neurological specialist.¹⁴ In addition, health information needs to be provided each time the patient interfaces with a health care provider.

Nurses usually provide a psychosocial supportive role to individuals who have experienced a TIA. The main aspects of providing support include directing patients to key services, and giving appropriate and accurate information regarding treatment and lifestyle changes for the purpose of preventing future strokes.¹⁴ Therefore, effective communication between patients and nurses is essential, especially within the first month post-TIA. Nurses are aware, from practical experience, that non-adherence to health care regimens is a major factor in the recurrence of strokes.^{15,16} One seldom explored, yet potentially powerful explanation for why patients encounter difficulties in making lifestyle changes and adhering to treatment regimes, could be subtle or overlooked changes in patients' cognition, or actual cognitive impairment. Problems within the brain of a person who has had a TIA may affect his/her ability to select, attend to, learn and/or remember information. Some cerebrovascular lesions are clinically silent or cause disorders in function so mild that the effect is hardly noticeable to the patient.¹⁷

Regarding the pathology of TIAs, one of the most common causes is atherosclerosis, which usually occurs in the internal carotid arteries.³ These two arteries supply blood to the prefrontal cortex (the anterior part of the frontal lobes of the brain) and the hippocampus (a structure located inside the medial temporal lobe of the cerebral cortex).³ When blood flow through one, or both, of the internal carotid arteries is impeded, cerebral ischemia occurs.

Animal models have provided clues to the nature of cognitive function impairment secondary to a cerebral ischemia. Cerebral ischemia, lasting at least 5 minutes in rats, has been found to be related directly to the extent of damage in the hippocampus.¹⁸ The pyramidal CA1 cells, in the hippocampus, are known to be very susceptible to ischemia.¹⁸ The hippocampus area of the brain plays an important role in both learning and memory processing. Research has shown that an ischemic event in the rodent brain leads to selective loss of pyramidal CA1 cells of the hippocampus, which slowly occurs over a two to three day period, with almost total destruction of the cells after four days.⁶ The cellular damage has been found to be present after a recovery period of one week.¹⁹ Tanaka and colleagues⁷ found, in Wistar rats, that cholinergic activity (an index of transmitter activity associated with learning and memory) in the frontal cortex markedly decreased 3 weeks after an ischemic event, but was restored six weeks later. The prefrontal cortex is another area significantly impacted by a TIA.^{2,3} This area of the brain is associated with cognitive functions, such as attention, working memory and executive attention (the main component of both attention and working memory).^{20,21} The findings of the aforementioned studies suggest that, in animal models, cognitive function may change, anywhere from a few days to nine weeks, after TIA symptoms occur.

Evidence suggests that cognitive problems are experienced, among humans, after a TIA occurs. Attention, working memory, and learning and memory are three main cognitive functions associated with the prefrontal cortex and hippocampus.⁵ Prior studies have confirmed that attention, working memory, and learning and memory impairment occur after one experiences TIA symptoms.^{8,9} In contrast, Sinatra and colleagues¹⁰ found individuals who had experienced TIA symptoms did not have

poorer performance in all verbal tests, than did those who had not experienced a TIA. However, the tests were administered one to three months after the occurrence of the last ischemic event.

Frontal lobe dysfunction, accompanying carotid stenosis, has been found to be associated with potential attention and working memory difficulties. For example, Rao and colleagues²² found two measures of frontal lobe function (verbal fluency and behavioral control) to be independent predictors of global cognitive impairment among individuals who have experienced a TIA. Moreover, Sachdev and colleagues²³ found cognitive deficits among individuals who had experienced a TIA to be characterized by disturbances of frontal functioning, but with less verbal memory impairment. As a whole, prior investigations have revealed conflicting findings regarding cognitive functioning among individuals who have experienced a TIA. Cognitive function may be affected by the time of measurement and the various tests administered. However, they indicate cognitive function changes, within a month, after a TIA event occurs. Clearly cognitive difficulties would impact negatively the learning, understanding and adoption of new health behaviors.

Thus, based upon the need to prevent a recurrent stroke, during the first month after a TIA event, and due to the conflicting findings regarding cognitive function, the aim of this study was to explore the three main areas of cognitive performance (attention, working memory, and learning and memory) 3, 10, and 30 days after TIA symptom occurrence.

Method

Design: A repeated measures, within-and-across subjects, design, using case-control technique, was utilized to examine the pattern of cognitive performance of individuals, who had experienced a TIA, 3, 10, and 30 days after TIA symptom

occurrence. Matched control subjects, after experiencing minor surgery, also were tested at the same intervals. Cognitive function has been studied primarily in Western cultures and, thus, norms may not be representative of Eastern cultures. The case-control study approach was used to obtain an index of normal cognitive function in a different culture.

Sample size

Sample size was calculated using the formula for ANOVA,²⁴ yielding 52 subjects, who had experienced a TIA, and 52 control participants, who had experienced minor surgery, with a statistical power of 0.80, an effect size of 0.25 and a significance level of 0.05. The total sample size was 104 persons.

Sample

After institutional ethics committee approval was granted, from the main author's academic institution and from all hospital settings involved in the study, subjects for both the TIA group and the minor surgery group were recruited. A convenience sample of 52 individuals who had experienced a TIA was drawn from the list of patients' who were admitted through the outpatient and emergency departments of three tertiary hospitals in Bangkok and one tertiary hospital in Ayutthaya province, Thailand. Selection criteria, included individuals who had experienced a TIA and were: (a) at least 24 years old; (b) able to read and write Thai; (c) able to take and respond to tests and questions; (d) without hearing loss, eye problems, history of substance abuse or dependency, diagnosis of cancer, HIV/AIDS, head injury, attention deficit hyperactivity disorder or any known neurological disorder other than a TIA; (e) not currently on prescription medications known to alter cognitive processing; (f) not depressed; and, (g) willing to participate in

the study. A volunteer registered nurse, from each outpatient and emergency department, was asked to assist the primary investigator in recruiting potential subjects for the TIA group. This was accomplished by the volunteer nurse identifying potential subjects, via their chief complaint, and then confirming, with a neurologist, their diagnosis of TIA and adherence to the selection criteria. Once potential subjects were identified, the volunteer nurses explained: the objective of the study; what the subjects' involvement would entail; that anonymity and confidentiality would be maintained; and, that the subject had the right to withdraw at any time, without negative repercussions. Potential subjects consenting to take part in the study were asked to sign a consent form and to provide their telephone number so that they could be contacted by the primary investigator. After receiving a subject's consent to participate, the researcher called the subjects for the purpose of setting up an appointment to introduce herself and to arrange for the three administrations of the research instruments.

