ISSN (Print) 1226-1750
ISSN (Online) 2233-6656
Journal of Magnetics 22(4), 702-708 (2017) https://doi.org/10.4283/JMAG.2017.22.4.702

Effects of Cerebral Cortex Activation on Bimanual Task Training with and without Dominant Hand for Chronic Stroke Patients Using Transcranial Magnetic Stimulation

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(Received 24 November 2017, Received in final form 19 December 2017, Accepted 20 December 2017)

The purpose of this study was to investigate the effect of cerebral cortex activation on bimanual task training in chronic stroke patients with or without dominant hand injury using transcranial magnetic stimulation. This study was performed on 26 chronic stroke patients who was performed the bimanual task training such as that are easy to use in daily task by dividing dominant hand affected group (n=13) and non-dominant hand affected group (n=13). To evaluate the cerebral cortical activity before and after training, we measured transcranial magnetic stimulation as the motor evoke potentials (MEP's). There were differences in cerebral cortical activation between the treatment period and groups in the bimanual task training according to presence or absence of dominant hand on the impaired side. For the effective cerebral cortex activation of stroke patients, it is necessary to select appropriate bimanual task training according to the presence of the damaged side and dominant hand, and to take into consideration the difference in the characteristics of the right and left cerebral hemispheres acting on the motor function.

Keywords : stroke, transcranial magnetic stimulation, motor evoke potentials, bimanual task training, cerebral cortex activation

1. Introduction

Stroke is a disorder that causes central nervous system damage due to cerebrovascular injury and is often associated with impaired motor function [1]. Loss of motor function results in decreased spontaneous muscle contraction of motor neurons and weakness, spasticity, fractionate movement ability, and higher-order planning deficit. In addition, the upper motor command planning disorder is characterized by primary motor cortex (PM), somatosensory cortex (SM), secondary sensory motor cortex, subcortical structure and corticospinal tract [2]. In particular, damage to the corticospinal tract results in hemiplegia, because 75-90 % of the corticospinal tract dominates the opposite side of the body [3]. Statistically, 45 % to 50 % of stroke patients have right hemiplegia, and 69 % of the patients develop motor impairment of the upper limb. And approximately 39 % of patients reported recovery of upper limb function [4]. On the other hand, about 65 % of stroke patients showed restoration of function of the lower limb and 15 % or less of patients showed complete recovery of function [5, 6]. This suggests that the impairment of motor function due to stroke is more damaging to the upper limb motor function than the lower limb. The use of human hands is one of the most important factors in individual functional activity, which plays an important role not only in ADL's but also in occupational and leisure activities [7]. Especially, in various self-care activities such as scissors, clothes, food cutting, grooming, and toileting, both hands are used simultaneously for effective task [8, 9]. A dominant hand is a hand that is used predominantly in performing a task such as ADL's and the motor function of the cerebral hemispherical cortex is asymmetrically developed depending on the characteristics of the dominant hand [10]. The asymmetrical development of the individual is explained by the cerebral laterality as the strengthening of the phenomenon that dominantly uses the dominant hand.

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The dominant hand was reported to be in right hand use in 80 % of normal subjects [11, 12]. In various task activities using both hands, dominant hand performs delicate manipulation and non-dominant hand plays a role to stabilize task [13]. In fact, the damage to the corticospinal tract of hemiplegic patients after stroke has resulted in hand dysfunction of the upper limb [3]. These results lead to frustration due to limitation of the use of hand function in the daily task performance of the patient and psychological and physical pain caused by it, resulting in poor motivation of the patient and difficulty in performing the function. Most stroke patients should use both hands to perform routine tasks. However, due to the muscle weak and the decrease of the agility on affected hand, most of the daily tasks are performed with the non-affected hands, which cause problems in the accuracy and efficiency of the task.

Dominant hand of human is crucial to the efficiency and accuracy of activities of daily living and leisure activities. In addition, the damage of the dominant hand is an important factor for upper limb rehabilitation. This is because the predominant hand dominates the accuracy and speed of the task execution compared to the non-dominant hand, so the presence or absence of the dominant hand is important for the recovery of the movement [14]. As a consequence, different motor learning effects of dominant hand and non-dominant hand may have a positive effect on recovery of upper limb stroke, taking into consideration the dominant characteristics of cerebral hemisphere. However, there are insufficient studies on the differential approach applied to recovery of upper limb in patients with right hemisphere affected by dominant hemisphere and those with left hemisphere affected by non-dominant hemisphere. Several approaches have been attempted to recover the upper limb movement and many studies have been reported to demonstrate the effectiveness on recovery of upper limb [15-17].

