Effects of Hand Intrinsic Muscle Facilitation and Functional Task Training on Cerebral Motor Evoked Potential after 1 Hz Low-Frequency rTMS in Stroke Patients

Sung-Ryoung Ma[1] and Bo-Kyoung Song[2]*

[1]Department of Occupational Therapy, Shinsung University, Dangjin-si 31001, Republic of Korea
[2]Department of Occupational Therapy, Kangwon National University, Samcheok-si 245710, Repubilc of Korea

The purpose of this study was to investigate the effects of hand intrinsic muscles facilitation and functional task training with 1 Hz repetitive transcranial magnetic stimulation (rTMS) on cerebral motor cortex activity in stroke patients and to investigate the effectiveness of stroke rehabilitation. In this study, 20 adult stroke patients were randomly selected and divided into two groups of 10 each other. In the experimental group, hand intrinsic muscles facilitation and functional task training were performed after 1 Hz low frequency for 20 minutes and simple upper limb task training was performed in the control group. To investigate the changes of cerebral motor cortex activity after intervention, we measured Motor evoked potential (MEP) amplitude and latency. In both groups, MEP amplitude increased and MEP latency decreased after intervention. There was a significant difference between the two groups in MEP amplitude and latency ($p < 0.01$) ($p < 0.05$). Therefore, hand intrinsic muscles facilitation and functional task training with 1 Hz low frequency (rTMS) of stroke patients showed positive results in MEP amplitude and latency change of the injured cerebral cortex after stroke.

Keywords : low frequency repetitive transcranial magnetic stimulation, motor evoked potential amplitude, motor evoked potential latency, hand intrinsic muscles facilitation

1. Introduction

Stroke is characterized by neurological deficits in sensory, cognitive, language, and motor functions due to cerebral vascular hemorrhage or cerebral ischemia, resulting in weakness of the body [1, 2]. Muscle weakness that occurs in stroke patients is the most common motor dysfunction [3, 4], which affects upper limb motor deficits in 75% of stroke patients [5, 6]. Therefore, one of the most important factors determining the prognosis of stroke can be the index of recovery of motor function [7]. The functional imbalance within the motor system following stroke [7] can be due to damage of the white axonal tracts connecting brain motor areas [8]. In particular, damage to the lateral corticospinal tract leads to disruption of the opposite upper limb and hand movement [9]. It is involved in selective movement, such as finger, face and toe movements, which affect the mobility and dexterity of the distal part of body [10]. Recently, various rehabilitation approaches have been introduced to improve upper limb motor function of stroke patients. Especially repetitive transcranial magnetic stimulation (rTMS) was introduced as a therapeutic modality for post-stroke upper limb hemiparesis [11, 12]. TMS utilizes the principle of generating a magnetic field in a short time after the electromagnetic coil is placed on the outer skin of the head and causing depolarization of the neuron located in the cerebral cortex when the electromagnetic field wave in the tissue reaches the appropriate intensity and time [13, 14]. For example, stimulation of the primary motor cortex (M1) can cause muscle activation as MEP, which is recorded by electromyography [15]. rTMS is also used to assess the residual function of the lateral corticospinal tract after stroke [16]. MEP using TMS have the advantage on evaluation of motor nerve pathway directly by stimulating the pyramidal neurons of the cerebral cortex [17].

Recently, it has been reported that rehabilitation using various approach together with rTMS have a positive effect on improvement of upper limb motor function in stroke patients. Lefaucheur et al. (2014) reported that low-frequency rTMS and hand focused occupational therapy were applied to non-injured patients in chronic stroke

patients, which positively affected motor recovery of upper limb [11, 12]. Based on previous study, we tried to confirm the difference on motor recovery of upper limb by applying the treatment program to recover the intrinsic muscle and task performance for improve hand strength of stroke patients after applying rTMS. Hand intrinsic muscles are not directly involved in the finger flexion, but are important for performing precise grip of the hands. In particular, lumbricals and interossei muscles play an important role in creating hand shapes and creating appropriate forces for various objects shapes [18]. In addition, Carr and Shepherd (2003) suggested that among the various functional tasks applied to patients with stroke, task activities that can improve actual daily activities can be an effective treatment [19]. In this study, we investigated the motor evoked potential amplitude (MEP amplitude) of impaired cerebral motor cortex of stroke patients after applying 1 Hz low frequency MEP amplitude and motor evoked potential latency (MEP latency) to determine the effect on cerebral activity in stroke patients.