Fifty-two individuals, who had undergone minor surgery (i.e. any surgical procedure that did not involve anesthesia or respiratory assistance, such as excision of a scar or suturing of a minor wound), but had no known hypertension, diabetes, vascular disease or history of a TIA or stroke, were recruited for the control group. Potential subjects were identified by way of their patient record, while they were being seen in an outpatient department of one of the selected hospitals. Each potential subject was demographically (age, gender and educational level) matched with a subject in the TIA group. Once potential control subjects were identified, the primary investigator provided them the same information subjects in the TIA group received. Those consenting to participate were asked to sign a consent form and appointments were made with them for the purpose of administering the three rounds of the research instruments.

Four subjects, who had experienced a TIA, had a stroke within 30 days of their initial symptoms. They and their four matching control subjects were removed from the study. As a result, four more individuals, who had experienced a TIA, as well as four matching control subjects, who had experienced minor surgery, were recruited and participated in the study. Thus, the attrition rate for the study was 7.69%

Instruments

A Demographic Data Questionnaire was used to obtain subjects' demographic characteristics, while their cognitive performance (attention, working memory, and learning and memory) was evaluated via eight different measures. Their cognitive performance assessment included the: Necker Cube Pattern Control Test (NCPCT); Digit Span Forward Test (DSFT); Trail Making A Test (TMAT); Barratt Impulsiveness Scale (BIS); Visual Analogue Scale (VAS); Digit Symbol Substitution Test (DSST); Digit Span Backward Test (DSBT) and, Hopkins Verbal Learning Test-revised (HVLTR).

The researcher developed Demographic Data Questionnaire obtained information on all subjects regarding their gender, age and educational level. Data obtained on those who had experienced a TIA, included their TIA symptoms, length of symptoms and illness history.

Attention, the first component of cognitive performance, was assessed via five tests that measured distractibility, impulsivity and irritability. Distractibility was measured using the NCPCT, DSFT and TMAT. Impulsivity was assessed using the BIS, while irritability was measured by way of the VAS. The NCPCT was developed as a direct test of one's "attentional capacity" (ability to inhibit a competing pattern stimulus) by using a cube with a width and length of 2 centimeters each and a depth of 1 centimeter.^{25, 26} Subjects may see the cube pattern in two different views, one when

looking at the foreground and the other when reversing to the background of the cube. To maintain one pattern, subjects have to mentally inhibit the alternative pattern. There are two assessment components to the NCPCT, for: 1) establishing a baseline of passive attention; and, 2) measurement of controlling, or effortful, attention.

In the first component, the subject is tested in two 30-second sessions (T1 and T2). The subject is asked to passively look at the cube. Each time the cube reverses or flips, the subject taps the researcher's hand. The researcher counts the number of flips that occur.

In the second component, the subject is tested in the two more 30-second sessions (T3 and T4). The subject is asked to try to keep the cube from flipping. Whenever, the cube reverses or flips, the subject also taps the researcher's hand. The numbers of flips that occur are counted. The values obtained from session T1 and session T4 are discarded. The value obtained in session T2 is subtracted from the value obtained in session T3, with the results being divided by the value obtained in session T2. This results is then multiplied by 100 for a percentage score $[(T3-T2)/T2 \times 100]$. The result was defined as the person's attentional capacity. TIA subjects who had a significantly higher mean NCPCT score than their matched control were determined to have distractibility

The DSFT examines verbal recall; attention capacity and working memory by having subjects retain a verbally stated series of numbers, and then repeated back in the correct order.²⁷ The number of digits in the sequence increases, with each successful repetition, until 9 digits are successfully repeated, or until the person fails, at a given sequence, after two attempts. The score is the highest number of digits successfully completed. Scoring is expressed in the form of a digit. Each item is scored 0, 1, or 2, with: 2 = passes both trials; 1 = passes only one trial; and, 0 = fails both trials. TIA subjects who

had significantly lower mean scores than their matched control were considered to have attention impairment and distraction.²⁸

Attention and concentration abilities, including visual-motor, conceptual tracking and sequencing skills, were measured by the TMAP.²⁹ This instrument is a timed (minutes) paper and pencil test, which consists of 25 encircled numbers randomly scattered over an 8x11 paper. Subjects are instructed to connect, in order, the series of numbers without lifting his/her pencil from the paper. TIA subjects, who spent significantly more time to complete the

test than their matched control, were determined to have poorer attention and concentration abilities.

Impulsivity was measured by the Barratt Impulsiveness Scale (BIS) short form,³⁰ which consists of 15 items with a 3 factor structure: poor-planning (5 items), motor impulsivity (5 items) and attention impulsivity (5 items). Since it originally was used with students, slight modifications of the situation in the questionnaire were made for this study. Each of two original questions on attention impulsivity was replaced by a more relevant question, as follows:

<u>Original:</u> I am restless at lectures and talks.	<u>New:</u> I am restless when listening to long talks.
<u>Original:</u> I squirm at plays or lectures	<u>New:</u> I squirm when listening to long talks.

The scores of the items of the BIS were rated on a 4-point Likert-type scale (1= rarely/never to 4=almost always). TIA subjects who had significantly higher scores, than their matched control, were considered to have high impulsivity.

Irritability was measured, using a Visual-Analogue Scale (VAS).²⁵ Subjects were asked to respond to two mood state items (patience and annoyance), which assess how they usually feel and how they currently feel. The four questions asked were:

1. How patient am I with others usually?
2. How patient am I with others right now?
3. How easily annoyed or irritated am I usually?
4. How easily annoyed or irritated am I with others right now?