Recently, one of the most studied methods for upper limb recovery approach is to simultaneously induce bilateral symmetrical movement and to verify the recovery effect of upper limb [18-20]. Induction therapy of bilateral symmetric movements simultaneously induces the movement of intact and damaged upper limbs and promotes activation of cerebral hemispheres in injured and cerebral hemispheres [18]. However, most of the tasks used in daily life do not use symmetrical hands and perform bilateral asymmetrical movements. The characteristics of these tasks are considered to be a more practical approach to the training of the upper limb in the training of the upper limb asymmetric movement therapy rather than bilateral symmetrical movement therapy.

This study used transcranial magnetic stimulation as a motor evoked potentials (MEPs) to evaluate cortical activation through bimanual task training. MEPs is a neurophysiologic test that uses transcranial magnetic stimulation to determine the conduction abnormality from the cerebral motor cortex and spinal nerve roots to the peripheral motor neurons, It is a safe and objective inspection method used for function and prognosis. Specifically, MEPs represents the degree of activity of the motor nerve, which is connected to the cerebral cortex and corticospinal tracts. This is because when the magnetic stimulation is used to directly and indirectly excite the cerebral cortex, is an action potential generated by contraction the skeletal muscle through the alpha motor neuron [21]. Therefore, MEPs is related to the excitation of the cerebral cortex, and the lack of induction of MEPs during proper magnetic stimulation indicates that the neuron or neural stem is dead or has a very high motor threshold. Barker *et al.* (1985) introduced the cerebral cortex magnetic stimulation technique, which proved useful in predicting functional recovery by directly stimulating the cerebral cortex motility without pain and observing the response of the limb muscles. And MEPs are more useful than predicting somatosensory evoked potentials (SEPs) in predicting functional recovery [22-24]. The purpose of this study was to investigate the difference in cerebral cortical activation with bimanual task training (BTT) and to compare the effects of both dominant and non-dominant hand injuries on patients with dominant hand hemiplegia and non-dominant hand hemiplegia using transcranial magnetic stimulation.

2. Materials and Methods

2.1. Subject

This study was performed on stroke patients who visited the B rehabilitation hospital in Republic of Korea. After conducting preliminary observations prior to the selection of the subjects, the subjects who had participated in the study were instructed about the contents of the study, the training period and other precautions. To investigate the subject's cortical activity, before and after test and retention test were performed after two weeks. Prior to carrying out this study, we approved the approval of the Institutional Life Research Ethics Committee of Yongin University (2-1040966-AB-N-01-20-1611-HSR-061-8) and adhered to the Helsinki Research Ethics Declaration. In this study, we performed Fugl-Meyer upper extremity function test and performed the study by selecting 13 patients with dominant hand hemiplegia and 13 patients with non-dominant hand hemiparesis among

26 patients with mild stage stroke between 58 and 66 points [25, 26]. The criteria for determining the dominant hand were tested based on the Edinburgh evaluation list [27]. This study selected patients with stroke who meet the following criteria: In stroke patients, the cause of hemorrhage/infarction was defined as a patient who had been diagnosed with hemiplegia for 6 months, who had no cognitive impairment (MMSE-K $\geq$ 24), and Fugl-Meyer upper extremity function test score of 58 or more but this subjects were excluded patients with severe internal carotid artery injury, patients with intracranial metal implants, and patients with a history of seizures. This study was carried out for 4 months after preliminary study for 4 weeks.

