

Yuji Inagaki , Kazunori Seki¹, Takahide Ogura², Takaaki Sekiya³, Yasunobu Handa¹

¹Department of Restorative Neuromuscular Rehabilitation, Tohoku University Graduate School of Medicine, ²Department of Noninvasive diagnostic imaging, Tohoku University Graduate School of Medicine, ³Department of Health & Welfare Science, Sendai University, Miyagi, Japan
*inagaki-yuji@m.tains.tohoku.ac.jp

Abstract

Recently, mirror therapy which focuses on moving unimpaired limb has been developed for patients with hemiplegia following stroke. In the present study, we used Electromyogram (EMG) triggered-FES (ETF) to move unilateral hand synchronously with contralateral voluntary hand movement while performing mirror therapy and investigated the effects on motor evoked potential (MEP) induced by transcranial magnetic stimulation (TMS) in thirteen healthy subjects. MEP was recorded from three muscles in the right arm; extensor carpi radialis (ECR), flexor carpi radialis (FCR) and first dorsal interosseous (FDI). The subjects performed 6 tasks as below: observation of a mark with only left hand extension movement (Task1), observation of resting right hand added to Task1 (Task2), observation of mirror reflection of left hand movement added to Task1 (Task3), observation of a mark and right hand movement induced by ETF (Task4), observation of moving right hand added to Task4 (Task5), and observation of mirror reflection of left hand movement added to Task4 (Task6). In ECR, mean amplitude of MEP (AMEP) in Task 4 ($P=0.049$) and Task 6 ($P=0.0427$) showed a significant increase comparing to Task 1. In FCR, statistically significant differences were not found. In FDI, AMEP in Task 2 ($P=0.0231$) and Task 5 ($P=0.033$) showed a significance increase comparing to Task 1. These results suggested that ETF combined with mirror therapy had a possibility to activate excitability of the primary motor cortex corresponding to the muscle that was electrically moved.

Keyword: EMG-triggered FES, mirror therapy, transcranial magnetic stimulation

1. Introduction

Hemiplegia is one of the most troubling sequelae of stroke, and it causes detrimental effects to motor execution ability. It is extremely expected to develop treatment procedure for improving function of upper extremity, because upper extremity is directly linked with the constrained activities of daily living.

Recently, mirror therapy which focuses on moving unimpaired limb has been developed for the patients with hemiplegia following stroke. In this therapy, mirror reflection of the moving hand in the healthy side is superimposed on the paretic hand and a patient continues to gaze the reflection during moving the healthy hand. There are several studies reporting some clinical effects of conventional mirror therapy for upper extremity impairments [1-3].

On the other hand, as a result of neurophysiological experiment, Fukumura et al.[5] reported that amplitude of motor evoked potential (MEP) induced by transcranial magnetic stimulation (TMS) increased when the subjects watched a mirror reflection of the voluntarily moving hand while the wrist joint in the contralateral side was passively moved with alternate flexion-extension by an experimenter. This study indicated combination of visual input through mirror reflection and passive movement augmented the primary motor cortex (M1).

In the present study, we used Electromyogram (EMG) triggered-FES (ETF) as a substitution of passive movement while performing mirror therapy and investigated the effects on MEP.

2. Methods

Thirteen (ten males, three females, 28.2 ± 8.1 years) neurologically healthy subjects participated in the study. All subjects were self-declared right hand dominant. They gave informed written consent prior to participation.

2.1 Task and experimental procedures

Subjects sat with a relaxed position on a reclining chair, and a custom-built mirror box was placed on a horizontal plate attached to the armrest of a reclining chair in front of a subject. They were asked to place both hands at neutral position in the mirror box. In this experimental setting, they performed 6 tasks as below (Fig 1).

Task1: the subjects executed repetitive extension movement of the left wrist in a box with frequency of 0.5 Hz for 90seconds. They continued making wrist extension and relaxation following a signal of a metronome (art metronome, Mu-tech Co.,Inc). During performing the task, the subjects visually fixated a small round mark (1cm diameter) on the box shielding both hands. Task2: in addition to the condition of Task1, the subjects visually fixated only resting right hand. Task3: in addition to the condition of Task1, the subjects only watched a mirror reflection of the moving left hand superimposed on the resting right hand positioned behind the mirror. Task4: in addition to Task1, the right wrist was extended by ETF synchronously with muscle contraction in the left forearm. We used a device for ETF developed by Futami [5]. Stimulation electrodes were attached on the right extensor carpi radialis (ECR) muscle and triggered EMG was obtained from the left ECR. This method makes it possible to move right hand by left hand movement. Task5: in addition to the condition of Task4, the subjects visually fixated only right hand being moved electrically. Task 6: in addition to the condition of Task4, the subjects watched a mirror reflection as same as Task3. The subjects were instructed not to move the right hand during Task1 ~3 and, to confirm resting state of right hand during performing these tasks, we observed background EMG discharge of right hand and forearm. All of the tasks were performed in random order.