For each of the four questions, subjects are asked to place a mark on a 100 mm line which has, at one end, “not at all,” and, “extremely so,” at the other end. For each of the two mood states, the placement of the mark on the 100 mm line, for the “usually” response, was compared to the placement of the mark, for the “right now” response. The distance,

in millimeters, was measured between the two marks. The larger the distance between the two marks, the greater the presence of irritability. TIA subjects who had significantly higher scores, on the difference between the “usual” and “right now” responses for the two mood states (patience and annoyance), than their matched controls, were considered to have higher irritability.

Working memory, the second component of cognitive performance, was assessed by way of the Digit Symbol Substitution Test (DSST) and Digit Span Backward Test (DSBT). The DSST is used to identify cognitive and cerebral dysfunction. This tool requires complex visual scanning and tracking perception, motor speed, and memory.³¹ The test consists of rows containing small blank squares, each paired with a randomly assigned number from one to nine. Above the rows is a printed key that pairs each number with a different symbol. The subject is required to scan the numbers and fill in the blank space with the symbols corresponding to each number, as rapidly as possible, within 90 seconds. The number of correctly matched symbols and numbers that are recorded, within

90 seconds, are counted. TIA subjects who had a significantly lower score, than their matched control, were considered to have a working memory deficit.

The Digit Span Backward Test (DSBT) measures working memory, which involves both the storage and manipulation of information.²⁷ Subjects are asked to repeat digits backwards after they are verbally stated by the researcher. The number of digits, in a sequence, increase, with each successful repetition, until 9 digits are successfully repeated, or until the subject fails at a given sequence, after two attempts. The score is the highest number of digits completed. Scoring is expressed in the form of a digit. Each item is scored 0, 1, or 2, with: 2 = passes both trials; 1 = one trial is passed; and, 0 points = both trials are failed. TIA subjects who had significantly lower mean scores, than their matched control subject, were considered to have working memory impairment.

Learning and Memory, the third component of cognitive performance, was assessed using the Hopkins Verbal Learning Test-R (HVLT-R).³² This tests examines three aspects of learning and memory: total recall, retention and recognition. The HVLT-R tasks include three learning trials (T1, T2 & T3), one 20-25 minute delayed recall trial (T4), and one yes/no delayed recognition trial (T5). The latter trial (T5) consists of a randomized list that includes the 12 target words and 12 non-target words, six of which are drawn from the same semantic categories as the target words. Raw scores are derived for total recall, delayed recall, retention (% retained), and a recognition discrimination index. The scores are measured as follow: 1) Total Recall = Trial 1 + Trial 2 + Trial 3; 2) Percent retained = (Trial 4 / Trial 3) x 100; and 3) Recognition = number of

hits of the T5 recognition trail / 12. TIA subjects who had significantly lower scores, than their matched control, were considered to have learning and memory deficits.

Since all instruments, except the Demographic Data Questionnaire, were written in English, they required translation into Thai and then back translation into English. The back translated English version of each instrument was compared to its original English version to make certain that no changes in meaning occurred. Permission to use and translate each of the copyrighted instruments was obtained prior to them being translated and used.

Instruments' validity and reliability: The primary researcher was trained in the use of the instruments by Dr. Barbara Therrien, School of Nursing, University of Michigan and Dr. Bruno Giordani, Director, Neuropsychology Section, Department of Psychiatry, University of Michigan, USA. Content validity of all instruments in Thai version was tested by four experts who were two psychologists, one medical doctor, and one neurologist. Face validity was assessed by administering the instruments to ten Thai elderly, who were not part of the study, for the purpose of evaluating cultural appropriateness, language, level of readability and clarity of instructions. Instrument items and instructions were revised accordingly, based upon feedback from the ten Thai elders. All instruments were pilot tested on 20 individuals, who met the study's inclusion criteria, but would not be part of the study. Based upon the pilot study data, test-retest reliability was assessed on the: NCPT, DSFT, DSBT, TMAT, DSST and HVLT-R. The BIS and VAS were tested by way of Cronbach's alpha. The reliabilities for all instruments were acceptable (r = .812 to .985).

Procedure

Each subject in both groups (TIA and matched control) was administered the battery of tests, by the primary researcher, in his/her respective home, on three separate occasions. Test administration occurred for those in the TIA group 3, 10 and 30 days after experiencing symptoms, while his/her matched control was administered the tests 3, 10 and 30 days after having minor surgery. The test environment was free of distractions (music, noise, people, or outside view) during the testing process. It took subjects approximately 50 minutes to complete all tests.

Results

No significant differences were found among the demographics between those who had experienced a TIA and those who had experienced minor surgery. The majority were middle-aged males, with a low level of education (see **Table 1**). Among those who had experienced a TIA, it was their first TIA episode. All of them had a history of hypertension and most (n =52; 100%) encountered physical weakness and difficulty speaking (n = 29; 55.70%) after experiencing their TIA. Their symptom duration ranged from 5 to 120 minutes, with a mean of 20 minutes (see **Table 2**).

Table 1 Demographic characteristics of the sample

Demographics	TIA		Control	
	n	%	N	%
Gender				
- Male	31	59.60	31	59.60
- Female	21	40.40	21	40.40
Age (years)				
< 40	2	3.80	2	3.80
40-49	19	36.50	19	36.50
50-59	21	40.40	21	40.40
60-70	10	19.20	10	19.20
Average	<i>Mean=52.52 (SD=7.97), Min-max = 37-69 years</i>		<i>Mean=52.52 (SD=8.00), Min-max=37-68 years</i>	
Education				
- Illiterate	7	13.46	7	13.46
- < Elementary school	7	13.46	7	13.46
- Elementary school	12	23.08	12	23.08
- Secondary school	8	15.38	8	15.38
- High school / Vocational school	6	11.54	6	11.54
- Diploma Degree / Vocational school	6	11.54	6	11.54
- Bachelors or Higher Degree	6	11.54	6	11.54

Table 2 Characteristics Related to Health Status (n = 52)

