Lateralization of Cortical Activity during Mirror Therapy detected by Electric Potential Induction measured by means of Motion trans-cranial Magnetic Stimulation.

Akita Kobayashi [1)], Toyohiro Hamaguchi [1)] *, Akiteru Takagi [2)]

Key words : Mirror Therapy, Tans-cranial magnetic stimulation, Induction of motion- potential, Motor area, Stimulation of nerve

Summary

The activation of left and right cerebral cortex induced by motion of upper limb during Mirror Therapy: MT: was studied by measuring motor-evoked potential (MEP) using trans-cranial magnetic stimulation (TMS).

Subjects were 10 neurologically healthy right handed males, age 21.9 ± 1.17 and their surface muscle potential was measured using surface muscle electrical potential meter at their right first dorsal inerosseus (FDI) at resting, image training (IT), MEP during Mt were compared.

Significant interaction was observed between on left and right ΔMEP (difference of MEP value) during IT and MT (F[3,36]-3.047, P=0.0278). MEP in stimulation of left motor area was significantly higher than right motor area stimulation (P<0.01).

Promotion of neural stimulation of left cerebral cortex motor area was suggested by this study. This study also suggests the possibility of difference of MT effect for left or right cerebral hemisphere depending on the side of disturbance.

Introduction

MT is a physical therapy creating an image of movement by using an optical illusion that the handicapped upper limb is in action through a mirror image of a healthy upper limb. The man's feeling is created by dynamic interaction of signal from sense receptor and optical images built in past [1,2)]. MT is a therapeutic method that alters the physical sense through optical illusion and successful results have been reported in cases of optically induced pain and paralysis of upper limb after stroke [3,4)]. The success of functional recovery in the case of motor paralysis of an upper limb after stroke by MT has also been reported in Japan [5)].

There are many reports of damage of the sense motor function in case of motor paralysis after stroke and patients visually believe in the immovability of damaged side together with sense of skin, muscle, joint and the other parts. Thus the image of motor paralysis is created due to cerebellum information management [2)]. Namely, there is a possibility of brain judging the real remaining capability to be more limited than it is. MT gives the illusion that the damaged upper and lower limbs is moving normally by showing in a mirror the other healthy moving limbs. It is able to create a capability corresponding to the remaining function by reconstructing a normal body image in the somatosensory area after the activation of motor area, building a normal motor function from the phantom [6,7)].

Though experiments using image processing of

1: Department of Physical Therapy, and 2. Department of Occupational Therapy, School of Medical technology, Niigata University of Health and Welfare
* Corresponding aouthor.: 1398 Shimami-cho, Niigata 950-3198, Japan
Tel/Fax: +81-25-257-4447, E-mail: hamaguti@nuhw.ac.jp

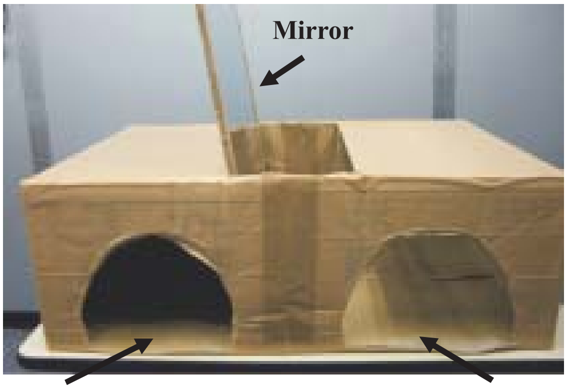

Fig.1. Mirror box.

Insert the healthy upper limb into the opening of a side of box and unhealthy one into the other. Healthy one is visible in the mirror. The subject feels damaged upper limb is moving normally due to illusion.

brain function, MT is neuro-physiologically shown to have the effect of stimulating the activation of motor area [8-10]. There is a functional localization in the left and right cerebral hemispheres. Thus, there are lateralization in the amount of the activation within the areas of optical and somatic sensation and the areas of the prefrontal, so called mirror neuron, area [11]. There is a report that MT presents a lighter sense-response of disturbance (in the case of no damage in left cerebral hemisphere [12]. The possibility exists for effectiveness of motion therapy of upper and/or lower limbs, if the difference in activation of left and right prefrontal area.

