The effect of computer-assisted cognitive rehabilitation and repetitive transcranial magnetic stimulation on cognitive function for stroke patients

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Abstract. [Purpose] This study investigated the effects of computer-assisted cognitive rehabilitation (CACR) and repetitive transcranial magnetic stimulation (rTMS) on cognitive function in patients with stroke. [Subjects and Methods] We enrolled 20 patients and divided them into CACR and rTMS groups. CACR and rTMS were performed thrice a week for 4 weeks. Cognitive function was measured with the Korean Mini-Mental State Examination (K-MMSE) and Lowenstein Occupational Therapy Cognitive Assessment-Geriatric (LOTCA-G) before and after treatment. The independent samples t-test was performed to test the homogeneity of K-MMSE and LOTCA-G before treatment and compare the differences in cognitive improvement between the CACR and rTMS groups. A paired samples t-test was used to compare cognitive function before and after treatment. [Results] Cognitive function of both the groups significantly improved after the intervention based on the K-MMSE and LOTCA-G scores. While the LOTCA-G score improved significantly more in the CACR group than in the rTMS group, no significant difference was seen in the K-MMSE scores. [Conclusion] We showed that CACR is more effective than rTMS in improving cognitive function after stroke.
Key words: Stroke, Computer-assisted cognitive rehabilitation (CACR), Repetitive transcranial magnetic stimulation (rTMS)

INTRODUCTION

Stroke, which is one of the most common diseases in adults, is generally accompanied by disabilities, and 50% of the patients sustain neurological damage[1)]. The major factor that interferes with independent daily activities is cognitive dysfunction resulting in deterioration of memory, alertness, attention, and language function[2)]. In general, 25% of the patients show dementia 3 months after a stroke, and 50–75% show partial cognitive dysfunction[3)].

Cognitive dysfunction reduces motivation and has a negative effect on functional recovery and returning to rehabilitation[4)]. Aside from motor function and emotional disabilities, it is the most problematic disability, and the importance of cognitive rehabilitation is being emphasized[5)]. Cognitive rehabilitation is a program designed to improve cognitive functions such as attention, memory, and concept formation ability, by systematically applying an intervention technique to improve cognitive processes[6)], which is necessary for stroke patients to improve their functional capabilities for performing daily activities and regaining independence[7)].

It consists of traditional and computerized cognitive training, which are currently used actively. Traditional cognitive training consists of pencil and paper activities, peg design, and puzzle activities that require functions of the damaged area, followed by a 1:1 intervention by a therapist. Therefore, the intervention varies depending on the therapist, and the feedback is not consistent[8)]. However, computer-assisted cognitive rehabilitation (CACR) makes use of a computer program specific to the damaged area of the patient, and the level of difficulty can be adjusted to suit the patient. In addition, it provides instant and direct feedback for their performance. Because the training results during treatment can be saved, the progress of a patient can be monitored, thus providing objective data for further studies[9)]. Since the first attempt at CACR by Glisky et al.[10)], many researchers have verified its effects[11)].

Many studies of CACR have been published in the last 10 years, and positive effects of cognitive rehabilitation on patients with stroke are being reported. Through an analysis of the studies on the cognitive rehabilitation after stroke published until 2002, Cicerone et al.[12)] reported that cognitive rehabilitation is beneficial (92.9% level). Lee et al.[13)] and Shin et al.[14)] treated patients with cognitive dysfunction after brain damage with CACR PSS CogRehab, which contains a problem-solving program that targets issues, such as de-

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fects in basic cognitive function, spatiotemporal perception, memory, and problem-solving skills. They reported improvement in short-term verbal memory, short-term visual perception memory, auditory and visual attention focus, and the performance of activities of daily living.

Recently, studies have focused on memory improvements occurring in response to noninvasive brain stimulation, such as repetitive transcranial magnetic stimulation (rTMS), which modulate the excitation of the cortex by varying the frequency of magnetic stimulation of specific brain regions[15]. Noninvasive brain stimulation is an emerging area of study in the fields of brain and neural rehabilitation and cognitive science[16]. The rTMS cognitive network was first introduced by Pascual-Leone and Hallett[17], who observed a decrease in the performance of working memory after the application of rTMS to decrease cerebral activities. They reported that the lateral prefrontal cortex plays an important role in working memory.