Demographics	TIA	
	N	%
Symptoms		
- weakness on left side	4	7.70
- weakness on right side	11	21.20
- speech difficulty	8	15.40
- weakness on left side & speech difficulty	2	3.80
- weakness on right side & speech difficulty	27	51.90
Duration of Symptoms (minutes)		
<10	1	1.90
10-59	48	92.30
>59	3	5.80
Average	Mean=20 SD=20.627 Min=5;	Max=120
Personal Illness History		
- Hypertension	26	50.00
- Hypertension & diabetes mellitus	12	23.10
- Hypertension & hyperlipidemia	6	11.50
- Hypertension, diabetes mellitus & hyperlipidemia	8	15.40

All variables met the assumptions underlying statistical testing for two-way analysis of variance (ANOVA) repeated with one factor. Results of the Necker Cube Pattern Control Test (NCPCT), Trail Making A Test (TMAT), Digit Span Forward Test (DSFT), Barrett’s Impulsiveness Scale (BIS), Digit Span Backward Test (DSBT), Digit Symbol Substitution Test (DSST) and Hopkins Verbal Learning Test-revised (HVLTR) showed a similar pattern. The main effect of time points and group, as well as the interaction effect of group by time points, were significant ($p < .05$; $.01$; $.001$). These findings imply that those who had experienced a TIA, as well as those who had minor surgery, had a different degree of attention, working memory, and learning and memory at each of the three time points (see **Table 3**).

Comparing mean scores of all tests performed revealed that those who had experienced a TIA displayed poorer performance than did those who had minor surgery, with respect to attention, working memory, and learning and memory at each of the three time points. Individuals who experienced a TIA also were found to have a similar pattern of impairment, which indicated some degree of impairment three days after TIA symptom occurrence. The mean scores of all tests showed increased impairment, among those who experienced a TIA, 10 days after they had TIA symptom occurrence. In contrast, the battery of test scores showed a change towards improvement 10 to 30 days after TIA symptoms occurred. However, those who experienced a TIA still exhibited poorer performance in cognitive performance than did those who had minor surgery (see **Figure 1**).

Table 3 Repeated measures ANOVA for TIA group and matched control group

	3 days Mean±SD	10 days Mean±SD	30 days Mean±SD	Group F	Time F	Group x Time F
Attention						
NCPCT						
TIA	-52.23±15.03	-48.74±12.80	-55.97±12.36	13.09***	10.90***	12.02***
Control	-59.99±12.01	-60.84±10.75	-60.73±11.06			
Trail Making a Test						
TIA	59.83±1.92	63.06±2.05	57.35±2.02	12.77**	45.90***	52.66***
Control	51.50±1.39	51.50±1.40	51.54±1.39			
DSFT						
TIA	11.88±1.82	10.96±1.77	12.46±1.82	11.45**	47.319***	30.90***
Control	12.82±0.24	12.81±0.24	12.98±1.82			
Barrett's Impulsivity						
TIA	27.10±0.50	27.35±0.48	26.76±0.52	27.65***	13.19***	4.37*
Control	23.27±0.50	24.75±0.48	22.98±0.52			
Irritability						
TIA	5.38±0.57	5.19±0.57	4.81±0.55	5.35*	1.06 ^{ns}	1.13 ^{ns}
Control	3.65±0.57	3.07±0.52	3.56±0.55			
Irritability						
TIA	5.48±0.50	4.71±0.50	4.33±0.47	4.43*	2.85 ^{ns}	0.56 ^{ns}
Control	3.65±0.62	3.46±0.61	3.17±0.59			
Working Memory						
DSBT						
TIA	6.92±0.25	5.83±0.24	7.13±0.27	15.74***	32.61***	55.22***
Control	7.98±0.24	8.06±0.25	7.85±0.25			
DSST^a						
TIA	34.58±1.36	32.52±1.34	35.40±1.34	16.97***	92.91***	59.43***
Control	41.50±1.13	41.23±1.13	41.54±1.15			
Learning & Memory						
HVLT -R						
- Total Recall						
TIA	20.54±0.71	19.10±0.40	22.06±0.64	11.27**	32.30***	30.30***
Control	23.17±0.53	23.37±0.52	23.40±0.52			
- Retained						
TIA	104.69±2.39	96.55±2.62	114.20±1.38	60.55***	12.98***	10.76***
Control	122.64±1.53	117.13±1.53	118.38±1.39			
- Recognition						
TIA	1.71±0.02	1.63±0.02	1.74±0.02	22.33***	58.53***	41.04***
Control	1.78±0.02	1.77±0.02	1.80±0.02			

