Effectiveness of Repetitive Transcranial Magnetic Stimulation for Improving the Verbal Memory of Patients with Anomic Aphasia in South Korea

Haewon Byeon

*[*1]Department of Speech Language Pathology, Honam University, Gwangju, 62399, Republic of Korea*
[*]Corresponding author E-mail: byeon@honam.ac.kr

Abstract

Background/Objectives: The objective of the present research was to evaluate the effects of the repetitive transcranial magnetic stimulation (rTMS) application to the patients with anomic aphasia on the verbal memory (VM).

Methods/Statistical analysis: This study was conducted on 31 patients, who were diagnosed with anomic aphasia due to the stroke. Subjects were randomly divided into a treatment group (receiving rTMS; n=16) and a control group (Sham TMS; n=15). The location of the rTMS stimulus was the left dorsolateral prefrontal cortex (DLPFC) and the 1Hz TMS was given 20 minutes per time and three times per week for four weeks. The positions of the electrodes of the Sham TMS group were identical to those of the treatment group and the stimulation stopped 30 seconds after the application. Verbal memory evaluation was conducted by using the Korean version of the Consortium to Establish a Registry of Alzheimer's Disease assessment battery (CERAD-K).

Findings: The results of the ANCOVA indicated that there were significant differences ($p < 0.05$) between the two groups in immediate verbal memory (IVM), recognition verbal memory (RVM), and delayed verbal memory (DVM). The results of parameter estimation showed that IVM, RVM, and DVM were significantly higher in the treatment group by 1.9, 2.0, and 2.1, respectively, than in the control group.

Improvements/Applications: The results of this study suggested that the repeated stimulation on the left dorsolateral prefrontal cortex using the rTMS could improve the VM of stroke patients.

Keywords: transcranial direct stimulation, verbal memory, language rehabilitation, aphasia, speech language pathology, rTMS

1. Introduction

The stroke is a collective term for the ischemic stroke, caused by the blood vessel obstruction, and the hemorrhagic stroke, caused by the blood vessel rupture. The stroke is the most common cause of death in South Korea and it leads to high social costs. As of 2010, the socioeconomic cost due to the stroke is estimated at $3.5 billion [1]. Particularly, even if the operation is successfully done, the stroke patient frequently experiences severe sequela of the stroke. An effective speech & language therapy is needed for the stroke patient to improve the quality of their lives and return to the society successfully.

The quality of life is recognized as an important factor in creating a treatment plan in the medical and health rehabilitation fields. Moreover, it is used to evaluate the dynamic effects of the disease, disability, and dysfunction, on an individual. Additionally, numerous studies have been actively conducted to evaluate the quality of life of patients with communication disorders such as Parkinson's disease and aphasia after a speech & language therapy [1]. Nevertheless, the effects of a language& speech therapy on the quality of stroke patient's life have not been studied enough.

Cognitive function is a mental activity including the acquisition, storage, retrieval, and use of knowledge [2]. It is defined as a comprehensive terminology that encompasses from low-level mental activities (e.g., attention and memory) to high-level mental activities (e.g., organizing ability, problem-solving ability, and abstract) [2]. Linguistic ability is important for the cognitive function to work successfully. The problem associated with the linguistic ability limits the range of rehabilitation treatment and decreases the patient's desire for rehabilitation owing to the difficulty in communicating with the medical staff [3]. The problem associated with the linguistic ability inhibits the successful rehabilitation of brain-injured patients [4]. Therefore, it is an important factor for determining the functional prognosis of the stroke patient after stroke.

Particularly, the damage of verbal memory is one of the main characteristics found in patients with aphasia after stroke [5]. Cummings et al. (1986) argued that the verbal memory is a broad concept including the knowledge about objects, facts, and concepts as well as the knowledge related to the rules and vocabulary of the language and it includes all types of cognitive processes approaching information from a memory system [6]. The impairment of the verbal memory of patients with aphasia results in a decrease in word output ability.