2. Theoretical Background

2.1. Principles of TMS

TMS is a brain stimulation method that non-invasively stimulates the cerebral cortex safely and effectively, with little or no pain, due to the fact that it is not weakened by strong resistance such as the skull or scalp and does not form a strong current density [20].

The effect of TMS is different depending on stimulation. A single pulse TMS depolarizes and discharges the cerebral cortex under stimulation points. For example, stimulating the primary motor cortex (M1) can cause MEP to be recorded with electromyography (EMG) [21]. In addition, rTMS, which repeats the stimulation rather than the single stimulus, causes a long lasting effect beyond the initial stimulation period. Therefore, rTMS may increase or decrease excitability to the cortical spinal cord depending on electromagnetic wave, the strength of the stimulus, the direction and frequency of the coil. The mechanism of action of rTMS is presumed to induce a similar synaptic efficacy change in relation to long-term potentiation and long-term depression. rTMS is divided into high frequency and low frequency depending on frequency. A high frequency of 5 to 20 Hz increases the response of the cerebral cortex, which can be seen to decrease the MEP threshold. Low frequency stimuli also stimulate below 1 Hz or at the same frequency, resulting in suppression of cortical responses [22].

In a previous study on the duration effect of TMS, the low-frequency rTMS stimulation showed a 31 - minute duration effect of stimulation when the stimulus intensity was 80-110 % of the motor threshold [23].

2.2. Transcallosal inhibition (TCI)

Neurons mediating transcallosal inhibition (TCI) are likely located in the primary motor area (M1) and project across the corpus callosum to exert their effect by exciting inhibitory interneurons locally in the M1 of the contralateral hemisphere. According to the TCI, in a normal state, both cerebral hemispheres regulate and compete with the opposite cerebral hemispheres, respectively [24].

3. Method

3.1. Subject

The study included adult stroke patients admitted in the department of rehabilitation medicine. A total of 20 patients were selected according to the criteria of the study and randomly assigned to each group. The subjects used a randomization to draw a numbered table in the box. The selection criteria of the subjects are as follows. Patients who were diagnosed with stroke through computed tomography (CT) or magnetic resonance imaging (MRI), patients who had been over 6 months of stroke, and volunteers Patients were selected. Patients with aphasia, cognitive impairment, unilateral neglect, visual field defect, or psychiatric or orthopedic disease were excluded.

3.2. Intervention methods

The selected 20 patients were randomly divided into two groups. Low frequency rTMS, hand intrinsic muscle facilitation, and functional task training were performed

Table 1. Introduction of an intervention program applied to both groups.

Experimental group	Control group
1. Low frequency rTMS (20 min)	Functional task program
– 1 Hz, 1200 pulse, 120% MT	(40 min)
2. Hand intrinsic muscle Facilitation	– Grip the cup
(10 min)	
– Specific activation of lumbricals	– Press a computer keyboard
– Specific activation of abductor digiti minimi	– Grip the small ball
– Specific activation of thenar eminence	– Move the stoking cone
3. Task application (10 min)	– ROM arc exercise
– Grip the cup	
– Press a computer keyboard	
– Grip the small ball	

in the experimental group and only five upper task programs were administered to the control group except the low frequency rTMS (Table 1). In both groups, 5 sessions per week and 40 sessions per session were equally intervened and two before and after evaluations were performed.

3.2.1. Low frequency recurrent cranial magnetic stimulation and motor evoked potentials

In this study, MagPro R30 was used to apply low frequency rTMS (Fig. 1). The MagPro R30 used in this study was a 70 cm diameter MagPro 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 MEP of primary motor area was measured by low frequency magnetic stimulation and the maximum magnetic field was 2.0 Tesla. The subject was measured in a supine position on the bed. In order to evaluate the motor evoked potential threshold in the first step, the hood was worn on the head so that the coordinate point stimulating the head of the subject could be easily found. The handle was positioned at a 45 degree angle from the centerline in the

Fig. 2. (Color online) Attached surface electrodes: first dorsal interosseous.

tangential direction of cerebral hemisphere. The first dorsal interosseous (FDI) was measured in order to measure MEP of the cerebral hemispheres, with the knobs tangential to the head of the cerebral hemisphere and at an angle of 45 degrees from the center line (Fig. 2). Before starting the intervention, a silver chloride electrode was attached to FDI and a ground electrode was attached to the arm to measure the EMG value. EMG values were recorded using mobile KEY POINT®.NET software. The signals were amplified to 100 mV/div and then filtered at 2 Hz to 10 KHz. The point at which the largest MEP appears at the recording potential of FDI is judged to be the motor cortical area of the corresponding muscle. The resting motor threshold was defined as the minimum stimulation intensity at which MEP greater than 50 µV was recorded at least 5 times during 10 times of stimulation. In addition, 1,200 pulses were applied to the cerebral hemispheres of the unsponsored cerebral hemispheres at a frequency of 1 Hz for 20 minutes to inhibit cerebral motor cortex at the level of 120% of the exercise threshold [23].