On et al.[16] reported an improvement in the accuracy of working memory (which is the basis of long-term memory and language learning and execution) after 1,000 rTMS sessions at 10 Hz and at 100% intensity of the exercise threshold. These effects on working memory were maintained up to 30 min after the final stimulation depending on the number of stimulations. Pape et al.[18] and Mally and Stone[19] found that rTMS has beneficial effects on the cognitive function and memory of patients with central nervous system diseases, such as stroke and degenerative brain diseases.

However, studies on which treatment method, CACR or rTMS, is more effective in improving cognitive function are lacking. Therefore, the purpose of this study was to examine which intervention, CACR or rTMS, was more effective in improving the cognitive functions of patients with stroke by setting the prefrontal cortex as the stimulation area when direct stimulation was possible among the areas of the brain.

SUBJECTS AND METHODS

The experimental procedure was sufficiently explained beforehand to the subjects, who voluntarily participated by signing the experiment consent form. This study was approved by the Institutional Ethics Committee of Namseoul University. The subjects comprised 20 right-handed stroke patients with left hemiplegia who were hospitalized in C Hospital in Cheon-An City, Republic of Korea. All the subjects were determined to be right-handed with the Edinburgh Handedness Inventory. The selection criteria included patients who were at least 6 months post stroke, had a Korea version of the Mini-Mental State Examination (K-MMSE) score ≤ 23 (the cognitive disability standard), were capable of voluntary movements of the contralateral arm, and could control the touch screen of the CACR with their hands. rTMS was applied according to the method described by On et al.[16] except for the frequency, and a TAMAS transcranial magnetic stimulator (CR Technology Co., Ltd., Daejeon, Korea) with a diameter of 96 mm and an figure-eight coil was used for TMS. After attaching a recording electrode to the first right dorsal interosseous muscle of the patients, it was stimulated under stable conditions after fixing a cloth with marks at a 1-cm intervals to the scalp. After finding

Table 1. Subject characteristics

Character-istics	Classification	CogRehab (n=10)		rTMS (n=10)	
		N	%	N	%
Sex	Male	5	50.0	4	40.0
	Female	5	50.0	6	60.0
Age (yr)	60−69	1	10.0	2	20.0
	70−79	7	70.0	5	50.0
	80−89	2	20.0	3	30.0
Lesion	Infarction	4	40.0	8	80.0
	Hemorrhage	6	60.0	2	20.0
Prevalence time (months)	≤12	1	10.0		
	≤24	5	50.0	7	70.0
	≥24	4	40.0	3	30.0

the hot spot where the maximal motor evoked potential was induced at the minimal intensity, the minimal intensity at which an evoked potential>50 μV was induced in more than 5 out of 10 stimulations was set as the resting motor threshold. The intensity of the rTMS was at 100% of the resting motor threshold, and the stimulation frequency was set at 10 Hz. The F3 point was stimulated according to the International 10/20 EEG recording system to stimulate the left prefrontal cortex. The stimulation was applied for 5 s, and restimulation was applied after a 55-s resting period. Stimulations of 1,000 times a day were repeated 20 times. The CACR and rTMS subjects (10 each) were randomly assigned, and the effects of each treatment intervention were not explained to them in order to prevent a treatment bias effect in the subjects.

This study was performed on 20 subjects after the contents of the experiment were sufficiently explained before the experiment, and they consented to the experiment participation agreement. All the subjects were hospitalized and received basic inpatient treatments, such as physical therapy and occupational therapy. After dividing the subjects into the 10 who received basic inpatient treatment and participated in the PSS Cogrehab FD Edition CACR and the 10 who received basic inpatient treatment and participated in the rTMS, the K-MMSE and Lowenstein Occupational Therapy Cognitive Assessment-Geriatric (LOTCA-G) were administered to both groups, and they were evaluated before and after the treatment intervention. The K-MMSE and LOTCA-G were used to evaluate cognitive function before and after the intervention, and the reliability coefficient of the K-MMSE was r=0.72, and that of the LOTCA-G was r= 0.84 in this study. The PSS CogRehab for the CACR group was performed for 20 min a day 3 times a week for 4 weeks. The rTMS was performed for 20 min a day 3 times a week for 4 weeks.

