ISSN (Print) 1226-1750
ISSN (Online) 2233-6656
Journal of Magnetics 24(4), 770-775 (2019) https://doi.org/10.4283/JMAG.2019.24.4.770

Effects of Action Observation Training with 1 Hz Low Frequency Repeated Transcranial Magnetic Stimulation on Cerebral Cortex Activity and Hand Function in Patients with Ideomotor Apraxia after Stroke

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(Received 14 November 2019, Received in final form 16 December 2019, Accepted 16 December 2019)

The aim of this study was to investigate the effects of action observation training with low frequency repeated transcranial magnetic stimulation (rTMS) on cerebral cortex activity and hand function in patients with ideomotor apraxia after Stroke. Fourteen patients were randomly divided into two groups which in action observation training (AOT) with 1 Hz low-frequency rTMS and AOT without rTMS. Motor evoked potential (MEP) amplitude and latency were examined by TMS for cerebral cortex activity and hand function was evaluated by manual function test (MFT). As a result, there was a significant difference in MEP amplitude in group, but only AOT with rTMS group was a significant difference in MEP latency and MFT. In addition, there was a significant difference of MEP amplitude, latency and MFT between groups. These results suggest that application of AOT and rTMS can have a positive effect on the recovery of hand function in ideomotor apraxia after patients.

Keywords : low frequency repeated transcranial magnetic stimulation, ideomotor apraxia, the motor evoked potential, amplitude, latency, cortical activity

1. Introduction

Most of stroke patients is the damage of the upper motor neurons of the cerebral hemisphere. In addition, sensory, perceptual, cognitive, and motor impairments appear and thus negatively affect functional activities such as activities of daily living (ADLs) [1]. However, unlike upper motor neuron syndromes after stroke, patients ideomotor apraxia (IA) with stroke have difficulty in independent ADLs despite the absence of muscle weakness, sensory loss, abnormal muscle tone, and walking ability. IA is a complex higher-order motor disorder caused by cerebral damage, which does not perform selective movement without damage to the corticospinal pathway [2, 3]. Clinically, IA is mainly seen in the left hemisphere lesion, and the left frontal lobe, parietal lobe damage, and corpus callosum are closely related [4]. In addition, the Wernicke area of the left temporal lobe is associated with the premotor cortex and the primary motor cortex, and the damage to this area is impaired by the ability to comprehend commands. It is accompanied by impaired motor planning and execution ability [5]. Thus, IA patients increase clumsiness in manipulating objects in ADLs and thereby impair their independent on functional activity [1]. Recently, neurorehabilitation based on neuroplasticity has been mainly performed in task-oriented training, which is recognized as a more efficient than traditional approach [6, 7]. Task oriented training focuses on active involvement in task performance rather than intervention by physical and occupational therapist engagements. It's motor learning method that adapts to the environment by providing specific tasks through functional movements in ADLs, focusing on the patient's active participation in task performance rather than intervention by the therapist. In addition, task-oriented training has been proposed as an effective method for restoring physical function by the damaged cerebral cortex in relation to motor and cognitive impairment after stroke on neurorehabilitation [6]. However, patients with IA due to

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impairment of cerebral motor planning and initiation program have many limitations on task-oriented motor learning using tasks. They also have many limitations in task-oriented motor learning using tasks, which are difficult to use the required task due to damage to the cortex area responsible for the motor planning and execution. To overcome these limitations, the newly proposed motor learning is action observation training (AOT) [8, 9]. AOT provides visual information and tactile kinesthetic information using task tools, which can help correct postural orientation and postural stability [10]. However, most of these approaches do not directly change the damaged cerebral cortex, but rather enhance function by promoting neuroplasticity through external stimuli and environmental changes [11]. Recently, to improve these limitations, non-invasive self-stimulation is used. repetitive transcranial magnetic stimulation (rTMS) is used to stimulate cerebral cortex activity by locally magnetic stimulation on specific areas of the cerebrum. This has been suggested as another approach for functional recovery in stroke patients. And using rTMS, it is possible to identify changes in cerebral cortex activity in neurorehabilitation. Transcranial magnetic stimulation (TMS) induces electrical currents in the magnetic field through rapid amplitude, which can lead to depolarization of motor neurons in the cerebral cortex by magnetic coils. In addition, it can be used to evaluate the excitability of cerebral cortex activity through the TMS equipment in clinical practice. 1 Hz low frequency rTMS suppresses the primary motor cortex and the rTMS above 5-10 Hz activates the same motor area. Corpus callosum also plays a key role in mediating U/L movement and coordination of left and right hands by connecting the left and right hemispheres. The interaction between the left and right hemispheres can be explained by transcallosal inhibition (TCI), and the motor threshold of the primary motor cortex can be controlled by magnetic stimulation. Recently, 1 Hz low frequency rTMS in affected hemispheres of stroke patients can increase the MEP amplitude on the primary motor cortex and unaffected hemisphere can decrease the MEP amplitudes in the primary motor cortex. Therefore, low frequency rTMS of unaffected hemispheres in stroke patients may promote U/L function [12]. Fadiga *et al.* (1995) confirmed the excitability of the corticospinal pathway by observing hand movements such as writing and grasping tasks using rTMS. And it suggested to help motivate the process and copy behavior [13]. Based on this previous study, we propose a functional recovery by confirming the excitability of corticospinal pathway in MEP after AOPT with rTMS as a new strategic method to IA patients.