*p<.05; **p<.01; ***p<.001

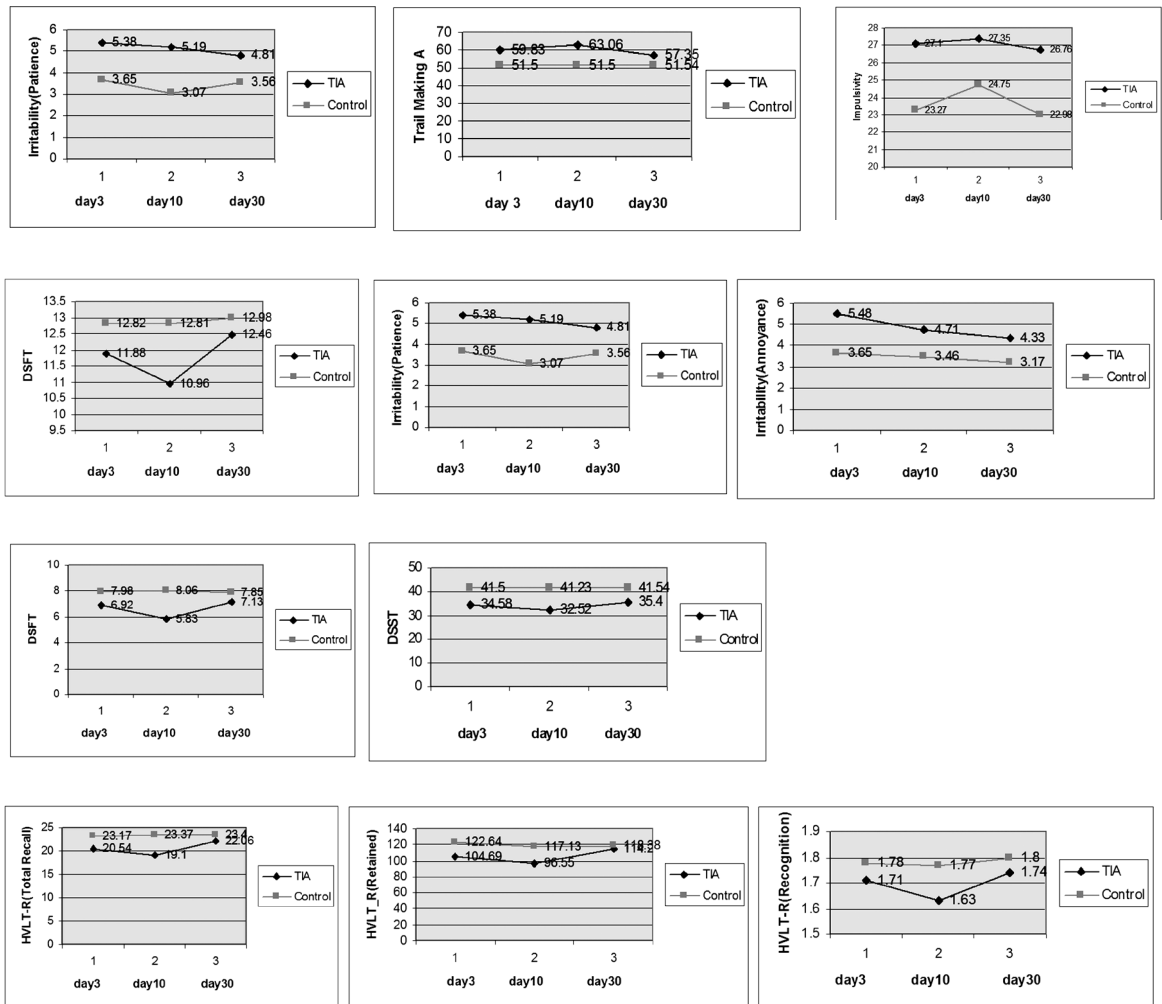


Figure 1 Comparison of the mean scores of the NCPCT, DSFT, TMAT, DSBT, DSST, and HVL T-R

The irritability score of those who experienced a TIA did not show, over the 30 day period, the same pattern of change as the other test scores. However, the mean irritability scores of those who had experienced a TIA suggested they were more irritable, at all three time points, than were those who had experienced minor surgery.

Discussion

The results provided evidence that compromised cognitive performance (attention, working memory, learning and memory) occur after a TIA. Most subjects presented with weakness and speech difficulties, which may have occurred secondary to a disturbance in their frontal lobe, and the lateral surfaces of their temporal and parietal lobes, due to ischemia.^{3,34} Thus, their symptoms may have contributed to their brain function.

Furthermore, the mean duration of TIA symptoms was 20 minutes, providing an indication of the extent of possible CA1 cell damage, in the hippocampus, and deficits in spatial learning. Confirmation of CA1 cell loss has been conducted, in rats, when ischemia has occurred for 5 and 10 minutes.¹⁷ The fact that those who had experienced a TIA had ischemia for approximately 20 minute helps explain why their cognitive performance was worse than those who had minor surgery. In addition, results of this study are supported by prior findings,^{35, 36} which show that persons with an obstructed carotid artery, who have experienced a TIA, can have lasting cognitive impairment, which affects their attention, memory and learning, despite recovery of their focal neurological deficits, such as weakness or speech difficulties.

Attention: Anatomical studies on attention impairment have cited findings regarding prefrontal and parietal lobe damage.²⁰ This study found impaired performance, at all three time points, when using measures of distractibility and impulsivity, two of the indicators of attention impairment. Attention is essential for effective functioning, since it is necessary for learning needed information.

Distraction manifests as failure to inhibit competing demands or loss of focus, while impulsivity is related to the loss of inhibition in the behavioral dimension. In this study, results from the BIS showed the same pattern as those of the distractibility tests (NCPCT, DSFT, TMAT). These results corroborate other studies, which concluded there are real attention deficits among individuals who have experienced a TIA.^{22, 23} In contrast, individuals who have experienced a TIA have been found to not necessarily show worse performance than those who have not experienced a TIA.¹⁰ However, this was found through the use of dissimilar tests from this study and without matched controls, based on gender and education.

In this study, an increase in distractibility and

impulsivity was found between days 3 and 10, and beginning improvement of cognitive function was noted between days 10 to 30. This may be related to the fact that body weakness is present when prefrontal and parietal lobes are damaged.²⁰ In addition, brain cells are known to remain damaged one week post-TIA symptoms.¹⁸ Another explanation for the worsening of attention capacity, at day 10, is that environmental and life demands may be increasing at that time, since subjects were trying to return to their normal life activities. It is likely that these demands overwhelmed their attention capacity, since their brain cells still were compromised. Beginning improvement of cognitive function may have been noted between days 10 to 30, since neurological recovery is known to generally occur during the first few weeks to months, post attack.³⁷ The fact that attention deficit was still found at day 30, among those who had experienced a TIA, most likely is related to the fact that, in Wistar rats, an increase in choline acetyltransferase activity in the frontal cortex and hippocampus, caused by hypofusion of cerebral blood flow in the forebrain, results in behavior deficits.⁷

Although the results of the irritability testing (VAS) did not show the same pattern as found with distraction or impulsivity, those who had experienced a TIA showed more irritability than did the controls at all three times of measurement. This may be because the irritability test was not sensitive enough, or the irritability change was too small, to detect the change. It is possible, also, the irritability test failed to adequately capture irritability, due to no specific situation being provided, or the subjects could not feel a change in their irritability.