2.2. Procedure

In this study, the BTT was chosen to perform the tasks that are easy to use in daily task in life. The contents of each task are as follows. (1) Hand washing task: Two-hand washing task training was performed using soap in the ADL room, and the therapist performed some tasks with some help as needed. (2) Dressing task: The patient was instructed to perform the task training using the both hands and to provide the therapist's assists if necessary. (3) Scissoring task: Using a 190cm x 70cm size scissors, one sheet of thick paper of A4 paper size was cut off with both hands, and the therapist performed some tasks with some help as needed. (4) Bottle lid picking task: Bottle lid picking task was performed by using bottle opener with bottle cap on beverage bottle, and the therapist performed some tasks with some help if necessary. (5) Strength training: Two hands are used to perform two-handed task training using the JAMAR® hand dynamometer and the therapist provides some help as needed. The task time per subject task was 6 minutes and all tasks were performed within 30 minutes and the order was randomized. Cerebral cortical activity was measured transcranial magnetic stimulation before BTT All subjects were treated 3 times a week, 12 weeks 36 times totally. After BTT, impaired cerebral cortical activity was reevaluated.

2.3. Measurement

2.3.1 Transcranial magnetic stimulation

In this study, MagPro R30 transcranial magnetic stimulation instrument was used to measure excitability of the cerebral cortex and the excitation of the cerebral cortex was measured by connecting a B65 butterfly coil stimulator with a diameter of 70 cm to the MagPro R30 instrument. The maximum magnetic field is 2.0 Tesla. All subjects used a rigid square pillow with no cushion to restrain the movement of the head after lying on a test table in a comfortable position to measure changes in excitability of the cerebral cortex. The positions of both arms were abducted slightly, the elbow joints were extended, the wrist joints were neutral, and the fingers were supine by the body in a finger extension. Then, subjects were asked to wear a hood with a coordinate on their scalp, and the motor threshold of the cerebral cortex was measured. The two points were the center point (Cz) at which the intersection of the midsagittal line and the interaural line connected from the nasion to the inion was measured. And crossed lines in a checker board shapes. The motor threshold of cerebral cortex was tangential to the damaged cerebral hemispherical scalp of the subject using a B65 butterfly coil stimulator. The handle was positioned at a 45-degree angle with the back pointing toward the back of the cerebral cortex. Before starting the study, to measure MEP's of the subject, silver/silver chloride electrode (Ag/AgCl) was applied to the first dorsal interosseous (FDI) were attached to the belly tendon montage, and the EMG values were measured by attaching the ground electrode to the arm. EMG values were recorded using mobile KEY POINT.NET® software and the signal was amplified to 100 mV/div and filtered

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

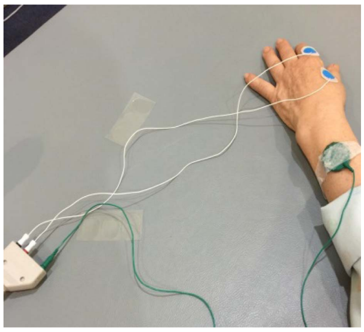

Fig. 2. (Color online) Attached surface electrodes: first dorsal interosseous muscles.

to 2 Hz to 10 KHz. To locate the motor cortex area of FDI, a single stimulus was given while moving slightly over the middle of the subject's brain using a B65 butterfly coil stimulator. The location of the largest MEPs in the recording potential of FDI was judged to be the motor cortical area of the muscle. The resting motor threshold is defined as the minimum stimulation intensity at which more than 50 μV of MEPs is recorded at least 5 times during 10 times of stimulation and the stimulation intensity is defined as the amplitude of MEPs stimulated with 120 % And latency values were measured 15 times to determine the average value [28].

2.2.2. Analysis

Statistical analysis was performed using the SPSS/WIN statistical program 20.0. The descriptive statistics were used for the general characteristics of the subjects, and the repeated two-way measures (ANOVA) were used to examine the change of each variable according to the training time and the group of the subjects. The statistical significance was $\alpha = 0.05$.

3. Results

3.1. General characteristics of subjects

A total of 26 patients with chronic stroke were included in this study. A total of 13 patients with dominant hand injuries were 7 men and 6 women, and 13 patients with non - dominant hand injuries were 6 men and 7 women. The mean age of subjects was 67.92 ± 6.46 years in dominant hand affected group (DHAG) and 58.15 ± 18.00 in non - dominant hand affected group (NDHAG). The duration of stroke was 3.31 ± 1.18 years for dominant hand injuries and 3.15 ± 1.15 years for non-dominant hand injuries (Table 1).