2. Materials and Methods

2.1. Subject

The subjects were selected from 14 patients with ideomotor apraxia after stroke. The criterion for selection was the mini-mental status examination korean version (MMSE-K) with more than 23 patients who could understand the research process and imitate AOT. They had also intact vision and hearing function with a person who can independently perform a manual function test with affected hand.

2.2. Assessment methods

2.2.1. TMS

This study measured the excitability of surface channels using the MAG PRO R30 TMS instrument, which stimulates neurons by generating a strong magnetic field to the subject (Fig. 1). The MAG PRO R30 used in this study was a 70 cm diameter MAG PRO butterfly coil (MCF-B65) stimulator connected to the MagPro R30, which is a non-invasive magnetic stimulation device that generates strong magnetic fields in the electromagnetic coil and passes through the skull. In this study, the motor evoked potential (MEP) of primary motor cortex was measured by low frequency magnetic stimulation and the maximum magnetic field was 2.0 Tesla. The subjects were placed in bed in a straight posture and the head was fixed. Both arms were rotated to the shoulder at an angle of 45 degrees and to the side of the body of the elbow joint at 0 degree. To measure motor threshold, a white hood with coordinates on the subject's head was worn on the scalp. The coordinates of the hood are the center point (Cz) at which the intersection of the midsagittal line and the interaural line connected from the nasion to the inoculum is defined as a center point in the form of a checkerboard. Then, in order to record the resting motor threshold through TMS to the cerebral motor cortex, the coil stimulator was

Fig. 1. (Color online) MagPro R30, Medtronic Inc., Skovlunde, Denmark.

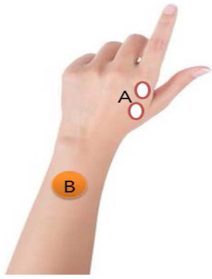

Fig. 2. (Color online) Attached surface electrodes (B) and first dorsal interosseous muscles (FDI) (A).

tangent to the cerebral hemispherical damage side scalp, with the handle pointing backward and at 45 degrees from the center line. In order to measure MEP of the subjects before the study, the first dorsal interosseous muscle (FDI) was attached to the belly tendon montage using electromyographic electrodes the ground electrode was attached to the frontal arm to measure MEP (Fig. 2). Electromyogram (EMG) values were recorded using a mobile KEY POINT.NET instrument and the signal was amplified to 100 mV/div and filtered at 2 Hz to 20 KHz. In order to find the primary motor cortex of FDI, the researcher placed a single stimulus while moving through the central sulcus of the subject while lying through the coil stimulator [14, 15].

2.2.2. Manual function test (MFT)

MFT, which is widely used as a tool to objectively evaluate U/L function in patients with central nervous system injuries such as stroke, traumatic brain injury, and Parkinson's disease, includes U/L movement and grip force It is divided into 8 items and evaluated. Record 1 point for each item check and 0 point if not possible. The total score of the MFT is 32 points. All subjects were performed before and after AOT.

2.3. Procedure

2.3.1. 1 Hz low frequency rTMS and AOT video

1 Hz low frequency rTMS was determined by the same MagPro R30 (Fig. 1), where the highest MEP appears at the recording potential of FDI as the motor cortex area of the muscle. Resting motor threshold is defined as the minimum stimuli intensity at which at least 5 of 10 stimuli are recorded at least 50 μV of MEP, and the intact side with 120 % of motor threshold at 1200 pulses. 1 Hz frequency was applied to the intact cerebral hemisphere for 20 minutes to suppress cerebral motor cortex [16]. The video presented in the AOT was used in the same way as the video and method used in the study by Lee and Kim (2011) [17]. The video consisted of five tasks: brushing, opening the bottle cap, drinking water, turning the bookshelf, and making phone calls. Five videos were taken by dividing the essential functions of daily life task into each task. Each motion was photographed on coronal, sagittal, and horizontal planes, and the subjects were edited so that they could observe the dynamics in three dimensions. AOT videos per task were 10-12 minutes [17].