Working memory: Results suggest those who had experienced a TIA had working memory impairment, as measured by the DSBT and the DSST. A consistent pattern of change in their working memory was found, over the three time periods, similar to the distraction and impulsivity

testing. One component of the working memory model is the central executive function, which is an attentional control system in the attention model. Executive function has been shown to be responsible for directing attention to relevant information, suppressing irrelevant information and inappropriate actions, and coordinating cognitive processes, when there is more than one task to be done at the same time.²¹ In this study, those who had experienced a TIA were found to have attention deficit. Thus, they had deficiencies in their working memory and were not able to manipulate all the information they received.

Another possible explanation of the finding is there is a relationship between the frontal lobes and working memory. Prior studies have shown the frontal lobes play an important role in working memory.³⁸ Electrophysiological recordings have demonstrated that some neurons, in the frontal lobes, fire only during the delay period of a working memory task.³⁹ Impairment of working memory means that information cannot be acquired, manipulated or used in a normal manner, significantly impacting what and how much one can learn and remember.

Learning and Memory: Learning and memory performance (assessed by the HVLT-R) of those who had experienced a TIA were lower than that of their matched controls. Thus, the pattern of learning and memory of those who had experienced a TIA appeared to be similar to the pattern of attention and working memory.

Impaired learning is known to be associated with ischemic damage to the temporal lobe, especially the hippocampus, which is supplied with blood by the internal carotid arteries. It has been found that CA1 cells, in the hippocampus of animals, are sensitive to ischemia and related to learning and memory.¹⁸ In addition, attention is needed to focus on the target of information before manipulating it by working memory. The working memory then manipulates the information and

transfers it to long term memory. These three main concepts appear to work together as a network. Thus, either attention or working memory deficits could influence one's ability to learn and remember, and have an indirect relationship with other cognitive impairments on learning. It is likely that the explanation, regarding the learning and memory deficits of those who have experienced a TIA, involves a combination of the above.

The pattern of change also may be explained by the delayed death of CA1 cells, after a carotid occlusion, in the hippocampus. Animal studies have revealed that after an ischemic event of at least 5 minutes, the cells change very slowly after two days; but are almost totally destroyed within four days.¹⁸ Therefore, those who have experience at TIA, at day three, may show less ability in learning and memory than they had pre-TIA, due to the decreased number of functioning CA1 cells. It also is possible that the destruction of CA1 cells continued, which may account for the worsening of learning and memory at day ten post-TIA.

In contrast, test scores, of those who had experienced a TIA, showed improvement, between day 10 and day 30. This may be related to the fact that the activity of the enzyme, choline acetyltransferase, has been found to be restored, in sham-operated rats, six weeks after a carotid ligation.⁷ In addition, choline acetyltransferase dysfunction has been shown to be correlated with discrimination learning disabilities in hypoperfused rats.⁷ Even though improvement was noted, among those who had experienced a TIA, at day ten, such an explanation may explain why their HVLT-R means scores, at day 30, were poorer than the HVLT-R means scores of their matched control. Prior research also found that individuals who had experienced a TIA subjects showed significant differences in their cognitive impairment, when compared to persons who had not experienced a TIA.²³

Conclusions, Recommendations and Limitations

This study found that impairment of attention, working memory, and learning and memory, but not irritability, occurred in the first few days after the presentation of TIA symptoms. The impairments were found to worsen, by day ten, but improved between day 10 and 30. However, it is not clear if there was continual regression before recovery, or if recovery had begun earlier than the tenth day. Regardless, nurses need to assess the ability of those who have experienced a TIA to receive information, particularly 10 days after their initial symptom occurrence. Further research is needed to measure cognitive performance at different times, i.e. at days 3, 5, 10, 15, 20 and 30 to help clarify the impairment pattern.

Moreover, the findings show that those who experienced a TIA may have had cognitive impairment before testing. Their cognitive impairment may have occurred before the presentation of their TIA symptoms. Since to demonstrate the effect of cognitive impairment, the relationship between cognitive impairment and an individual's ability to learn and remember are required, comparison of cognitive performance, among those who have TIA symptoms and individuals who do not have TIA symptoms should be explored.

Although irritability among those who had experienced a TIA did not change within 30 days of their occurrence of symptoms, they were found to have more irritability than their matched controls, at all three times of measurement. Even though the instrument used to measure irritability had a high reliability, the individual items used within the instrument need to be further examined, since it is possible they were not sufficiently

sensitive to detect changes in the subjects' irritability. In addition, the use of qualitative questions, in future studies, may be needed to enhance measurement and interpretation of irritability.

Finally, the primary researcher, who had been trained to administer all the tools used, as well as to score and measure the results, did so solely by herself. Therefore, unintentional biases in the measurement and reporting of data may have occurred.

Implications for Nursing Practice

The findings may stimulate nurses and other health care providers to consider patients' ability to think, receive information, and learn, particularly 10 days after having experienced the occurrence of TIA symptoms. If any information is to be given, during this time, families or relatives probably are the key persons to help those who have experienced a TIA receive suggestions and instructions from nurses and other health care providers. Moreover, individuals who have experienced a TIA should be cautioned to think before they act, especially since impulsivity often leads to falls, accidents and mistakes.

Furthermore, nurses should implement therapies to help those who have experienced a TIA deal with their cognitive changes. Examples of restorative techniques, which may assist to improve learning and memory, include: using vivid pictures to capture attention; limiting competing stimuli (TV); doing one task at a time; speaking slowly; using short sentences during instructions to facilitate working memory; putting important pieces of information first and last during short instruction periods; and, building in repetition and demonstration of tasks.^{25, 40}

Acknowledgements

The lead author wishes to thank the Faculty of Nursing, Mahidol University and the Commission of Higher Education for their scholarship, as well as the Thailand Nursing Council for Nursing and Midwifery for the grant which supported this study.