MT, which requires image formation, may be effective in the case of no damage in left semi-sphere of cerebrum, because the disturbance of space recognition and physical recognition often occurs in left hemi-sphere damage of cerebrum. If we assume that left hemi-sphere of cerebrum plays an important role in MT, the lateralization may appears in the motor area during MT. This study compared the activation of left and right cerebral cortex read by MEP induced by stimulating of the motor areas of cerebrum cortex by TMS.

Methods

1. Subjects.

Ten healthy right handed adult males, age 21 ± 1 years og age were cosen after the informed consent. They had no neurological abnormalities. Handedness was judged by hand survey sheets developed by Kameyama and Oddy et al. and modified by Shioura and confirmed that all subjects were right handed.

2. Equipment used.

Mirror box shown in Fig.1, muscle surface potentiometer, fixture for neck-breast, fixture for forearm, weights, metronome, TES equipment (MAGSTIM200, Miyuki Techics Co.), goniometer were employed.

MT was carried out by using a mirror box which was prepared from cardboard. It may be easily made from card board box in which one can place forearms to thefingers and a mirror. The preparation method of mirror box is as follows: prepare two openings on both side, large enough to set both upper arms into each openings. A mirror is set on the upper surface of box and an opening is made so that image on the mirror can be seen through this. It is important that the damaged upper limb should not be observed but only the normal upper limb reflected in the mirror should be visible. Thus, the upper opening must be minimal so that the limb with damage is not seen.

In MT, the damaged upper limb and healthy upper limb are inserted into the box through different opening. The mirror should be adjusted to reflect the healthy arm and the other one should not be visible through the mirror. Under this condition, the healthy arm is visible in the position of the disturbed arm. This creates, in the patient, an illusion as though the disturbed arm is moving normally.

3. Position of limbs.

Fig.2. Scene of measurement.
MEP is read from left FDI when right cerebrum hemisphere has dominant stimulus, make facing B surface of stimulation coil upward.

Participants were asked to sit on a chair and place both arms on a table. To measure the electric potential of cerebrum induced by the illusion, the damaged arm with fixed with a plastic prosthesis and a weight on the arm joint. During measurement, both arms were fixed, to overlap the healthy and the disturbed arm illusion in the mirror keeping elbow angle at 120°, outer and inward angle in center, hip joint and knee angle at 90° breast-lumbar and neck breast angle at 20°.

4. Recording of magnetic stimuli and induced potential.

The stimulation points of cerebrum was from the parietal to the finger-controlling cerebral motor area following 10-20 method. To keep a constant position of head and circular coil during MT, prosthetic fixation of neck-breast was used and stimulation was carried out (Fig.2).

When the face of MTS coil is turned upward, the left cerebral hemi-sphere will be dominantly stimulated, but in B position, face upward, right hemi-sphere will be dominantly stimulated. When MEP from right FDI, under the fixing of right upper limb, takes A position facing upward but when MEP from left FDI in fixing the left upper limb, it takes the B position facing upward. Ten single stimulation were repeated in each trial with interval of minimum 5 seconds.

The strength of stimuli was 60% of the power of TMS machine. Moreover, to relax the patient, a desensitization was performed three times by trial stimulation before TMS. TMS stimulation was started after confirming the absence of sympathetic contraction of fixed side of upper limb.

FDI was chosen for detection muscle by TMS in TMP and the position of probe system was placed from second finger bone tip to near muscle abdomen side of first finger. Surface probes were used to lead of MEP signal and dipole induction method was used with a distance of 20 mm. apart. MEP lead from FDI was integrated on personal computer with sampling frequency of 1 kHz. Via pre-posted amplifier (DPA-10, Diamedical Co.), and amplifier (DPA 2078, Diamedical Co.). The obtained muscle potential diagram was used to calculate the maximum number for each measurement after smoothing with wave rectification with the analytical softwear for muscular potential (Chart & ScoPe AD Instruments).