2.3.2. Training procedures

This AOT was performed 3 times a week for 3 months. The subjects were performed in TMS room where all harmful environments were blocked to maximize the training on motion training through video watching. AOT consisted of five tasks and the subject sat on a chair with a backrest and watched the motion observation video played on the monitor through a computer on the desk. AOT video was reproduced at a normal speed at first, then at a speed twice as slow as the second. The third was regenerated at normal speed and observed [17]. Approximately 15 minutes of AOT per task was played and after watching the motion, the subjects imitated the task training like video and practiced the task by using one hand or two hands according to each task. The therapist intervened as needed during task training.

2.4. Data Analysis

This study used the SPSS 22.0 program for windows. Descriptive statistics were used for Mean and standard deviation of age and duration in general characteristics of subjects. The Mann-Whitney U test was used to determine the MEP amplitude, MEP latency, and MFT before and after intervention in the groups. Wilcoxon signed rank test was performed to determine the difference of MEP amplitude, MEP latency, and MFT between the groups. All statistical analyzes were performed at $\alpha = 0.05$ significance level.

3. Results

3.1. General Characteristics of Subjects

AOT with rTMS group was 4 males, 3 females, and 7 patients. The mean age was 60.57 years old. AOT group was 3 males and 4 females, and the mean age was 61.42 years (Table 1).

3.2. Comparison of MEP amplitude, latency before and after interventions in two group

The comparison of MEP amplitude changes in AOT with rTMS group showed a significant increase ($p < 0.05$) before and after the intervention with an evaluation of

Table 1. General characteristics of subjects.

Variables		AOT with rTMSG (N=7)	AOTG (N=7)
Gender	Male	4	3
	Female	3	4
Age		60.57±6.97	61.42±8.62
Lesion type	Hemorrhage	3	2
	Infarction	4	5
Time from stroke to rehabilitation (months)		13.43±4.66	14.71±5.56

M ± SD: M: mean, SD: standard deviation, AOT: action observational therapy, rTMSG: repetitive transcranial magnetic stimulation group, AOTG: action observational therapy group.

0.35 mV at 0.12 mV before and after intervention. In comparison with the change in MEP latency, there was a significant decrease ($p < 0.05$) before and after mediation from 25.87 ms to 22.33 ms after intervention (Table 2). The comparison of MEP amplitude change in AOT groups, significant increase was observed between 0.14 mV before intervention and 0.23 mV after intervention ($p < 0.05$). In comparison with the change in MEP latency, there was reduced from 24.99 ms before intervention to 23.77 ms after intervention and then decreased to 1.22 mV. There was no significant difference (Table 2).

3.3. Comparison of MFT before and after intervention in groups

In the comparison of MFT changes, AOT with rTMS group showed significant increase from 24.57 points before intervention to 26.00 points after intervention ($p < 0.05$) (Table 3). In the MFT comparison of AOT group, there was no significant difference between before and after intervention from 22.71 points to 23.43 points ($p > 0.05$) (Table 3).

3.4. Comparison of MEP amplitude, latency and MFT before and after intervention between two groups

As shown in Table 4, there was significantly difference in the comparison of MEP amplitude and MEP latency after intervention between the two groups ($p < 0.05$) (Table 4).

Table 2. Comparison of MEP amplitude, MEP latency before and after intervention in the groups.

Variables		Pre-test	Post-test	*z*	*p*
		M±SD	M±SD		
AOT with rTMSG (N=7)	MEP amplitude (mV)	0.12±0.03	0.35±0.07	-2.366	.018*
	MEP latency (ms)	25.87±1.15	22.33±0.85	-2.384	.017*
AOTG (N=7)	MEP amplitude (mV)	0.14±0.05	0.23±0.05	-2.366	.018*
	MEP latency (ms)	24.99±1.03	23.77±1.36	-2.366	.128

*p < .05, M±SD M: mean SD: standard deviation, MEP: motor evoked potential, AOT: action observational therapy, rTMSG: repetitive transcranial magnetic stimulation group, AOTG: action observational therapy group.

Table 3. Comparison of MFT before and after intervention in the groups.