SPSS version 20.0 was used for statistical analysis of the data in this study. The general characteristics of the subjects were calculated with numbers and percentages. General characteristics of the subjects are presented in Table 1. Independent samples t-tests were performed to test the homogeneity of the MMSE-K and LOTCA-G scores of the subjects before the treatment intervention. To compare the

Table 2. Changes in K-MMSE and LOTCA-G cognitive function before and after the intervention

Material	Intervention	Before	After
		Mean±SD	Mean±SD
K-MMSE	rTMS (n=10)**	17.90 ± 2.470	19.50 ± 2.369
	Cogrehab (n=10)**	18.00 ± 1.886	20.30 ± 2.058
LOTAC-G	rTMS (n=10)*	68.70 ± 6.464	70.50 ± 6.223
	Cogrehab (n=10)**	71.70 ± 4.945	76.80 ± 4.442

K-MMSE: Korean Mini-Mental State Examination; LOTCA-G: Lowenstein Occupational Therapy Cognitive Assessment-Geriatric; SD: standard deviation; rTMS: repetitive transcranial magnetic stimulation; Cogrehab: cognitive rehabilitation; *p<0.05; **p<0.01.

Table 3. Comparison of cognitive function differences between the rTMS and CogRehab groups

	rTMS (n=10)	CogRehab (n=10)
	Mean±SD	Mean±SD
K-MMSE	1.60 ± 1.430	2.20 ± 1.317
LOTAC-G*	2.00 ± 1.563	5.10 ± 3.348

K-MMSE: Korean Mini-Mental State Examination; LOTCA-G: Lowenstein Occupational Therapy Cognitive Assessment-Geriatric; SD: standard deviation; rTMS: repetitive transcranial magnetic stimulation; Cogrehab: cognitive rehabilitation; *p<0.05.

Table 4. Comparison of LOTCA-G details in the CogRehab group

Intervention CogRehab (n=10)	Material LOTAC-G	Before	After
		Mean±SD	Mean±SD
	OT	12.90±0.738	13.20±1.033
	PT**	12.30±1.360	13.50±1.080
	SP	8.90±1.287	9.20±1.398
	MP	10.70±0.823	10.90 ±0.738
	VO**	11.10±1.197	13.60±1.647
	TO	3.40±0.843	3.40±0.843
	MR*	10.00±1.333	10.40±1.265
	AT*	2.80±0.632	3.20±0.422

LOTCA-G: Lowenstein Occupational Therapy Cognitive Assessment-Geriatric; SD: standard deviation; Cogrehab: cognitive rehabilitation; OT: orientation; PT: perception; SP: spatial perception; MP: motor praxis; VO: visuomotor organization; TO: thinking operation; MR: memory; AT: attention and concentration; *p<0.05; **p<0.01.

cognitive function of the subjects before and after the treatment, a paired samples t-test was performed. To compare the differences in cognitive function improvements between the CACR group and the rTMS group, an independent samples t-test was performed. The level of statistical significance α was set at 0.05.

RESULTS

The cognitive functions of both the rTMS and CACR groups significantly improved after the intervention based on the K-MMSE and LOTCA-G scores (p<0.05) (Table 2). While the improvement in the LOTCA-G score in the CACR group was more significant than that in the rTMS group (p<0.05), no significant difference was found in the K-MMSE scores (p >0.05) (Table 3). In the CACR group, significant improvements were shown in the details of the LOTCA-G, including PT (perception), VO (visuomotor organization), MR (memory), and AT (attention and concentration) (p<0.05) (Table 4).

DISCUSSION

The reality of the rehabilitation of stroke patients is that the treatments are focused on the recovery of physical function rather than on improvements in cognitive function. Cognitive function is an important parameter by which the prognosis of the damage caused by a stroke can be gauged and that determines the quality of the patient's subsequent life.

This study was conducted to determine the effects of CACR and rTMS on cognitive function improvements in stroke patients. Based on the K-MMSE and LOTCA-G scores, the cognitive function of both the rTMS group and the CACR group improved significantly after the intervention (p<0.05). Similar to the results of the study by On et al.[16] that showed improvement in the working memory function of 10 healthy adults as a result of rTMS applied to the left prefrontal lobe to improve working memory, it is likely that the cognitive function improvements in the rTMS group were due to improvements in working memory.

In both, the CACR and rTMS groups, the improvement in the LOTCA-G scores was greater than that in the K-MMSE scores. Kim[20] also reported greater improvements in the LOTCA-G scores than in the K-MMSE scores in their study that measured changes in cognitive function resulting from CACR. As shown by Appelros[21] and Cho et al.[22], although the MMSE is a reliable and valid tool commonly used for evaluating cognitive function in patients with brain damage, the K-MMSE, compared with the LOTCA-G, does not properly reflect the effects of CACR and rTMS because it lacks the evaluation criteria to assess the management function changes that correspond to higher cognitive functions.