5. Procedure.

Three motions, (1) resting, (2) IT and (3) MT were chosen for this study. Three measurements were carried out three times on left cerebral hemisphere dominant stimulation (right upper limb was fixed) and right cerebrual hemi-sphere dominant stimulation, all together 6 times. The order of measurement was resting, IT and MT in all of the cases. To be unbiased, the measurement for 5 subjects were started from right upper limb fixed and for the other 5 subjects from left upper limb fixed, after observing their learning process for motion.

(1) For resting: the subjects were directed to

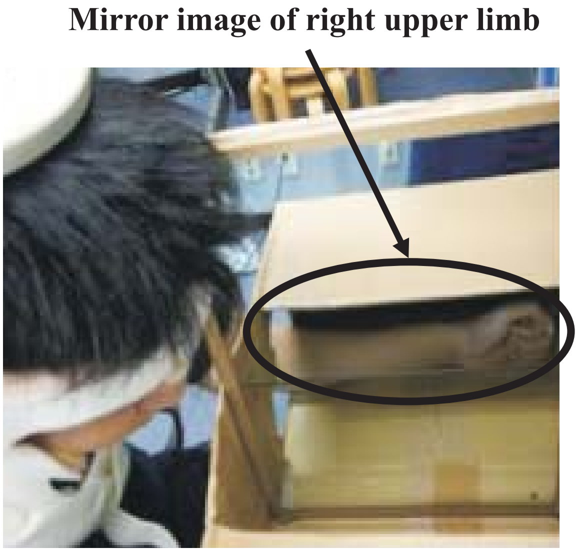

Fig.3. MT operation.
Left upper limb is fixed behind mirror and the image in the mirror is of the right upper limb.

maintain their posture and not move as much as possible during measurements.

(2) IT work: Subjects were asked to imagine that fixed arm would move as free fingers holding motion with rhythm. Motion through imaging was performed by watching the fixed upper limb. The timing for TMS stimulation was adjusted with the beginning of the gripping action by the subject in rhythm.

(3) MT work: Subjects were asked to imagine the fixed upper limb was performing a grabbing motion by watching the mirror image of moving unfixed upper limb (Fig.3). After the measurement, subjects were asked to verbally answer about the illusion condition during motion work.

6. Statistical analysis.

The averages of 10 MEP values obtained in resting, IT and MT from left and right side were taken. To compare the MEP values obtained by stimulating left and right cerebrum hemi-sphere, the MEP value during resting was subtracted from IT and MT. Those values of left and right were compared after adjusting for the shape of cerebral hemisphere and the position of stimulation. Two way analysis of variance (ANOVA) was employed for statistical analysis.

Results

ΔMEP, the difference between the value read from the FDI by stimulating right cerebrum cortical motor area and the FDI by stimulating left cerebral cortical motor area, was compared. A significant interaction was observed between left and right ΔMEP values obtained in IT and MT ($F[3, 36]=3.047$, $P=0.0278$). ΔMEP (altered MEP value) was much higher during MT with right upper limb fixed and dominant stimulation to left cerebrum cortical motor area than during MT with left upper limb fixed and dominant stimulation of left cerebrum cortical motor area for finger movement (Post-hoc, Bonferroni, $P=0.0088$). Also, with comparison of the value increase during IT and during MT, the tendency is obvious in the latter case ($P=0.08$) (Fig.4).

All subjects agreed upon the feeling of illusion during MT. To the question about the difference between left and right upper limb fixing over motion illusion, five out of ten subjects reported a stronger illusion in left upper limb fixation while one felt strange with right upper limb fixation and the other four did not notice any difference.

Discussion

This study shows an effective interaction between IT and MT and a higher potential is observed upon stimulation of MEP lead from left FDI by stimulating right cerebral cortical motor area than from right FDI by stimulating left cerebral cortex. A significant activation of left cerebral cortex by MT was suggested by an incease of MEP due to the activation of cerebrum cortex.

