



Original Article

The effects of repetitive transcranial magnetic stimulation (rTMS) on depression, visual perception, and activities of daily living in stroke patients

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Abstract. [Purpose] The present study aimed to investigate the effects of repetitive transcranial magnetic stimulation (rTMS) on visual perception, depression, and activities of daily livings (ADLs) in stroke patients. [Subjects and Methods] Forty-four stroke patients were divided equally into an experimental group that underwent rTMS and a control group that underwent mock rTMS. Changes in patient visual perception, depression, and ADLs were evaluated. All subjects underwent treatment for 20 minutes, 5 times per week, for 4 weeks. Beck Depression Inventory (BDI), Motor-free Visual Perception Test (MVPT) and Functional Independent Measurement (FIM) were respectively used to assess depression, visual perception and ADLs. [Results] The experimental group showed significant improvements in depression, visual perception, and ADLs between week 1 and 4, between week 1 and 8, and between week 4 and 8. Meanwhile, the control group showed no differences between week 1 and 4, and although, like in the experimental group, a significant difference was observed in depression and visual perception between Week 1 and 8, there was no significant difference in ADLs. [Conclusion] These demonstrate that rTMS has a positive impact on visual perception, depression, and ADLs.

Key words: Repetitive transcranial magnetic stimulation (rTMS), Activities of daily livings (ADLs), Visual perception

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INTRODUCTION

Stroke is one of the three leading causes of death in South Korea and its incidence is gradually increasing. Specifically, with a mortality of 48.2 persons per 100,000 population in 2014, stroke was the 3rd most common cause of death¹⁾. In stroke patients, impaired visual perception not only reduces the overall ability to perform activities of daily living (ADLs), but also causes difficulties in differentiating between objects or letters²⁾. Because of the negative effects of unilateral neglect and decreased spatial awareness on overall ADLs, and particularly in dressing, hygiene, movement, independent living, and learning new behaviors, impaired visual perception has a major impact on rehabilitation³⁾. Visual function is crucial for independent ADLs in stroke patients, and restoring normal visual perception has been reported to be an important factor in improving performance of ADLs⁴⁾.

Furthermore, impairments in ADLs can cause stroke patients to experience psychological problems, including depression⁵⁾. Thinking about the difficulty of returning to a pre-injury state tends to make stroke patients avoid society and contact with others⁶⁾. This leads to depressive moods as a result of low self-esteem, lack of energy, and sleeping disorders⁶⁾. Hence, to

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improve independent daily living in stroke patients, it is necessary to take into account psychological factors like depression, as well as perceptual factors, such as visual perception.

Improving depression, visual perception, and performance of ADLs in stroke patients requires changes in neuroplasticity^{4, 7}. One method of inducing changes in neuroplasticity is non-invasive neurostimulation, in which the activity of the neural cortex is controlled by applying stimuli directly to the cortex without surgery^{4, 7}. Representative non-invasive methods include transcranial direct current stimulation (tDCS), which uses direct current electrical stimulation, and repetitive transcranial magnetic stimulation (rTMS), which uses magnetism⁷. rTMS is one of the physical factors used in physical therapy using magnet⁸. rTMS is based on the principle of using a magnetic field formed by a coil to induce depolarization in neurons in a manner similar to conventional electrical stimulation⁷. rTMS, in which TMS is applied in short, repeated bursts, is known to induce changes in the excitability of the cerebral cortex for a certain length of time⁹. Typically, low frequencies less than 1 Hz cause inhibition of the cerebral cortex, and high frequencies greater than 5 Hz increase excitability¹⁰.

When the non-invasive method of rTMS is used in stroke patients, it is effective in improving motor function in the limbs, enhancing cognitive function, reducing depression, and alleviating dysphagia^{7, 9, 10}. Thus, previous studies have shown that rTMS can help in the rehabilitation of stroke patients.

However, few studies have simultaneously investigated the physical function of visual perception, the psychological factor of depression, and the independent rehabilitation indicator of ADL performance. Moreover, no research has evaluated the changes induced by the co-use of rTMS and occupational therapy. Therefore, this study aimed to investigate the impact of rTMS applied to the affected side of stroke patients, on depression, visual perception, and ADL performance.