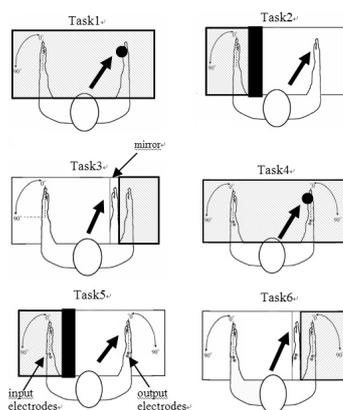


Fig. 1. Schematic illustration of the experimental setup. The arrow in each task represents where the subjects were asked to look.

2.2 Transcranial magnetic stimulation

TMS was performed using a Magstim 200 stimulator (Magstim company LTD, GB) connected to a figure-eight coil with an external diameter of 9 cm. The stimulating coil was placed on the left scalp over the optimal site for eliciting responses in the right

extensor carpi ulnaris (ECU) muscle using surface electrodes. TMS was delivered with 1.2 times intensity of the motor threshold at rest and great care was taken to maintain the position of the coil during recording MEP. MEPs were amplified with a band pass of 10~3000 Hz. Analogue outputs from the signal processor were digitized at a sampling rate of 1.5k Hz and saved in a computer for offline analysis.

2.3 Recording of MEP

MEPs were recorded from the right ECR, flexor carpi radialis (FCR) and first dorsal interosseous (FDI) muscle using disposable surface electrodes. The distance between electrodes was 2 cm. Each pair of the electrodes was placed over the center of the muscle belly. The reference electrode was placed over the left olecranon. EMG signals of ECU were used only to monitor MEP responses during tasks. At least 10 waves of MEP were obtained immediately after completion of each task.

2.4 Analysis

The waves of MEP recorded at a task were averaged and peak-to-peak amplitude of an averaged MEP was measured to calculate mean MEP amplitude (AMEP) in each task.

Task1 was defined as a control task, and each value of AMEP from task2 to 6 was compared to that of task1 respectively using Wilcoxon's signed-rank test. The level of statistical significance was defined by $p < 0.05$.

3. Results

Statistical significance of the value of AMEP between Task1 and others were shown in Table1. In ECR, Task2 showed a tendency of significant increase ($P=0.0504$) and Task4 ($P=0.0499$) and Task6 ($P=0.0427$) showed a significant increase comparing to Task1. In FCR, statistically significant differences were not found between Task1 and other tasks. In FDI, Task2 ($P=0.0231$) and Task5 ($P=0.033$) showed a significant increase comparing to Task 1. Additionally, Task 4 had a tendency to be significantly larger than Task 1 ($P=0.0653$). We observed no obvious background EMG discharge appeared on the right hand and forearm during performing the task1 ~3.

Table 1. Statistical significance of the value of AMEP between Task 1 and others

vs Task1	Task2	Task3	Task4	Task5	Task6
ECR	*	—	**	—	**
FCR	—	—	—	—	—
FDI	**	—	*	**	—

*: $P < 0.1$, **: $P < 0.05$, —: Not significant.

4. Discussion and Conclusions

The present study tested whether the visual sensation relating to motor imagery and electrically induced proprioceptive sensation modulated excitability of M1 dominating unilateral upper extremity under the condition of repetitive movement in contralateral upper extremity.

Extension of the left wrist was repeated voluntarily through all of the tasks. It could be postulated, therefore, that motor imagery constructed by muscle contraction of left ECR and movement of the left wrist relating to joint sensation was easy to be projected to contralateral side during performing each task. AMEP in both ECR and FDI increased in Task2, and did not increase in Task3. One of the differences between Task2 and Task3 was observation

modality. The subjects directly observed their right hand and the electrodes on FDI in Task2 though the right forearm was not observed. There are some studies reporting that both observing moving hand and observing resting hand facilitated MEP in the resting hand [6,7]. The result in Task2, therefore, suggests projection of motor imagery, constructed by unilateral movement, to the contralateral side can be facilitated by direct observation of the target side. In Task3, on the other hand, visual sensation was only input from the mirror reflection of the moving left hand. Funase et al.[7] reported MEP amplitude of FDI and FCR was increased during observation of contralateral self-movement through a mirror as same as observation without mirror. They recorded MEP, however, during performing self-movement and compared its amplitude with resting state, while we recorded MEP after completion of the task and self-movement was performed even in Task1 as control. It can be speculated that, at least under the condition of unilateral hand movement, indirect observation of moving hand through a mirror is disadvantageous to project motor imagery to the resting hand comparing to direct observation of the resting hand.