The difference in visuomotor organization scores (a LOTCA-G evaluation item) before and after the intervention was the largest (Table 3), indicating that the effect was likely due to the visuospatial training effect of CACR, which is a visuospatial perception training program. PSS CogRehab appeared to cause an overall improvement in visuospatial perception. The absence of a sensitive measure for it supports the finding that the improvement in the LOTCA-G score was bigger than that in the K-MMSE score.

In a study on the effects on cognition, visuospatial perception, and daily life resulting from a Korean computer-based cognitive rehabilitation program (CoTras), Park et al.[23] showed that the improvement in the visuomotor organization score, a LOTCA item used as a tool to assess cognition, was largest. Our results support the findings of Lee et al.[13], who used CACR on stroke patients, and found an improvement in

the scores for all LOTCA-G areas of the subjects, especially in cognition and visuomotor organization.

rTMS, which is noninvasive brain stimulation technique, can stimulate the cortex using a local magnetic wave induced on the head surface. Many studies, such as those on depression, attention disorders, schizophrenia, sleep disorders, and Parkinson's disease, have used this feature to excite the cerebral cortex without surgery or anesthesia. The clinical effects have not been verified, except for depression in the study on rTMS by Choi and Jeong[24], and this was attributed to the various technical variables such as the stimulation intensity, location, frequency, pulse width, interval between stimuli, type of coils, time, number of treatments, gap between procedures, and treatment time. In fact, information on cognitive function changes with rTMS is lacking in stroke patients.

Ko et al.[25] noted side effects that can cause seizures in normal humans when rTMS is applied above the threshold intensity for a long time. Therefore, they recommend its use within the permitted safety standard range. However, even within this range, patients may feel discomfort because of the unique sounds that occur during stimulation and facial muscle contractions. In this study, we experienced difficulty in selecting new subjects because 4 subjects dropped out due to discomfort. In addition, the high equipment cost is likely to make its clinical use difficult.

Our results show a greater improvement in cognitive function by CACR than rTMS. In addition, rTMS caused discomfort in the subjects (a stability issue). Thus, rather than a rTMS technique, a computerized cognitive rehabilitation program would be more appropriate to improve cognitive function after stroke. However, in their review on computerized cognitive rehabilitation programs, Kim et al.[26] suggested that there are potential problems in each computerized cognitive rehabilitation program and that a larger number of subjects should be studied to verify the clinical usefulness.

Although a number of recent studies on CACR-induced cognition improvements have been reported from Korea, studies on cognition improvement by rTMS are still lacking. Most studies have examined improvements in working memory, which is a function of the prefrontal cortex. Furthermore, no study that has compared cognition improvement by CACR to that by rTMS has been reported domestically.

The cognitive improvements in stroke patients might be improved if studies combine the two interventions (CACR and rTMS) so that they can be both applied to subjects and use proper evaluation tools that can verify the effects. In addition, it would be clinically significant to investigate the effects of cognition function improvements on the performance of daily activities by patients with stroke.

There were a number of limitations in this study. Firstly, it was difficult to generalize the results because of the small number of subjects. Secondly, there was no follow-up study on whether the effects of cognitive function improvements were long term. Thirdly, the influence of drugs on the results cannot be excluded because the subjects continued their dementia- and depression-related medication during the course of the study.

REFERENCES

1) Duncan PW, Goldstein LB, Matchar D, et al.: Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. Stroke, 1992, 23: 1084–1089. [Medline] [CrossRef]

2) Kim GY, Han MR, Lee HG: Effect of dual-task rehabilitation training on cognitive and motor function of stroke patients. J Phys Ther Sci, 2014, 26: 1–6. [Medline] [CrossRef]

3) Desmond DW, Moroney JT, Paik MC, et al.: Frequency and clinical determinants of dementia after ischemic stroke. Neurology, 2000, 54: 1124–1131. [Medline] [CrossRef]

4) Diamond PT, Felsenthal G, Macciocchi SN, et al.: Effect of cognitive impairment on rehabilitation outcome. Am J Phys Med Rehabil, 1996, 75: 40–43. [Medline] [CrossRef]

5) Cho YN, Jung JH, Kim HG: A study on cognitive dysfunctions of stroke patients. J Kor Soc Cogn Rehabi, 2012, 1: 37–50.