SUBJECTS AND METHODS

The subjects in this study were patients with a diagnosis of stroke who had been hospitalized between 1st January 2015 and 30th June 2016. Subjects were selected unilateral neglect and a diagnosis of right hemisphere ischemic or hemorrhagic stroke. Patients were excluded from the study if (1) they had severe cognitive impairment that made it difficult to understand instructions; (2) they had seizures, severe head trauma, a metal skull implant, or a pacemaker; or (3) they showed an unstable neurological state. All participants completed a consent form, and the study protocol was approved by an institutional review board (Kaya IRB-159). The general characteristics of the participants are shown in Table 1. There were no differences between the two groups in general characteristics.

For rTMS, we used the STM9000 (Standard, EB-Neuro Inc., Italy), which has been officially approved by the FDA. The rTMS stimulus was targeted at P3, over the left parieto-occipital cortex, and at P4, over the right parieto-occipital cortex. In order to set the motor threshold before stimulation, a cotton cap with a grid ($1 \times 1 \text{ cm}^2$) was fixed to the scalp from the nasion to the inion, a magnetic stimulus was applied to the cranium, and the motor-evoked potentials were measured¹¹. Low-frequency rTMS stimulation was applied to P3 on the left, healthy side, using a 1-Hz stimulus at 90% motor threshold, 4 times, for 5 minutes at a time, separated by 1-minute intervals. High-frequency rTMS was applied to P4 on the right, affected side, using a 5-Hz stimulus at 90% motor threshold, 20 times, for 5 seconds at a time, separated by 55-second intervals. The mock stimulus used the same protocol as low-frequency rTMS, except that the coil was not placed against the skull, and the stimulus was applied in the vertical direction¹². After performing the motor-free visual perception test (MVPT), we selected subjects who met the inclusion criteria. The 44 subjects who met the inclusion criteria were randomly assigned to a group. Over 4 weeks, the subjects received either rTMS or mock rTMS for 20 minutes, 5 times per week. Conventional rehabilitation therapy was performed after the procedure. In addition, both the experimental group and the control group underwent mock rTMS for 5–8 weeks after the experiment. The rehabilitation therapy focused on visuospatial neglect, and was conducted at a difficulty matched to each patient's abilities. All groups were evaluated pre-intervention, post-intervention (4th week of the study), and at 4 weeks post-intervention (8th week of the study). In this study, the Beck Depression Inventory (BDI) was used to evaluate depression, the MVPT was used to evaluate visual perception, and the Functional Independence Measure (FIM) was used to evaluate ADLs.

SPSS 21.0 was used for the statistical analysis of the collected data. Frequency analysis was performed for the subjects' general characteristics, and repeated measure analysis of variance with post-hoc testing was used to compare the intervention effects between the two groups. Statistical significance was tested using a significance level of $\alpha=0.05$.

RESULTS

A summary of the general features of the sample ($n=44$) is provided in Table 1. rTMS had a significant effect on depression, visual perception, and ADLs in the experimental group, and there were also significant differences between the effects in week 1 and week 4, and between the effects in week 4 and week 8 ($p<0.05$). In the control group, there was no difference between the effects in week 1 and week 4. There was a significant difference in depression and visual perception in week 8 compared to Week 1, but there was no significant difference in ADLs ($p<0.05$) (Table 2).

Table 1. The general characteristics of the subjects (N=44)

Categories	Items	Experimental group		Control group	
		N	%	N	%
Gender	Male	18	81.8	13	59.1
	Female	4	18.2	9	40.9
Age (yrs)		52.6 ± 10.6		64.3 ± 11.5	
Paretic side	Left	22	100	22	100
	Right	0	0	0	0
Time since stroke (month)	>12	11	50.0	10	45.5
		8	36.4	8	36.4
Cause of disease	Cerebral infarction	11	50.0	15	68.2
	Cerebral hemorrhage	11	50.0	7	31.8

Table 2. Comparison of depression, visual perception and ADL within control and experimental group after intervention