The mirror neuron found by Ggentilucci et al. are localized in left and right frontal cortex (F5 for Macaca monkey, human : prefrontal motor

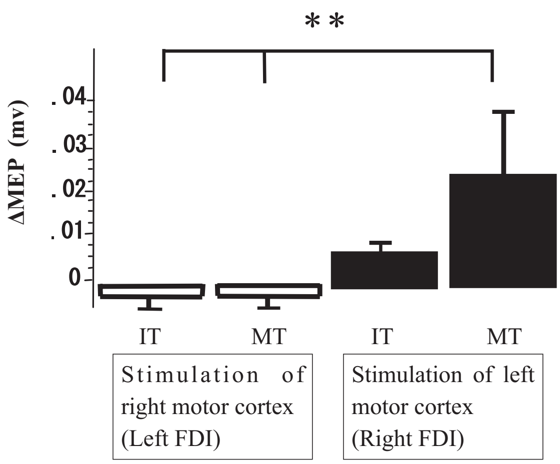

Fig.4. Comparison of ΔMEP during left/right IT and MT.

A meaningful interaction of left/right ΔMEP during IT and MT was recognized (F[3, 36]=3.047, P=0.0278). ΔMEP value (altered value of MEP) in right upper limb fixed and dominant stimulation of the finger locus in motor area of left cerebrum cortex was given was shown to be much higher relative to left upper limb fixed and dominant stimulation of the finger locus in motor area of right cerebrum cortex (ANOVA, F[3. 36]=3.05, P<0.03). *Post-hoc, Bonferroni, P=0.0088, n=10.

area)[13]. According to the PET study by Rudi et al. on motion image, the image induced by self motion has much stronger relation with left cerebral hemisphere [14]. Location of cerebrum function of self imaging are mostly in lower parietal lobe of left hemisphere, complementary motor area, primary motor area and somatosensory area, with some function of right hemisphere in cerebellum and precuneus. It is conceivable that this study also suggests the activation of prefrontal area, surrounding complementary motor area of left hemisphere, and parietal association area by strengthening of self-image formation by mirror image illusion during MT.

To increase the effect of MT, it is important to believe in self generalization of mirror image of healthy side as the damaged upper limb and to build an image of the moving arm. I t is hoped that left cerebral hemisphere, especially left complementary motor area, and left lower parietal lobe are not damaged. There is a report that MT is effective for mild cases, and thus there is a possibility that MT is effective for the case without damage in left cerebral hemisphere [10]. It may be difficult to obtain a body image of paralyzed arm, if the damage of sensor paralysis is critical, and the effect from brain function is conceivable.

The brain function to treat motion information optically is associated with ventral motor frontal area [15,16], and the fact that MT is superior to IT in motion illusion may suggest that the motion imaging can be recognized easily by an optical sensation. MT uses induction of motion sense as moving by self (sensation that moving damaged side by one's own ability). Precuneus is related to focused eye movement and is the area of control center of various senses like vision and physical movement, and fusion of optical and bodily sensation [19,20]. The primary motor area (periphery of complementary motor area) is connected with parietal association area and has the functions of joining the optical and motor information and of alteing and inducing optical information to motor information [21-23].

Right FDIΔMEP increase confirmed during MT in this study suggests a activation of left complementary motor area and parietal primary joint area as well as primary motor area. More subjects felt stronger illusion of right upper limb mirror image in place of left upper limb when the question was asked in which case you felt a stronger illusion. Some of them mentioned that motion with not trines upper limb is more difficult, relative to trained upper limb creating a mirror illusion, and thus more difficult to form motion image. There is a possibility that recognition of gaps between expected motion image and clumsy actual movement was recognized by right cerebral hemisphere and thus relatively reduced the function of left cerebral hemisphere leading to difficulty in inducing the illusion. A simple movement by trained hand activates the motor are of the opposite side and same side of cerebellum [24-26]. All of the subjects in this study were right handed and thus it was conceivable that trained arm influenced neuron stimulation of left motor area.

This study showed that left cerebral cortex could be meaningfully activated by MEP of TMS during MT. It is considered that neuronal signals from complementary motor area and parietal associaton area activates the motor area but the mechanism for that is not understood. Also it is unclear that why neural base speculated as mirror neuron is dominant in left hemisphere. However, the effectiveness of MT for left hemi paralysis patient after stroke is possibly due to this localization of brain function. Nevertheless, various stimulation mechanisms are involved between central nerve to peripheral muscle in stimulation transfer. To understand the therapeutic mechanism of MT, the more detailed studies on localization of brain function and the order of activation during MT by means of analysis of brain by PET and FMRI are needed.

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