AMEP in FCR did not show any change through all of the tasks. The right FCR was in the state with no observation and no corresponding movement of the left forearm. In the study on motor imagery, MEP amplitude in the task with motor imagery of unilateral wrist flexion was facilitated significantly not only in FCR but also in ECR in the ipsilateral side. In the present study, however, the subjects were not instructed to image movement of extension in the right hand. This might be one of reasons explaining no change of AMEP in FCR.

AMEP in both ECR and FDI also increased in Task4. Since no visual sensation was given in this situation, the factor relating to such an increase was only electrical stimulation (ES) applied to right ECR. It is invalid to postulate ES has a direct effect to project motor imagery. Khaslavskaja et al.[9] reported increase of MEP amplitude in the tibialis anterior following ES to the peroneal nerve. This indicated ES could provoke motor activation due to cutaneous, muscle, and joint proprioceptive afferent feedback to the corresponding area of M1. In Task4, the result of AMEP increase in FDI might imply remote effect of afferent signals originated from ES to ECR and no change of AMEP in FCR suggests contribution of reciprocal Ia inhibition via spinal cord.

Interpretation of the results in Task5 and Task6 is complex and difficult. In FDI, AMEP increased in Task5 but did not increase in Task6. This result may be interpreted as summation of Task2~4, that is, both direct observation and ES provided augmentation of MEP and observation of mirror reflection disturbed it. In ECR, however, the results in Task5 and Task6 were reversed. No change of AMEP in Task5 suggests direct observation of the moving right hand inhibits the facilitating effect of ES. Meanwhile increase of AMEP in Task6 indicates observation of the moving left hand through a mirror is beneficial to regain the facilitating effect of ES. When healthy subjects observed video clips of natural and unnatural hand-orientation movement, MEP was facilitated significantly during observation of natural hand orientation [10]. Electrically induced movement by ETF might be visually unnatural for the healthy subjects. If so, mirror reflection could correct unnatural motor imagery to natural one and assist the facilitating effect of ES.

References

- [1] Ramachandran VS, Roger-Ramachandran D. Synaesthesia in phantom limbs induced with a mirror. *Proc R Soc Lond B Biol Sci*, 263:377-386, 1996
- [2] Altschuler EL, Wisdom SB, Stone L. Rehabilitation of hemiparesis after stroke with a mirror. *Lancet*, 353:2035-2036, 1999
- [3] Yavuzer G, Selles R, Sezer N, et al. Mirror therapy improves hand function in subacute stroke: A randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, 89:393-8, 2008
- [4] Futami R, Seki K, et al. Application of Local EMG-Driven FES to Incompletely paralyzed Lower Extremities. Proc. of 10th annual conference of IFESS, 204-6, 2005
- [5] Fukumura K, Sugawara K, Tanabe S, et al. Influence of mirror therapy on human motor cortex. *International Journal of Neuroscience*, 117:1039-48, 2007
- [6] Garry MI, Loftus A, Summers JJ. Mirror, mirror on the wall: viewing a mirror reflection of unilateral hand movements facilitates ipsilateral M1 excitability. *Experimental Brain Research*, 163:118-22, 2005
- [7] Funase K, Tabira T, Higashi T, et al. Increased corticospinal excitability during direct observation of self-movement and indirect observation with a mirror box. *Neuroscience Letters*, 419:108-12, 2007
- [8] Kasai T, Kawai S, Kawanishi M, et al. Evidence for facilitation of motor evoked potentials induced by motor imagery. *Brain Research*, 744:147-50, 1997
- [9] Khaslavskaja S, Sinkjaer T. Motor cortex excitability following repetitive electrical stimulation of the common peroneal nerve depends on the voluntary drive. *Experimental Brain Research*, 162: 497-502, 2005
- [10] Maeda F, Kleiner-Fisman G, Pascual-Leone A. Motor facilitation while observing hand actions: specificity of the effect and role of observer's orientation. *The American Physiological Society*, 87:1329-35, 2002