		Pre-test	Post-test	*z*	*p*
		M±SD	M±SD		
MFT (score)	AOT with rTMSG (N=7)	24.57±1.99	26.00±1.58	-2.236	.025*
	AOTG (N=7)	22.71±1.22	23.43±1.1	-1.890	.059

*p < .05, M±SD M: mean SD: standard deviation, MFT: manual function test, AOTG: action observational training group, rTMSG: repetitive transcranial magnetic stimulation group.

Table 4. Comparison of MEP amplitude and MEP Latency between two groups.

		AOT with rTMSG (N=7)	AOTG (N=7)	*z*	*p*
		M±SD	M±SD		
MEP amplitude (mV)	Pre-test	0.12±0.03	0.14±0.05	-.836	.40
	Post-test	0.35±0.07	0.23±0.05	-2.366	.02*
MEP latency (m/s)	Pre-test	25.87±1.15	24.99±1.03	-1.354	.18
	Post-test	22.19±0.93	23.77±1.36	-2.111	.04*

*p < .05, M±SD M: mean SD: standard deviation, MEP: motor evoked potential, AOT: action observational therapy, rTMSG: repetitive transcranial magnetic stimulation group, AOTG: action observational training group.

Table 5. Comparison of MFT between two groups.

		AOT with rTMSG (N=7)	AOTG (N=7)	*z*	*p*
		M±SD	M±SD		
MFT (score)	Pre-test	24.57±1.99	22.71±1.25	-1.746	.081
	Post-test	26.00±1.58	23.43±1.10	-2.522	.012*

*p < .05, M±SD M: mean, SD: standard deviation, MFT: manual function test, AOT: action observational therapy, rTMSG: repetitive transcranial magnetic stimulation group, AOTG: action observational training group.

3.5. Comparison of results between two groups

As shown in Table 5, there was significantly difference in the comparison of MFT after intervention between the two groups ($p < 0.05$) (Table 5).

4. Discussion

In neurorehabilitation, various approach have been introduced as a method of restoring hand function of stroke patients, and AOT is being implemented as a new therapeutic strategy approach. neurorehabilitation approach including AOT, can be explain that external stimuli through somatosensory feedback affects neuroplasticity of the cerebral cortex, and as a result, it is expected to recover of the damaged the cerebral cortex. Recently, with the development of medical magnetic technology, TMS is newly introduced in various neurorehabilitation. TMS generates a magnetic field within a short time and turns into an electric field within the tissue, which effectively activates nerve cells in the cerebrum, as the electric field waves cause depolarization of nerve cells located in the cerebral cortex. Cerebral cortex activity can regulate UMNs according to magnetic stimulation intensity and frequency. Low frequency rTMS below 1 Hz can more safely and effectively suppress abnormally active motor neuron areas, and high frequency rTMS above 5 Hz can damage nerve cells in the injured cerebral hemisphere. It has the advantage that it can be activated more easily. rTMS can also be easily applied to localized areas without causing pain in stroke patients [18]. This low frequency rTMS can activate the primary motor cortex, which can more accurately identify changes in cerebral cortex with MEP amplitude and MEP latency obtained from TMS. The purpose of this study was to examine the differences in cerebral cortex and hand function and 1 Hz low frequency rTMS was applied to the primary motor cortex of unaffected hemisphere 3 times a week for 3 months in patients with chronic stroke. At the same time, we compared the differences in intervention protocols with changes in cerebral cortex and hand function, compared with the AOT with rTMS and AOT without rTMS. As a result, both AOT with rTMS and AOT reduced MEP amplitude and decreased MEP latency due to stroke, which can be thought to increase the excitability of the corticospinal pathway, which contributed to the damaged primary motor cortex. The comparison between the two groups confirmed that rTMS and AOT interventions were more effective. Injured side cerebral hemispheres in stroke patients show higher threshold values for cerebral activity, lower amplitude, and delayed latency [19]. It is very important to change the motor threshold of brain activity to restore hand function. Therefore, the combination of rTMS and AOT for the enhancement of brain activity is very important in promoting functional activity by activating damaged cerebral hemispheres in a short time. In this study, MFT was performed to investigate the changes of hand function which is that consists of motor, grasp and manipulation components in hand. As a result of this study, it was confirmed that there was a significant difference after the intervention between two group. It is thought that the combination of rTMS and AOT can effectively change the excitability of the cerebral motor cortex in neurorehabilitation after stroke. Recently, various task-oriented training has been applied for reactivation of cerebral motor cortex. Especially, repetitive performance of tasks that give meaning to subjects is positive for neurological changes in the cerebral cortex. However, IA after stroke have difficulty in handling the tools and they are limited in performing task training. they have characteristic damages to intraparietal sulcus, superior parietal lobule, and superior temporal sulcus [20]. In previous studies, low frequency rTMS for 5 days helped to restore the U/L function after brain damages. This suggests that low frequency rTMS positively supports cerebral cortex activity [21]. In addition, it can be a positive aid for neurorehabilitation and motor learning, including magnetic stimulation for effective cerebral cortex and restoring hand function [22]. Lastly, the study showed that the primary motor cortex was found to have increased activation with non-invasive low frequency rTMS in the cerebral intact area, as well as generalized rehabilitation for restoring hand function. It is expected that the cells can be activated and give a positive result and can be used as an important basis for restoring hand function.