The cognitive therapy, which includes the linguistic ability after the occurrence of the stroke, can be divided into the drug therapy and the cognitive rehabilitation. The most two typical cognitive rehabilitation therapies are the traditional cognitive rehabilitation therapy, by utilizing various paper-and-pencil tasks or block manipulation tasks, and the computer-based cognitive rehabilitation therapy. However, these cognitive rehabilitation treatments are difficult to perform depending on the individual

ability of a therapist or the level of a patient's cognitive level [5]. Therefore, methods to stimulate the brain nerve non-invasively related to cognitive function have been studied [5].

In recent years, the repetitive transcranial magnetic stimulation (rTMS) has been used for the cognitive rehabilitation of stroke patients. It directly stimulates the cerebrum to promote or suppress the excitability of the cerebral nerve. The conventional cognitive rehabilitation enhances language performance by increasing brain plasticity and changing the stimulation approach (e.g., auditory sense and visual sense) and the surrounding environment. However, rTMS is a non-invasive therapy method that induces the changes in neural plasticity by regulating the brain activation and it is known to significantly improve the brain activation of patients with neurologic disorders [7].

Multiple studies have reported that rTMS may increase the effectiveness of cognitive rehabilitation therapy by activating the cerebral nerve of stroke patients [8]. These studies have shown that rTMS not only promotes the physical functions (e.g., kinesthesia, balance, and leg movements) of stroke patients [9] but also helps them recover emotional functions (e.g., depression) and enhance cognitive abilities (e.g., executive functions, attention, and short-term memory) [10]. Previous studies also have revealed that rTMS has an effective treatment as well as neurophysiological effects [11]. The rTMS is safe without a side effect even applying it for 20-30 minutes continuously and it can be used along with other rehabilitation exercises [11]. These are advantages for the rTMS.

Although previous studies have reported that the rTMS is effective in activating the cerebral function of stroke patients, previous studies evaluating the effects of the rTMS on the stroke patients were limited to exercise, perception, and cognitive abilities. Moreover, there are not enough studies examining the effects of the rTMS on the verbal ability. The objective of this study was to evaluate the effects of the rTMS application to the patients with anomic aphasia on the verbal memory (e.g., immediate memory, recall memory, and delayed memory).

2. Methods

2.1. Research participants

The present study was conducted on 31 patients, who were diagnosed with anomic aphasia due to the stroke in Seoul and Incheon rehabilitation hospitals from Aug 01 to Dec 31, 2017, for three weeks. The selection criteria of study subjects are as follows: (1) who provided the written consent of the subject or guardian before participating in the study; (2) who was diagnosed with anomic aphasia according to the Korean-The Western Aphasia Battery (K-WAB) [12]; and (3) who did not have depression according to short-form geriatric depression scales(SGDS-K) [13]. Subjects were randomly divided into a treatment group (receiving rTMS; n=16) and a control group (Sham TMS; n=15) [Figure 1].

2.2. Measurement

2.2.1. Verbal Memory

Verbal memory evaluation was conducted by using the Korean version of CERAD-K [14] composed of ten lists of immediate memory words and twenty items recognition memory words. The CERAD-K is a standardized semi-structured clinical assessment tool for evaluating dementia and it is currently translated into 12 languages and used in over 40 countries. The CERAD-K is composed of verbal fluency (animal category), Boston naming test (15 item subset), Korean version of MMSE (MMSE-K), constructional praxis, word list memory, word recall, word recognition, and trail making test A & B. This study utilized the verbal learning test, composed of ten lists of immediate memory words and 20 items of recognition memory words, included in the