3.2. Comparison of MEPs amplitude and incubation time of DHAG and NDHAG with BTT

The amplitudes of MEPs of DHAG were increased to .13 mV before the study and to .43 mV after the study and decreased to .34 mV after 2 weeks. The MEPs amplitude of the NDHAG increased from .12 mV before the study to .23 mV after the study and decreased to .20 mV after 2 weeks (Table 2). The results showed that there was statistically significant difference between the groups after the training ($F = 1.082$, $p < .001$)($F = 78.608$, $p < .001$)($F = 17.427$, $p < .001$) (Table 3). The incubation period of DHAG decreased from 24.76 msec before the study to 21.90 msec after the study and to 21.96 msec after 2 weeks. The latency of NDHAG decreased from 24.37 msec before the study to 23.52 msec after the study, and increased to 23.60 msec after 2 weeks (Table 2).

Table 1. General characteristics of subjects (n=26).

Variable		DHAG (n=13)	NDHAG (n=13)
Age (years)		67.92 ± 6.46	58.15 ± 18.00
Gender	Man	7	6
	Woman	6	7
Lesion side	Rt. hemisphere	0	13
	Lt. hemisphere	13	0
Lesion type	Hemorrhage	4	5
	Infarction	9	8
Duration of Neurorehabilitation after stroke (years)		3.31 ± 1.18	3.15 ± 1.15
Handness	Rt side	13	13
	Lt side	0	0

M ± SD M: Mean SD: Standard Deviation DHAG: dominant hand affected group
NDHAG: non-dominant hand affected group

Table 3. Comparison of the MEPs amplitude and training time between groups.

Variable	SS	df	MS	F	*p*
Between-subject					
group	.284	1	.284	18.082	.000***
Error	.376	24	.016		
Within-subject					
Time	.581	2	.290	78.608	.000***
Time * Group	.129	2	.064	17.427	.000***
Error	.177	48	.004		

***$p < .001$

Table 2. Comparison of MEPs amplitude and latency in each group with BTT

Group		Pre test	Post test	Retention test
MEPs amplitude (mV)	DHAG	0.13 ± 0.039	0.43 ± 0.132	0.34 ± 0.122
	NDHAG	0.12 ± 0.030	0.23 ± 0.085	0.20 ± 0.061
MEPs latency (msec)	DHAG	24.76 ± 0.759	21.90 ± 0.794	21.96 ± 1.279
	NDHAG	24.37 ± 1.036	23.52 ± 0.706	23.60 ± 0.734

M ± SD M: Mean SD: Standard Deviation DHAG: dominant hand affected group
NDHAG: nondominant hand affected group

Table 4. Comparison of the MEPs latency and training time between group

Variable	SS	df	MS	F	*p*
Between-subject					
group	17.933	1	17.933	10.262	.004**
Error	41.939	24	1.747		
Within-subject					
Time	57.800	2	28.900	79.091	.000***
Time * Group	17.805	2	8.902	24.342	.000***
Error	17.555	48	.366		

$^{**}p < .01$, $^{***}p < .001$

There was statistically significant difference between the training period and the latency period change between the two groups (F = 10.262, $p < .01$). In addition, there was a statistically significant difference (F = 79.091, $p < .001$) between the training period and the group interaction (F = 24.342, $p < .001$) (Table 4).

4. Discussion

The purpose of this study was to investigate the difference of cerebral cortical activation according to difference of dominant hand and non - dominant hand in BTT in 26 hemiplegic patients after stroke. Representations can be generated on the primary motor cortex (M1) with transcranial magnetic stimulation, and the MEPs average amplitude values obtained through it can be used to more accurately identify changes in the corresponding regions [29]. Characteristically, the affected side of stroke patients has higher stimulation thresholds, lower MEPs mean amplitude values, and latency delay of MEPs than non-affected ones [30-34]. In this study, BTT related to activities of daily living was performed in the same way for both groups, three times a week for a total of 12 weeks and 30 minutes. In order to confirm the effect of BTT with transcranial magnetic stimulation, Representations factors such as MEPs mean value and delayed latency time of impaired cerebral cortex M1 were measured three times. After the BTT, both groups showed changes in MEPs mean amplitude increase and delayed latency time reduction before, after and the retention test. Staines *et al.* (2001) [35] performed unilateral movement training (UMT) and BTT for patients with left hemiparesis after acute stroke. In the UMT, the supplementary motor cortex (SMA) of the right hemisphere was activated in the fMRI when performing the task of picking up the left hand. However, when performing the task of catching with the right hand, M1, SMA, primary sensory cortex (S1). In acute stroke, BTT was able to activate cerebral cortex of M1, S1, and SMA of bilateral cerebral hemispheres when performing repetitive grasping tasks, thereby increasing cerebral cortical excitability of bilateral cerebral hemispheres, It can be important for reorganizations [35]. In addition, previous study suggest that increasing the MEPs amplitude value through intensive and repeated BTT in chronic stroke patients may help improve the damaged cerebral cortex [33].