3.2.2. Hand intrinsic muscle facilitation and functional task training program in experimental group

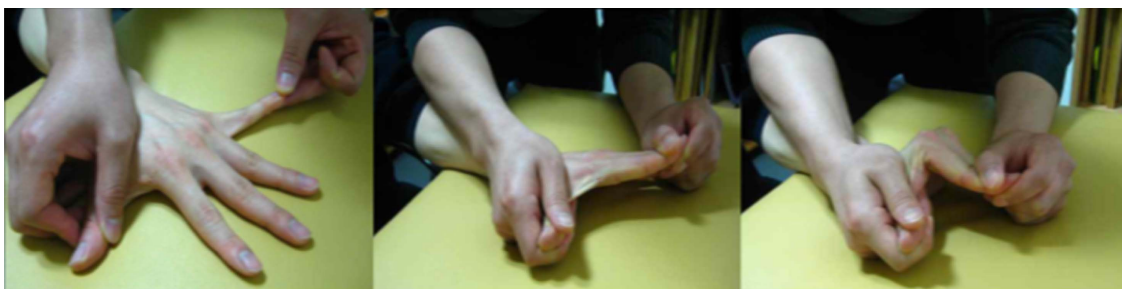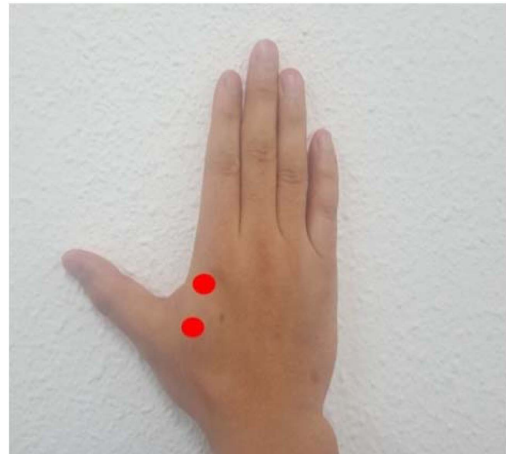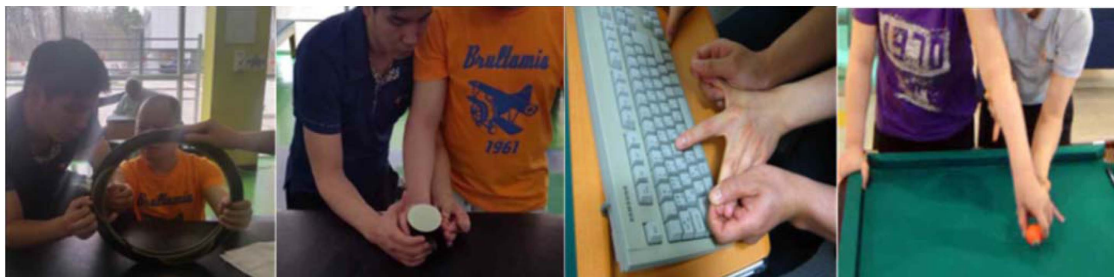**Fig. 1.** (Color online) MagPro R30, Medtronic Inc., Skovlunde, Denmark.

Fig. 3. (Color online) Specific activation of lumbricals, abductor digiti minimi and thenar eminence muscles.

Fig. 4. (Color online) Specific functional activation as grip the cup, press a computer keyboard and grip the small ball.

This study, hand intrinsic facilitation and functional task training program were modified according to the target program by referring to the task application program of Ma and Yang (2018) and Sue Raine's (2013) [24, 17]. The hand intrinsic facilitation programs consisted of specific activation of lumbricals, abductor digiti minimi and thenar muscles as hand intrinsic muscles (Fig. 3). The functional task training program consisted of grip the cup, press a computer keyboard, and grip the small ball in hand and upper limb (Fig. 4).