CERAD-K. The immediate memory word test score is summed after three runs and the total score is 30 points. The total score of the recognition memory word and the delayed memory word were 10 points each.
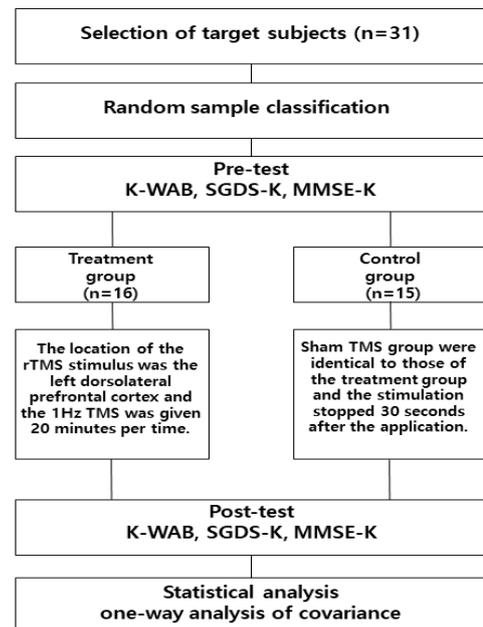

Figure 1: Design of study

2.2.1.1 Immediate Verbal Memory (IVM)

Ten word cards were presented to a subject at an interval of 10 seconds per word and the subject was asked to read the word loudly. Afterward, the subject recalled as many words as possible and wrote it on a piece of paper. This procedure was conducted three times. Ten words were presented in a different order for each time. For each time, correctly memorized word was considered one point with the full marks of 10. The final score was calculated by adding the scores of three executions and the highest score was 30 points.

2.2.1.2 Recognition Verbal Memory (RVM)

It is a test evaluating the linguistic recognition memory by recognizing if a word was in the previous immediate memory word list or not by presenting the ten words used in the immediate memory word along with new impeditive ten words. The final score is calculated by adding the number of correct 'yes' and correct 'no' responses and subtracting 10 from it. The highest score is 10 points.

2.2.1.3 Delayed Verbal Memory (DVM)

It is a linguistic delayed memory test. It asks a subject to recall the ten words presented in the immediate memory word test 20 minutes after. The final score is calculated by adding one point for each correctly recalled word and the highest score is 10 points.

2.2.1.4. Short form Geriatric Depression Scales (SGDS-K)

Yesavage et al. [15] developed GDS, which is a self-report depression scale composed of 30 items. Afterward, Cho et al. [13] standardized the scale (SGDS-K) in Korean with downsizing it to 15 items because the conventional test takes too much time. This study used SGDS-K.

2.2.1.5. Korean-the Western Aphasia Battery (K-WAB)

K-WAB [12] is a tool to diagnose aphasia and assess the severity of it. The test consists of an oral language test and a written language test. The former is composed of self-speaking, listening,

naming, and repeating and the latter consists of reading and writing.

2.2.1.6. MMSE-K

The overall cognitive level was measured by using MMSE-K [16]. MMSE-K consists of the orientation for time and space, registration, recall, concentration, calculation, visuospatial function, and language function. Scores ranged from 0 to 30:no cognitive impairment for 24-30, mild cognitive impairment for 18-23, and severe cognitive impairment for 0-17.

2.2.2. RTMS

BioCon-1000Pro (Mcube Technology Co, Seoul, Korea) was used for rTMS. The location of the stimulus was the left dorsolateral prefrontal cortex (DLPFC) and the TMS was given 20 minutes per time and three times per week for four weeks [Figure 2], [Figure 3]. In the first week, 1Hz stimulation was continued for 10 seconds at the interval of 30 seconds and it was conducted 24 times (total 240 pulses). The amount of stimulation was increased to 720 pulses in the second week and it increased to 1,000 pulses in the third week.

The positions of the electrodes of the Sham TMS group were identical to those of the treatment group and the stimulation stopped 30 seconds after the application. The intervention was designed in the way that the subjects did not recognize the stimulation status during the 30 minute session.

