Disappearance of unaffected motor cortex activation by repetitive transcranial magnetic stimulation in a patient with cerebral infarct

The ipsilateral motor pathway from the unaffected motor cortex to the affected extremity is one of the motor recovery mechanisms following stroke (Jang, 2011). Because stroke patients who had shown recovery by this mechanism usually showed poorer motor function, compared with patients who showed recovery by other mechanisms, several researchers have considered this mechanism as a maladaptive plasticity (Jang, 2013).

Change in activity of the ipsilateral motor cortex by various rehabilitative interventions, including repetitive transcranial magnetic stimulation (rTMS), has been reported (Mansur et al., 2005; Takeuchi et al., 2005; Liepert et al., 2007; Kirton et al., 2008; Nowak et al., 2008; Takeuchi et al., 2008; Conchou et al., 2009; Khedr et al., 2009; Takeuchi et al., 2009; Greffes et al., 2010; Jang, 2011). Many studies have reported that application of rTMS on the unaffected hemisphere could result in improvement of the motor function of the affected hand in stroke patients (Mansur et al., 2005; Takeuchi et al., 2005; Liepert et al., 2007; Kirton et al., 2008; Takeuchi et al., 2008; Khedr et al., 2009; Takeuchi et al., 2009). In addition, a few functional neuroimaging studies have demonstrated the immediate effect of a single session of rTMS on the unaffected motor cortex in stroke patients (Nowak et al., 2008; Conchou et al., 2009; Greffes et al., 2010). However, no functional neuroimaging study on the effect of application of rTMS on the unaffected motor cortex for several sessions in stroke patients has been reported. In this study, we report on a patient with a cerebral infarct in whom activation of the unaffected motor cortex disappeared after application of rTMS for 2 weeks, as evaluated by fMRI.

A 50-year-old right-handed male patient exhibited severe paralysis of his left upper and lower extremities after coronary artery bypass graft surgery for treatment of coronary artery disease. He was diagnosed as having an infarction in the right middle cerebral artery (MCA) territory, including the precentral knob (Figure 1A). Four weeks after onset, he was transferred to the rehabilitation department of a university hospital in order to undergo rehabilitation. The patient exhibited severe weakness of the left hand (finger flexor: Medical Research Council (MRC)[2–4], finger extensor: MRC[0]) with moderate weakness of other muscles of the left upper and lower extremities (MRC[2–4]) (Table 1).

The patient underwent a comprehensive rehabilitative management program, including movement therapy, medications and neuromuscular electrical stimulation therapy. After 4 weeks of intensive rehabilitation (8 weeks after onset), the patient showed motor recovery of the left hand (finger flexor: MRC[4], finger extensor: MRC[3]) with other muscles as MRC 4–4+. He was able to perform some fine motor activity, as much as 5 (normal range: 13.8 ± 1.5) on the Purdue pegboard score [Kim et al., 1994], however, grade 3 mirror movements (strong and sustained repetitive movement) on Woods and Teuber’s study were observed in the right fingers during movement of the left fingers (Woods and Teuber, 1978). At 10 weeks after onset, the fine motor ability of the left hand showed improvement, with a Purdue pegboard score of 7, and no mirror movement of the right fingers were observed during movements of the left fingers.

Blood oxygen level-dependent (BOLD) fMRI measurements using the echo planar imaging (EPI) technique were performed twice, at 8 weeks and 10 weeks after onset, using a 1.5-T Philips Gyroscan Intera scanner (Hoffman-LaRoche, Ltd., Best, the Netherlands) with a standard head coil. The patient was examined while in a supine position and was firmly immobilized in order to prevent motion in the fMRI scanner. Using a block paradigm (21-second control, 21-second stimulation: 3 cycles), hand grasp-release movements (1 Hz) were performed for stimulation. SPM 8 software (Wellcome Department of Cognitive Neurology, London, UK) running in the MATLAB environment was used for analysis of fMRI data. Statistical parametric maps were obtained, and voxels of cluster level were considered significant at a threshold of uncorrected \( P < 0.001 \).
Figure 1 T2-weighted and functional MRI (fMRI) images of a 50-year-old male patient with right middle cerebral artery occlusion (MCAO) exhibiting severe paralysis of his left upper and lower extremities. (A) T2-FLAIR images showing an infarct in the right middle cerebral artery territory including the precentral knob (blue arrow). (B) Bilateral primary somatosensory–motor cortices (S1Ms) were activated during movement of the affected (left) hand on 8-week fMRI images. On 10-week fMRI images, the left SM1 activation (red arrows) had disappeared and activation of the right primary somatosensory cortex (blue arrows) was observed during movements of the left hand. By contrast, bilateral SM1 were activated during movements of the right hand on both 8-week and 10-week fMRI images.

period. In conclusion, we demonstrated the disappearance of activation of the unaffected motor cortex by 12 sessions of rTMS in a stroke patient. Recovery of motor function of the affected hand appeared to have occurred through bi-hemispherical reorganization, and, subsequently, peri-lesional reorganization. Because the methods and results of this study can be applied for rehabilitation in stroke patients who show activity of the unaffected motor cortex, we believe that our results have important implications for stroke rehabilitation. However, because it is a case report, this study is limited. Conduct of further complementary studies involving larger numbers of cases is warranted.

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Table 1 Changes of motor function in the patient with cerebral infarct

| Weeks after onset | Onset | 4 | 8 | 10 |
|------------------|-------|---|---|----|
| MRC Shoulder abductor | 2 | 2* | 4 | 4 |
| Elbow flexor | 2 | 2* | 4 | 4 |
| Finger flexor | 0 | 2 | 4 | 4 |
| Finger extensor | 0 | 0 | 3 | 4 |
| Hip flexor | 2 | 3* | 4* | 4 |
| Knee extensor | 2 | 4* | 4* | 4 |
| Ankle dorsiflexor | 2 | 4* | 4* | 4 |
| PPT | 0 | 0 | 5 | 7 |
| MM | – | – | G3 | G0 |

Medical Research Council (MRC): 0, no contraction; 1, palpable contraction, but no volitional movement; 2, movement against resistance equal to the maximum resistance overcome by the healthy side; 3, movement against resistance less than the maximum resistance overcome by the healthy side. Mirror movement was assessed with the modified Woods and Teuber scale: grade 0, no clearly imitative movement on contralateral homologous regions; 1, very mild MM or increased tone; 2, a slight but unsustained repetitive movement; 3, a definite repetitive movement, less than ½ range of motion (ROM) of the metacarpophalangeal joint in the unaffected hand; 4, a stronger repetitive movement, more than ½ ROM of the metacarpophalangeal joint in the unaffected hand; 5, a movement equal to that expected of the intact hand. PPT: Purdue pressure test; MM: Mirror movement. Movement: –: uncheckable.