3.2.3. Functional task program in control group

Control group intervened for 40 minutes in all five tasks such as grip the cup, press a computer keyboard, grip the small ball, moving the stocking cone, and range of motion exercise and arc exercise applied in control group.

3.3. Assessment methods

3.3.1. Evaluation of amplitude and latency of cerebral motion evoke potentials

The amplitude and latency of cerebral MEP were measured in the same manner as rTMS using MagPro R30 (Mag-Venture, Farum, Denmark) for low frequency rTMS (Fig. 1).

3.4. Statistical analysis

The results of the collected data were analyzed using SPSS 18.0 program for Windows (IBM Corp., Armonk, NY, USA). The descriptive statistics and the frequency analysis were performed for the general characteristics of the subjects. The data collected through the research showed that all the variables were distributed normally. In order to investigate the differences in treatment effects between before and after the group, a corresponding sample paired t-test was conducted and an independent sample t-test was performed between the groups. The statistical significance was $\alpha = 0.05$.

4. Results

4.1. General characteristics of subjects

The general characteristics of the experimental, control subjects are shown in (Table 2).

4.2. Comparison of effects before and after intervention in experimental group

In comparison of changes in MEP amplitude of experimental group, there was a significant increase ($p < 0.001$) before and after intervention from 0.129 mV before intervention to 0.329 mV after intervention. There was also a significant decrease ($p < 0.001$) in pre and post intervention intervals ($p < 0.001$) between the pre-intervention evaluation and the intervention evaluation at 27.36 ms and 23.79 ms, respectively (Table 3).

Table 2. General characteristics of subjects.

Variables		EG (N=10)	CG (N=10)
Gender	Male	7	6
	Female	3	4
Age		43.90 ± 6.67	44.80 ± 5.24
Lesion type	Hemorrhage	6	7
	Infarction	4	3
Lesion side	Right	5	6
	Left	5	4
Time from stroke to rehab (months)		24.10 ± 5.99	23.40 ± 6.94

M ± SD M: mean SD: standard deviation, EG: experimental group, CG: control group

Table 3. Comparison of results before and after with experimental group.

	Pre-test	Post-test	
	M ± SD	M ± SD	p
MEP amplitude (mV)	0.129 ± 0.00	0.329 ± 0.02	.000[***]
MEP latency (ms)	27.36 ± 2.83	23.79 ± 1.81	.001[***]

***$p < .001$ M ± SD M: mean SD: standard deviation

Table 4. Comparison of results before and after with control group.

	Pre-test	Post-test	p
	M ± SD	M ± SD	
MEP amplitude (mV)	0.120 ± 0.10	0.296 ± 0.17	.000***
MEP latency (ms)	28.91 ± 3.02	27.10 ± 3.54	.002**

**p < .01, ***p < .001 M ± SD M: mean SD: standard deviation

Table 5. Comparison of cerebral activity before and after intervention between two groups.

	EG (N=10)	CG (N=10)	p
	M ± SD	M ± SD	
MEP amplitude (mV)	0.200 ± 0.01	0.176 ± 0.02	.010**
MEP latency (ms)	−3.56 ± 2.27	−1.81 ± 1.31	.049*

*p < .05, **p < .01 M ± SD M: mean SD: standard deviation, EG: experimental group, CG: control group

4.3. Comparison of MEPs amplitude and MEPs latency before and after intervention in control group

In the comparison of changes in MEPs amplitude of CG, pre-intervention evaluation 0.120 mV and post intervention evaluation 0.296 mV showed a significant increase (p < 0.001) before and after intervention. There was also a significant decrease (p < 0.01) in pre and post-intervention interventions (28.91 ms, 27.10 ms) in the comparison of changes in MEPs latency (Table 4).

4.4. Comparison before and after intervention between two groups

As a result of comparing before and after intervention, the MEP was 0.200 mV for experimental group and 0.176 mV for control group, which was statistically significant (p < .01) before and after intervention compared to control group respectively. The MEPs latency was −3.56 ms in experimental group and −1.81 ms in control group. The experimental group showed a statistically significant decrease (p < .05) before and after intervention compared to control group (Table 5).