2.3. Statistical Analyses

The study originally intended to conduct repeat measures ANOVA in order to compare the changes in verbal memory before and after the intervention. However, this study analyzed the differences in verbal memory after treatment by conducting ANCOVA with using pre-test scores (e.g., verbal memory, RVM, and delayed verbal memory) as covariates. All analyses were performed using R version 3.5.1 win.
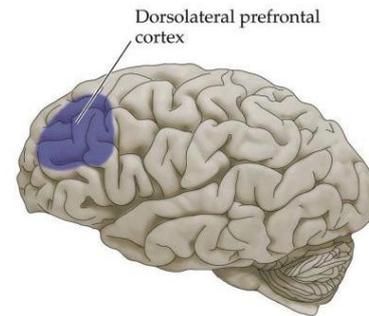

Figure 2: Example of configuration of rTMS

Figure 3: Location of stimulus: DLPFC

3. Results

3.1. Characteristics of Study Participants

The Characteristics of research participants are shown in Table 1. Chi-square test and independent t-test were conducted to evaluate the differences between treatment and control groups at the baseline level and the results showed that there were no significant differences between treatment and control groups in terms of sex, duration after onset, education, age, MMSE-K, K-WAB, and SGDS-K.

Table 1: The Characteristics of research participants

Variables	TG (n=15)	CG (n=17)	p
Age (year±SD)	62.50±8.13	63.88±9.15	0.870
Gender			0.456
Male	5	7	
Female	8	10	
Level of education (year)	9.58±2.12	9.32±2.50	0.860
Time since stroke (month)	10.95±3.18	12.15±4.53	0.297
MMSE-K	20.58±1.28	21.30±1.75	0.456
K-WAB	82.2±4.58	84.3±5.81	0.633
SGDS-K	8.58±2.55	9.10±3.05	0.870

* TG=Treatment group (rTMS); CG=Control group (Sham TMS)

3.2. Changes in Immediate Memory, Recognition Memory, and Delayed Memory According to Intervention

Pre- and post-tests were conducted for the treatment and control groups in order to evaluate the changes in IVM, RVM, and DVM according to the intervention [Table 2]. The interaction between the pre-test and treatment was analyzed in order to test if the data satisfied the basic assumptions of ANCOVA. The results showed that the interaction was not significant so it was confirmed that the pre-test and the slope of the regression analysis were identical between the two groups. Moreover, the Levene test revealed that their variances were homogeneous.

The results of the ANCOVA indicated that there were significant differences between the treatment and control groups in IVM, RVM, and delayed verbal memory (p<0.05). The results of parameter estimation showed that IVM, RVM, and DVM were significantly higher in the treatment group by 1.9, 2.0, and 2.1, respectively, than in the control group.
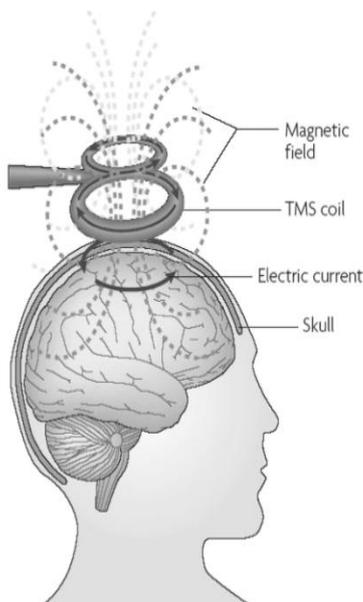
Table 2: Changes in immediate memory, recognition memory, and delayed memory according to intervention: ANCOVA

Variables	Treatment group (rTMS)		Control group (Sham TMS)		p-value
	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx	
IVM	13.31±1.48	15.88±1.50	13.23±1.50	13.81±1.51	<0.001
RVM	4.29±1.07	7.18±1.31	4.33±1.05	5.13±1.23	<0.001
DVM	4.03±0.85	6.88±1.35	4.11±0.71	4.85±1.13	<0.001

Pre-Tx=Pre-treatment; Post-Tx =Post-treatment

4. Discussion

The results of this study confirmed the effects of low-frequency rTMS on IVM, RVM, and delayed verbal memory. rTMS may increase or decrease the activation of the cerebral cortex in the local region. The rTMS of 1 Hz or less is considered a low frequency (LF-rTMS) and that of 5 Hz or higher is called a high frequency (HF-rTMS). LF-rTMS decreases the excitation of the cerebral cortex, while HF-rTMS increases the excitation of the cerebral cortex by increasing the size of motor evoked potential [17].