5. Conclusion

The purpose of this study was to investigate the activity of the cerebral cortex and hand function before and after intervention between AOT with rTMS group and AOT group. in 12 patients with stroke. As a result, there was a significant difference in the MEP amplitude in two groups, but only in AOT with rTMS group in the MEP latency and MFT. In addition, the two groups showed significant differences in both MEP amplitude, MEP latency and MFT. Based on these results, it is considered that neurorehabilitation program including low frequency rTMS should be actively used for restoring hand function in patients with IA after stroke.

Acknowledgements

This study was supported by 2017 Research Grant from Kangwon National University (No. 620170145).

References

[1] V. Pomeroy, S. M. Aglioti, V. W. Mark, D. McFarland, C. Stinear, S. L. Wolf, M. Corbetta, and S. M. Fitzpatrick, Neurorehabil Neural Repair **25**, 33 (2011).
[2] R. C. Rguarda and C. D. Marsden, Brain **123**, 860 (2000).
[3] L. A. Wheaton and M. Hallett, J. Neurological Sciences **260**, 1 (2007).
[4] B. Hanna-Pladdy, K. M. Heilman, and A. L. Foundas, Brain **124**, 2513 (2001).
[5] K. M. Heilman, L. J. Rothi, and E. Valenstein, Neurology **32**, 342 (1982).
[6] B. H. Dobkin, Nat. Clin. Pract. Neurol. **4**, 76 (2008).
[7] C. J. Winstein and S. L. Wolf, Stroke recovery and rehabilitation, Demosmedical, New York (2008) pp 267-306.
[8] L. Cattaneo and G. Rizzolatti, Arch. Neurol. **66**, 557 (2009).
[9] G. Rizzolatti and L. Craighero, Annu. Rev. Neurosci. **27**, 169 (2004).
[10] J. S. Frank and M. Earl, Phys. Ther. **70**, 855 (1990).
[11] C. I. Park and J. H. Moon, Rehabilitation Medicine. Hanmi-book, Seoul (2007) pp 407-460.
[12] S. R. Ma, M. S. Han, and B. K. Song, J. Magn. **22**, 696 (2017).
[13] L. Fadiga, L. Fogassi, and G. P. Rizzolatti, J. Neurophysiol **78**, 2608 (1995).
[14] P. A. Rossini, A. T. Barker, A. Berardelli, M. D. Caramia, G. Caruso, R. O. Cracco, M. R. Dimitrijević, M. Hallett, Y. Katayama, C. H. Lücking, A. L. Maertens de Noordhout, C. D. Marsden, N. M. F. Murray, J. C. Rothwell, M. Swash, and C. Tomberg, Electroenceph. Clin. Neurophysiol **91**, 79 (1994).
[15] R. Traversa, P. Cicinelli, M. Oliveri, M. G. Palmieri, M. M. Filippi, P. Pasqualetti, and P. M. Rossini, Clin Neurophysiol **111**, 1695 (2000).
[16] P. M. Rossini, A. T. Barker, A. Berardelli, M. D. Caramia, G. Caruso, R. Q. Cracco, and A. M. De Noordhout, Electroencephalogr. Clin. Neurophysiol **91**, 79 (1994).
[17] M. L. Lee and J. M. Kim, Kor. J. Neuro. Rehab. **1**, 51 (2011).
[18] M. K. Sohn, J. H. Moon, J. W. Song, and D. S. Park, J. Korean Acad. Rehabil. Med. **15**, 278 (1991).
[19] P. M. Rossini and F. Pauri, BrainRes. Rev. **33**, 131 (2000).
[20] S. H. Johnson-Frey, R. Newman-Norlund, and S. T. Grafton, Cereb Cortex **5**, 6 (2004).
[21] F. Fregni, P. S. Boggio, and A. Pascual-Leone, Stroke **37** 2115 (2006).
[22] N. Takeuchi, T. Tada, M. Toshima, T. Chuma, Y. Matsuo, and K. Ikoma, J. Rehabil. Med. **40**, 298 (2008).