References

1. Coull AJ, Lovett JK, Rothwell PM. Population-based study of early risk of stroke after transient ischemic attack or minor stroke: implications for public education and organization of services. *BMJ*. 2004; 328: 326-8.
2. Johnston SC, O'Meara ES, Manolio TA, Lefkowitz D, O'Leary DH, Goldstein S, Carlson MC, Fried LP, Longstreth WT. Cognitive impairment and decline are associated with carotid artery disease in patients without clinical evident cerebrovascular disease. *Ann Intern Med*. 2004; 40(4): 237-48.
3. Kasner SE, Gorelick PB. Prevention and treatment of ischemic stroke. Philadelphia (PA): Elsevier; 2004.
4. Rao R. The role of carotid stenosis in vascular cognitive impairment. *Eur Neurol*. 2001; 46: 63-9.
5. Ouyang YB, Voloboueva LA, Jun Xu L, Giffard RG. Selective dysfunction of hippocampal CA1 astrocytes contributes to delayed neuronal damage after transient forebrain ischemia. *J Neurosci*. 2007; 27(16): 4253-60.
6. Kirino T. Delayed neuronal death in the gerbil hippocampus following ischemia. *Brain Res*. 1982; 239: 57-9.
7. Tanaka A, Ogawa N, Asanuma M, Kondo Y, Nomura M. Relationship between cholinergic dysfunction and discrimination learning disabilities in Wistar rats following chronic cerebral hypoperfusion. *Brain Rep*. 1996; 729: 55-65.
8. Mononen H, Lepojarvi M, Kallanranta T. Early neuropsychological outcome after carotid endarterectomy. *Eur Neurol*. 1990; 30: 328-33.
9. Benke T, Neussl D, Aichner F. Neuropsychological deficits in asymptomatic carotid artery stenosis. *Acta Neurol Scand*. 1991; 83: 378-81.
10. Sinatra MG, Boeri R, DelTon F, Fornari T. Neuropsychological evaluation in transient ischemic attack and minor stroke. *J Neurol*. 1984; 231: 194-7.
11. Iddon JL, Sahakian BJ, Kirkpatrick PJ. Uncomplicated carotid endarterectomy is not associated with neuropsychological impairment. *Pharmacol Biochem Behav*. 1997; 56: 781-7.
12. Stark MA, Cimprich B. Promoting attentional health importance to women's lives. *Health Care Women Int*. 2003; 24: 93-102.
13. Royal College of Physicians of England and Wales. National sentinel stroke audit, 2006. London (UK): Royal College of Physicians; 2007.
14. Clinical Guidelines for Stroke and TIA Management: A guide for general practice. [cited 2008 Oct 10]; Available from: <http://www.racgp.org.au/Content/NavigationMenu/ClinicalResources/RACGPGuidelines/ClinicalGuidelinesforStrokeandTIAManagement200810StrokeGuidelinesFull.pdf>.
15. Rauch M, Turkoski B. Developing realistic treatment standards in today's economic climate: Stroke survivor education. *J Adv Nurs*. 1999; 30(2): 329-34.
16. Arunatit N, TangtroungpairjW. The prediction of risk factors to recurrent stroke in Prasat neurological institute. *J Prasat Neurol Inst*. 1996; 1(2): 46-55.
17. Selnes OA and Vinters HV. Vascular cognitive impairment: Nature clinical practice. *Neurology*. 2006; 2: 538-47.
18. Briones TL, Therrien B. Behavioral effects of transient cerebral ischemia. *Biol Res Nurs*. 2000; 1(4): 276-86.
19. Smith ML, Bendek G, Dahlgren N, Rosen I, Wieloch T, Siesjo, BK. Models for studying long-term recovery following forebrain ischemia in the rat. A 2-vessel occlusion model. *Acta Neurol Scand*. 1984; 69(6): 385-401.
20. Casey B. Disruption of inhibition control in developmental disorders: A mechanistic model of implicated frontostriatal circuitry. In: Siegler R, McClelland J, editors. *Mechanisms of cognitive development: The Carnegie Symposium on Cognition*, Vol.28. Hillsdale (NJ): Erlbaum; 2000. p. 327-46.

21. Baddeley A, Logie R. Models of working memory: Mechanisms of active maintenance and executive control. In: Miyake A, Shah P, editors. Working memory: The multiple component model. Cambridge (UK): Cambridge University Press; 1999. p. 28–61
22. Rao R, Jackson S, Howard R. Neuropsychological impairment in stroke, carotid stenosis, and peripheral vascular disease: A comparison with healthy community residents. *Stroke*. 1999; 30: 2167–73.
23. Sachdev PS, Brodaty H, Valenzuela MJ, Lorentz L, Looi J, Wen W, Zagami AS. The neuropsychological profile of vascular cognitive impairment in stroke and TIA patients. *Neurol*. 2004; 62: 912–9.
24. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale (NJ): Lawrence Erlbaum Association; 1988.
25. Cimprich, B. Attentional fatigue and restoration in individuals with cancer. [dissertation]. Ann Arbor (MI): University of Michigan; 1990.
26. Brewer T, Therrien B. Minor injury: New insights for early nursing care. *J Neurosci Nurs*. 2000; 32(6): 311–17.
27. Wechsler D. Manual for the adult intelligence scale-III. San Antonio (TX): Psychological Corporation; 1997.
28. Lezak MD. Neuropsychological assessment. Oxford (UK): Oxford University; 2004.
29. Demakis G. Frontal lobe damage and tests of executive processing: A meta-analysis of the Category Test, Stroop Test, and Trail Making Test. *J Clin Exp Neuropsychol*. 2004; 26: 441–50.
30. Spinella M. Normative data and a short form of the Barrett Impulsiveness Scale. *Int J Neurosci*. 2007; 117: 359–68.
31. Lezak M. The neuropsychological examination and interpretation. In: Lezak MD, editor. Neuropsychological assessment. 3rd ed. New York (NY): Oxford University Press; 1995.
32. Brandt J, Benedict R. The Hopkins verbal learning test-revised. Lutz (FL): Psychological Assessment Resources; 2001.
33. Brandt J. The Hopkins verbal learning test: Development of a new verbal learning test with equivalent forms. *Clin Neuropsychol*. 1991; 5: 125–42.
34. Hankey GJ, Warlow CP. Transient ischemic attacks of the brain and eye. Philadelphia (PA): Saunders; 1994.
35. Bakker FC, Klijn CJM, Jennekens-Schinkel A, Kappelle LJ. Cognitive disorders in patients with occlusive disease of the carotid artery: A systematic review of the literature. *J Neurol*. 2000; 247: 669–76.
36. Hemmingsen R, Mejsholm B, Boysen G, Engell HC. Intellectual function in patients with transient ischemic attacks (TIA) or minor strokes. *Acta Neurol Scand*. 1982; 66:145–59.
37. Teasell R, Bayona NA, Bitensky J. Plasticity and reorganization of the brain post stroke. *Top Stroke Rehabil*. 2005; 12(3): 11–26.
38. Zarahn E, Aguirre G, D’Esposito M. Temporal isolation of the neural correlates of spatial mnemonic processing with fMRI. *Cognitive Brain Res*. 1999; 7 (3): 255–68.
39. Fuster JM, Alexander GE. Neuron activity related to short-term memory. *Science*. 1971; 173: 652–4.
40. Parente R, Herrmann D. Retaining cognition techniques and application. Austin (TX): PRO-ED; 2003.