5. Discussion

Stroke rehabilitation is to acquire a way to compensate for the patient's disability through the process of learning and adaptation. In addition, a variety of rehabilitation approaches have been proposed in order to improve the functioning of the patients by continuously training their functional tasks according to the patient's level. Previous stroke rehabilitation did not directly change the brain, which is the cause of the lesion. Most of the rehabilitation was to enhance neuroplasticity through proper external

stimulation and environmental changes [27].

Recently, rTMS has been applied in stroke rehabilitation to apply hand therapy or goal-oriented tasks together. Kakuda *et al.* (2011) reported a reduction in muscle tone and an improvement in upper limb motor by applying task training after 15 days of rTMS in stroke patients with upper limb stiffness [28]. In this study, the amplitude and latency of the MEP amplitude of the injured cerebral cortex in stroke patients were evaluated by applying rTMS and hand therapy and tasks based on the previous studies. The results were as follows. First, there was a statistically significant increase before and after intervention between groups. Therefore, the intervention methods of the experimental group and control group were found to be effective in increasing the amplitude of MEP amplitude and decreasing MEP latency time. Second, the experimental group was statistically significantly higher than the control group in the latency of the MEP amplitude and MEP latency. These results suggest that transcallosal inhibition (TCI), hand therapy and application of TMS have a positive effect on cerebral activation. TCI is explained by the theory that both cerebral hemispheres regulate and compete with each other in the normal brain. Control and competition of the cerebral hemispheres are inhibited by TCI through the corpus callosum in the lobe of the brain because they control each other [24]. However, as with stroke patients, damage to one hemisphere leads to imbalance of cerebral cortical activity between the two cerebral hemispheres and impaired cerebral hemispheres receive strong inhibition from the unsponsored cerebral hemisphere, negatively affecting motor performance give. [29]. In this study, low - frequency rTMS was applied to the unaffected cerebral hemisphere to improve the MEP by reducing the unaffected cortical activity and activation of the affected cerebral hemisphere based on TCI. In addition, it is suggested that the impaired upper limb has a positive effect on the cerebral motor cortex by promoting the motor function and task performance by applying the hand intrinsic muscle facilitation and functional task training.

MEP is related to the excitability of the cerebral cortex, which means that the MEP is not induced during magnetic stimulation, which means that the nerve cell or nerve stem is dead or has a very high motor threshold and the positive impact of training [25]. In previous studies, the TMS evaluation of the primary motor area of the cerebral cortex reported that patients with higher MEP in the affected upper limb muscle within 30 days of stroke were more likely to recover function than those with lower MEP [30].

Stroke patients are delayed in MEP latency because of a decrease in the number of pyramidal neurons, an increase

in temporal dispersion, a slower activity in the pyramidal nerve cell group of the affected motor cortex, a premotor cortex, The slow activity of the corticospinal tract of the supplementary motor cortex, the slow regeneration of slow activity in invading muscles, and the contribution of nerve fibers with slow conduction from the unaffected cerebral hemisphere [31, 14]. In conclusion, the decrease in the latency of the MEP latency in this study may be an index to predict the improvement of the motor ability by inducing the MEP more rapidly. Traversa *et al.* (2000) reported that a gradual decrease in the MEP latency period was accompanied by clinical improvement and a similar trend in patients with subacute stroke. A shorter incubation period can be expected in patients with chronic stroke who have differences due to differences in each individual, but whose functional status is relatively good [14, 32]. In order to improve the upper limb motor function of stroke patients, the proposed intercostal cranial magnetic stimulation, intervention of hand training and functional task training improves MEP in affected cerebral cortex, which may cause neuroplasticity. This study is limited in that it is difficult to generalize the results due to few subjects and cannot measure the change of motor function. In addition, there was no investigation of the stimulation time of the TMS duration of the after effect. This study is limited in that it is difficult to generalize the results due to the small number of subjects and the change of motor function of the subject cannot be measured.

6. Conclusions

This study showed that the residual effect of 1 Hz rTMS during 20 min and the application of the hand intrinsic muscle facilitation to the task decreased the motor - induced latency and the latency of motor - induced latency in the injured cerebral cortex. This study showed that the improvement of the MEP amplitude and MEP latency in the affected cerebral cortex were significantly reduced by the functional task training and hand intrinsic muscle facilitation after the low frequency rTMS. Recently, a variety of rehabilitation intervention methods have been applied to improve the motor function of stroke patients. rTMS and simultaneous hand therapy and functional task training can help improve damaged brain function. They may improve neurophysiological and kinematic functions and may be an effective approach for stroke patients with impaired motor function.

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