		1 week	4 weeks	8 weeks	post hoc
		Mean ± SD ^{a)}	Mean ± SD ^{b)}	Mean ± SD ^{c)}	
Experimental group	Depression	25.8 ± 2.3	17.2 ± 3.4	15.5 ± 3.3	a>b,c
	Visual perception	14.9 ± 6.2	24.4 ± 5.1	29.0 ± 5.3*	a<b,c
	ADL	66.6 ± 7.8	78.2 ± 6.1	79.6 ± 6.4*	a<b,c
Control group	Depression	25.5 ± 1.9	23.9 ± 4.1	22.3 ± 5.1	a<c
	Visual perception	15.6 ± 4.4	18.9 ± 6.2	21.4 ± 5.1*	a<c
	ADL	67.2 ± 7.9	69.9 ± 7.6	71.3 ± 7.6	/

*p<0.05

DISCUSSIONS

This study divided 44 stroke patients into an experimental group, that underwent rTMS, and a control group, that did not undergo rTMS. We investigated changes in depression, visual perception, and ADLs in these groups, with the aim of exploring the implications of non-invasive electrical stimulation in occupational therapy for stroke patients.

The advantages of rTMS are the feasibility of local stimulation and non-irritation of the skin⁹⁾. Meanwhile, unlike conventional methods of rehabilitation therapy in patients with brain injury, it induces direct changes in neuroplasticity¹¹⁾. In rTMS, a frequency less than 1 Hz is considered low-frequency, and causes inhibition in the cerebral cortex; a frequency greater than 5 Hz is considered high-frequency, and increases excitation in the cerebral cortex. Hence, this study used low-frequency rTMS, which was also effective at improving visual perception in a study by Kim et al¹²⁾. Moreover, we investigated the effects on depression, visual perception, and ADLs in stroke patients.

In the experimental group in the present study, the depression score of 25.8 ± 2.3 at baseline decreased to 17.2 ± 3.4 in Week 4 following rTMS, and remained lower, at 15.5 ± 3.3, in Week 8, when rTMS was no longer performed. There were significant differences between baseline and Week 4, and between baseline and Week 8. These results are consistent with those of Gray et al.¹³⁾, who reported that rTMS was effective at reducing depressive moods. In that study by Gray et al.¹³⁾, high-frequency rTMS was applied to the dorsolateral prefrontal cortex of a single stroke patient 15 times during a 3-week period, and a decrease in depression was reported. Those results demonstrate that, in addition to the known effects of low-frequency rTMS, high-frequency rTMS also has a positive effect on depression. The present study used MVPT, which is a well-known instrument for evaluating visual perception, and found that the baseline score of 14.9 ± 6.2 in the experimental group increased to 24.4 ± 5.1 after 4 weeks of rTMS. Although scores increased further to 29.0 ± 5.3 by week 8, the difference between week 4 and week 8 was not significant. These results show a pattern similar to unilateral neglect, which is another subdomain of visual perception. For example, when low- and high-frequency rTMS were performed 10 times over 2 weeks in 27 patients, a greater improvement in visual perception was observed in the group that underwent rTMS (Kim et al.)¹²⁾, suggesting that the rTMS used in the present study was effective at improving visual perception. Here, it is thought that low-frequency rTMS affected the excitation of the affected cerebral cortex by inhibiting the unaffected cortex. These results could also be interpreted as low-frequency stimulation causing disinhibition of neurons in the affected area and resulting in relative activation of the unaffected area. The improvement in visual perception and the decrease in unilateral neglect between week 4 and 8 can be considered similar to an increase in the control group. In other words, conventional occupational therapy also has a positive effect on visual perception and unilateral neglect. ADLs were also improved by rTMS, and a study by Emara

et al.¹³⁾ demonstrated the positive effect of 4 weeks of high-frequency rTMS on ADLs. This positive effect was evidenced by improved upper limb function. These results suggest that the positive impact of high-frequency rTMS on ADLs in the present study were mediated by improvements in visual perception.

rTMS had a significant effect on depression, visual perception, and ADLs in the experimental group, and there were also significant differences between the effects in week 1 and week 4, and between the effects in week 4 and week 8 ($p < 0.05$). In the control group, there was no difference between the effects in week 1 and week 4. There was a significant difference in depression and visual perception in week 8 compared to week 1, but there was no significant difference in ADLs ($p < 0.05$). This study has some limitations. The results are difficult to generalize due to the small number of objects, also other factors influencing ADL have not been investigated. Therefore, future studies should investigate a larger number of patients in order to allow generalization of the results, also it should be conducted as a continuous research on a visual perception and improvement of ADL in patients with stroke.

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