ประสิทธิภาพในการเรียนรู้จดจำของผู้ที่เคยมีอาการสมองขาดเลือดชั่วคราว: สมาธิ กระบวนการจำ การเรียนรู้และความจำ

วิชชุดา เจริญกิจการ, สายพิณ เกษมกิจวัฒนา, Barbara Therrien, อรพรรณ ไตสิงห์, ธวัชชัย วรพงศธร

บทคัดย่อ: การศึกษาไปข้างหน้า (prospective study) นี้มีวัตถุประสงค์เพื่อ ประเมินประสิทธิภาพการเรียนรู้จดจำ 3 ด้านหลัก ได้แก่ สมาธิ (attention) กระบวนการจำ (working memory) และการเรียนรู้และความจำ (learning and memory) ของผู้ที่มีอาการสมองขาดเลือดชั่วคราว (TIA) คัดเลือกกลุ่มตัวอย่างแบบสะดวก (convenient sampling) จากผู้ที่เคยมีอาการสมองขาดเลือดชั่วคราว 52 คน ที่มารับการรักษาที่หอผู้ป่วยนอกและหน่วยฉุกเฉิน จากโรงพยาบาลระดับตติยภูมิ 4 แห่ง ในประเทศไทย และผู้ที่เคยได้รับการผ่าตัดเล็ก (กลุ่มควบคุม) 52 คน จากผู้ที่มีอาการสมองขาดเลือดชั่วคราวจากโรงพยาบาลระดับตติยภูมิ 1 แห่งในประเทศไทย

เครื่องมือที่ใช้ได้แก่ แบบทดสอบ Necker Cube Pattern Control, Trial A, Digit Span Forward, Barratt Impulsiveness Scale, Irritability Assessment Scale, Digit Symbol Substitution, Digit Span Backward, และ Hopkins Verbal Learning เก็บรวบรวมข้อมูลโดยการทดสอบและสัมภาษณ์ 3 ครั้ง ในวันที่ 3, 10 และ 30 หลังจากมีอาการสมองขาดเลือดชั่วคราว วิเคราะห์ข้อมูลด้วยสถิติการวิเคราะห์ความแปรปรวนแบบวัดซ้ำ

ผลการวิจัยพบว่า ผู้ที่เคยมีอาการสมองขาดเลือดชั่วคราว มีสมาธิ กระบวนการจำและการเรียนรู้และความจำ เปลี่ยนแปลงในช่วง 30 วันหลังจากมีอาการสมองขาดเลือดชั่วคราว โดยประสิทธิภาพการเรียนรู้จดจำทั้ง 3 ด้านหลัก ต่ำกว่ากลุ่มควบคุมในวันที่ 3 หลังเกิดอาการสมองขาดเลือดชั่วคราว ยกเว้นเรื่องอารมณ์หงุดหงิด(Irritability) และมีประสิทธิภาพต่ำลงอีกในวันที่ 10 แต่ประสิทธิภาพนั้นกลับดีขึ้นในวันที่ 30 อย่างไรก็ตามประสิทธิภาพการเรียนรู้จดจำทั้ง 3 ด้านของกลุ่ม TIA ต่ำกว่ากลุ่มควบคุมทุกช่วงของการประเมิน

ข้อเสนอแนะจากผลการศึกษา พยาบาลและบุคลากรทางด้านสาธารณสุขควรตระหนักถึงความสำคัญในการรับข้อมูลข่าวสารของผู้ที่เคยมีอาการสมองขาดเลือดชั่วคราว โดยเฉพาะวันที่ 10 หลังเกิดอาการ ผู้ป่วยอาจขาดสมาธิ ตัดสินใจเร็ว และความสามารถในการเรียนรู้และความจำลดลง ญาติควรมีส่วนร่วมช่วยในการรับฟังคำแนะนำจากทีมสุขภาพเพื่อช่วยดูแลผู้ป่วยให้ปฏิบัติตามแผนการรักษาต่อที่บ้านได้อย่างถูกต้อง

วารสารวิจัยทางการแพทย์ 2009; 13(3) 199 - 215

คำสำคัญ: ประสิทธิภาพในการเรียนรู้จดจำ ผู้ที่เคยมีอาการสมองขาดเลือดชั่วคราว สมาธิ กระบวนการจำ การเรียนรู้และความจำ

ติดต่อที่: วิชชุดา เจริญกิจการ, RN, PhD candidate, คณะพยาบาลศาสตร์ มหาวิทยาลัยมหิดล ประเทศไทย E-mail charoenkitkarn@yahoo.com
สายพิณ เกษมกิจวัฒนา, RN, DNSc. รองศาสตราจารย์ คณะพยาบาลศาสตร์ มหาวิทยาลัยแม่ฟ้าหลวง จังหวัดเชียงราย ประเทศไทย
Barbara Therrien, RN, PhD, FAAN. Associate Professor, School of Nursing, University of Michigan, Ann Arbor, Michigan, USA.
อรพรรณ ไตสิงห์, RN, DNSc. ผู้ช่วยศาสตราจารย์ คณะพยาบาลศาสตร์ มหาวิทยาลัยมหิดล ประเทศไทย
ธวัชชัย วรพงศธร, Ph.D. รองศาสตราจารย์ คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล ประเทศไทย