6) Berrol S: Issues in cognitive rehabilitation. Arch Neurol, 1990, 47: 219–220. [Medline] [CrossRef]

7) Zorowitz RD, Gross E, Polinski DM: Effects of problem-oriented willed-movement therapy on motor abilities for people with post stroke cognitive deficits. J Disabil Rehabil, 2002, 24: 666–679. [CrossRef]

8) Bang YS: The effects of task oriented activities on the cognitive function and performance of activities of daily living in stroke patients. J Korean Soc Occup Ther, 2007, 15: 49–61.

9) Lee YM, Lee CR, Hwang BJ: effects of computer-aided cognitive rehabilitation training and balance exercise on cognitive and visual perception ability of the elderly. J Phys Ther Sci, 2012, 24: 885–887. [CrossRef]

10) Glisky EL, Schacter DL, Tulving E: Computer learning by memory-impaired patients: acquisition and retention of complex knowledge. Neuropsychologia, 1986, 24: 313–328. [Medline] [CrossRef]

11) Jeong WM, Hwang YJ, Youn JC: Effects of a computer-based cognitive rehabilitation therapy on mild dementia patients in a community. J Kor Gerontological Soc, 2010, 30: 127–140.

12) Cicerone KD, Dahlberg C, Malec JF, et al.: Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. Arch Phys Med Rehabil, 2005, 86: 1681–1692. [Medline] [CrossRef]

13) Lee SA, Jeong MS, Chae KJ: The effects of the computer-assisted cognitive rehabilitation on cognition, perception, activities of daily living on traumatic head injury patients. J Korean Soc Occupationa Ther, 2001, 9: 123–133.

14) Shin SH, Ko MH, Kim YH: Effect of computer-assisted cognitive rehabilitation program for patients with brain injury. J Korean Acad Rehab Med, 2002, 2: 1–8.

15) Webster BR, Celnik PA, Cohen LG: Noninvasive brain stimulation in stroke rehabilitation. NeuroRx, 2006, 3: 474–481. [Medline] [CrossRef]

16) On SH, Park CI, Lee BH, et al.: Effect of prefrontal repetitive transcranial magnetic stimulation the enhancement of working memory. J Korean Acad Rehab Med, 2008, 32: 501–505.

17) Pascual-Leone A, Hallett M: Induction of errors in a delayed response task by repetitive transcranial magnetic stimulation of the dorsolateral prefrontal cortex. Neuroreport, 1994, 5: 2517–2520. [Medline] [CrossRef]

18) Pape TL, Rosenow J, Lewis G: Transcranial magnetic stimulation: a possible treatment for TBI. J Head Trauma Rehabil, 2006, 21: 437–451. [Medline] [CrossRef]

19) Mally J, Stone TW: New advances in the rehabilitation of CNS diseases applying rTMS. Expert Rev Neurother, 2007, 7: 165–177. [Medline] [CrossRef]

20) Kim YG: The effects of Korean computer-based cognitive rehabilitation program (CoTras) for the cognition and ADL in stroke. J Korean Soc Occup Ther, 2011, 19: 75–88.

21) Appelros P: Characteristics of Mini-Mental State Examination 1 year after stroke. Acta Neurol Scand, 2005, 112: 88–92. [Medline] [CrossRef]

22) Cho YN, Kim HK, Kwon HC: The effects of computerized cognitive rehabilitation on cognitive function post-stroke patients. J Kor Special Edu Rehabil Sci, 2012, 51: 261–278.

23) Park SW, Park IH, You SJ: The effects of Korean computer-based cognitive rehabilitation program (CoTras for the cognition and visual perception and ADL in brain injury. Soc Occup Ther Aged Dement, 2013, 7: 47–57.

24) Choi JW, Jeong BS: Practical review of Transcranial magnetic stimulation. J Korean SocBiol Ther Psychiatry, 2005, 11: 5–11.

25) Ko MH, Jeong YC, Seo JH, et al.: The effect of sub-threshold 10 Hz repetitive transcranial magnetic stimulation on motor cortical excitability. J Korean Acad Rehab Med, 2006, 30: 436–430.

26) Kim HJ, Lee SY, Kam KY: A review of computer-assisted cognitive rehabilitation (CACR). Soc Occup Ther Aged Dement, 2008, 2: 35–46.