Many previous studies evaluated the effects of a LF-rTMS on patients with aphasia. For example, Abo et al. (2012) [18] examined the effects of rTMS treatment on the severity of aphasia of non-fluent aphasic patients and reported that the treatment improved the verbal abilities. Moreover, Naeser et al. (2011) [19] applied a LF-rTMS to chronic non-fluent aphasic patients and reported that these patients significantly improved in a picture naming task and their response time reduced significantly as well.

Moreover, some previous studies examined the treatment timing of rTMS. Heiss et al. (2013) [20] applied a LF-rTMS treatment to subacute aphasic patients for 20 minutes per day for 10 days and found that it significantly increased the achen aphasia test score of them.

This study examined the effects of the rTMS on subacute anomic aphasic patients and the results showed that the rTMS group had significantly higher IVM, RVM, and DVM scores than the control group, which was similar to the results of previous studies. It is speculated that the 1Hz LF- rTMS could influence the excitement of cerebral cortex by reducing the excitement of the intact cerebral cortex. Particularly, the LF-rTMS is known to regulate the spontaneous neuronal activity like neuro regulators. The results of our study implied that the DLPFC and the prefrontal lobe, which are central parts related the language process and memory, could be activated by rTMS and the rTMS could affect the memory.

Klaus & Schutter (2018) [21] confirmed that the DLPFC is associated with language processing as a part of the complex cortical network. The results of this study suggested that the neural activation of the DLPFC could improve verbal memory. However, it is difficult to conclude this speculation because the cognitive process can be activated by the connected surrounding area as well as a specific single area of the brain. Therefore, more experimental studies are needed to prove the effects of rTMS in the future.

The limitations of the study are as follows. First, it is hard to generalize the results of this study to all patients with anomic aphasia due to stroke because this study had a small sample size. Second, this study could not confirm the persistent of the effects using a long-term follow-up. Follow-up studies are required to confirm the effects of the rTMS using various statistical analyses including repeated measures ANOVA.

5. Conclusion

The results of our study suggested that the repeated stimulation on the DLPFC using the rTMS could improve the verbal memory of stroke patients. Randomized and placebo-controlled phase III studies using a large-size sample is needed to confirm the results of this study.

Acknowledgment

References

[1] Kim HJ, Hue JH, Lee MH, Kang HY, Ji SH, Nam JM, et al. Cost-effectiveness analysis of national prevention programs for cardiovascular diseases. Seoul: Management Center for Health Promotion; 2007.

[2] Fuster JM. Cortex and mind: Unifying cognition. New York: Oxford University Press; 2003.

[3] Dorze GL, Brassard C.A description of the consequences of aphasia on aphasic persons and their relatives and friends, based on the WHO model of chronic diseases. Aphasiology. 1995 Aug:9(3):239-55. DOI.org/10.1080/02687039508248198.

[4] Bartlett G, Blais R, Tamblyn R, Clermont RJ, MacGibbon B. Impact of patient communication problems on the risk of preventable adverse events in acute care settings. CMAJ. 2008 Jun;178(12):1555-62. DOI: 10.1503/cmaj.070690.

[5] Cicerone KD, Dahlberg C, Malec JF, Langenbahn DM, Felicetti T, Kneipp S, et al. Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. Arch Phys Med Rehabil. 2005 Aug;86(8):1681-92.

[6] Cummings JL, Houlihan JP, Hill MA. The pattern of reading deterioration in dementia of the Alzheimer type: Observations and implications. Brain Lang. 1986 Nov;29(2):315-23. DOI.org/10.1016/0093-934X(86)90051-9.

[7] Barwood CHS, Murdoch BE, Whelan BM, Lloyd D, Riek S, O'Sullivan JD, et al. Improved language performance subsequent to low-frequency rTMS in patients with chronic non-fluent aphasia post-stroke. Eur J Neurol . 2011 Dec;18(7):935-43.