This study also was to investigate the difference in cerebral cortical activation according to presence or absence of dominant hand when performing BTT related on activities of daily living. BTT, which is currently performed in many studies, uses a simple repetitive training method that moves the same task symmetrically. In addition, it did not consider the asymmetry of movement and the characteristics of dominant hand and non - dominant hand in relation to the hand manipulation ability used for solving tasks in activities of daily living. Therefore, in order to improve the limitation of the previous study, this study used BTT included in functional activities considering asymmetry and cerebral hemisphere predominance when performing BTT and induced to use the affected upper limb as much as possible during training period. As a result, it was confirmed that BTT was applied to the DHAG after the training, and there was a difference in activation of cerebral cortex between DHAG and NDHAG. In addition, these results are similar to those of the previous study, which suggests that dominant hand can recover faster than non-dominant hand, especially in BTT with both hands [31]. And it can be confirmed that bimanual task training applied to stroke patients can affect recovery depending on presence or absence of injured side even if it is the same task training. These results show that the mean amplitude of cerebral cortical MEPs increased more significantly after the training and in the retention test than before the training in DHAG. Even though BTT is the same, it is considered to be one of the important factors affecting upper limb recovery due to differences in cortical activity due to dominant hand and non - dominant hand differences. There are two main reasons why BTT can make a difference in upper limb recovery depending on the presence or absence of dominant hand on the affected side. First, the lateralization of the right and left cerebral cortex due to the predominant cerebral hemisphere may cause different characteristics of motor function. Based on this hypothesis, it can be explained that the recovery result may be different even if the BTT is performed according to the cerebral hemisphere lesion. In the previous study using fMRI, the cerebral cortex activity in the right and left fingers was examined. The left cerebral cortex showed cerebral cortical activity when the right and left fingers were moved. But in the right cerebral cortex, activation of the cerebral cortex was observed only in the movement of the left finger [12]. And that there was a difference in the bimanual coordination of hand according to the hemisphere lesion difference. Characteristically, damage to the left hand cerebral hemispherical damage was not only in the contralateral side but also in the ipsilateral side. In the right cerebral hemispherical lesion, only the upper limb showed damage. This suggests that the left cerebral hemisphere is more involved in two-handed control [36]. In addition, BTT in this study further increased activation of the left cerebral cortex because the right hand plays a role of mobility and the left hand plays a role of stability when performing tasks. The use of the right hand is much more frequent than that of the left hand. This is explained by the study that cerebral cortical activity increases simultaneously in fMRI as the movement increases [35, 37]. The previous studies can be explained that the cerebral cortical activity increases simultaneously with the increase of the fMRI. The limitation of this study is that it is difficult to generalize to all stroke patients because only mild chronic stroke patients are selected. Therefore, it is necessary to confirm the limitation of the study and to suggest the BTT for the acute phase, subacute phase, and chronic phase stroke according to the episode of onset in future studies. In addition, upper limb approach in the clinic tends to generalize to the simple hemiplegia without considering the damage of dominant hand. This is thought to be the result of not recognizing the difference of different exercise recovery characteristics of dominant hand and non - dominant hand according to dominance of cerebral hemisphere. Therefore, based on the results of this study, BTT related to functional activities is selected rather than fixed task training applying both hand symmetrical movements in applying hand therapy to stroke patients. In addition, individualized hand therapy should be considered in consideration of different approach of right and left cerebral hemispheres.

5. Conclusion

In this study, we used transcranial magnetic stimulation to examine cerebral cortical activity in BTM. This study suggests that it is necessary to select appropriate BTT according to the presence of the damaged side and dominant hand, and to take into consideration the difference in the characteristics of the right and left cerebral hemispheres acting on the motor function.

Acknowledgment

This study was supported by 2014 Research Grant from Kangwon National University.

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