[8] Min DK. Changes in the sensory function after Transcranial Direct Stimulation on dorsolateral prefrontal cortex area. J Korea Acad Industr Coop Soc. 2015 Jan;16(1):445-52. DOI:10.5762/KAIS.2015.16.1.445.

[9] Liebetanz D, Nitsche MA, Tergau F, Paulus W. Pharmacological approach to the mechanisms of transcranial DC- stimulation- induced after- effects of human motor cortex excitability. Brain. 2002 Oct;125(10):2238-47. DOI.org/10.1093/brain/awf238.

[10] Cho HS, Cha HG. Effects of Trunk Pattern Exercise in proprioceptive neuromuscalar facilitation integrated Transcranial Direct Stimulation on function of lower extremity in stroke patients. J Korea Acad Industr Coop Soc. 2014 Jun;15(11):6767-73. DOI:10.5762/KAIS.2014.15.11.6767.

[11] Lang N, Siebner HR, Ward NS, Lee L, Nitsche MA, Paulus W, et al. How does transcranial DC stimulation of the primary motor cortex alter regional neuronal activity in the human brain?. European Journal of Neuroscience.2005; 22(2):495-504.

[12] Kim HH, Na DL. Paradise· Korean version-Western aphasia battery (K-WAB). Seoul: Paradise welfare foundation; 2001.

[13] Cho MJ, Bae JN, Suh GH, Hahm BJ, Kim JK, Lee DW, et al. Validation of Geriatric Depression Scale, Korean Version (GDS) in the assessment of DSM-III-R major depression. J Korean Neuropsychiatr Assoc. 1999 Jan;38(1):48-63.

[14] Woo JI. The Korean version of CERAD neuropsychlogical assessment batter. Seoul: Seoul University publishing department; 2002.

[15] Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and Validation of a Geriatric Depression Screening Scale: a preliminary report. J Psychiatr Res. 1982-1983;17(1):37-49. DOI.org/10.1016/0022-3956(82)90033-4.

[16] Park JH, Kwon Y. Standardization of Korean version of the Mini-Mental State Examination (MMSE-K) for use in the elderly. Part II. Diagnostic validity. J Korean Neuropsychiatr Assoc. 1989;28:508-13.

[17] Sasaki N, Mizutani S, Kakuda W, Abo M. Comparison of the effects of high-and low-frequency repetitive transcranial magnetic stimulation on upper limb hemiparesis in the early phase of stroke. J STROKE CEREBROVASC. 2013 May;22(4):413-8. DOI:https://doi.org/10.1016/j.jstrokecerebrovasdis.2011.10.004.

[18] Abo M, Kakuda W, Watanabe M, Morooka A, Kawakami K, Senoo A. Effectiveness of low-frequency rTMS and intensive speech therapy in poststroke patients with aphasia: a pilot study based on evaluation by fMRI in relation to type of aphasia. Eur J Paediatr Neurol. 2012 Oct;68(4):199-208. DOI.org/10.1159/000338773.

[19] Naeser MA, Martin PI, Theoret H, Kobayashi M, Fregni F, Nicholas M, et al. TMS suppression of right pars triangularis, but not pars opercularis, improves naming in aphasia. Brain Lang. 2011 Dec;119(3):206-13. http://DOI.org/10.1016/j.bandl.2011.07.005.

[20] Heiss W, Hartmann A, Rubi-Fessen I, Anglade C, KrachtL, Kessler J, et al. Noninvasive brain stimulation for treatment of right- and left-handed poststroke aphasics. Cerebrovasc Dis. 2013 Nov;36(5-6):363-72. DOI:10.1159/000355499.

[21] Klaus J, Schutter DJ. (2018). The role of left dorsolateral prefrontal cortex in language processing. Neuroscience. 2018 May;377:197-205. DOI.org/10.1016/j.neuroscience.2018.03.002.