Cortical Activation Changes Associated with Motor Recovery in Mild Hemiparetic Patients with Corona Radiata Infarct

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Abstract. [Purpose] We attempted to demonstrate the changes in cortical activation with motor recovery in hemiparetic patients who showed mild weakness at onset and excellent recovery, using functional MRI (fMRI). [Methods] Six patients (mean age 49.83 ± 8.75) with corona radiata infarct were recruited for this study. The motricity index for the upper extremity, the Medical Research Council classification for finger extensors, and the modified Brunnstrom classification were used to determine the motor function of the affected upper limb. fMRI was performed twice, after onset and after recovery, at 1.5 T in parallel with hand grasp-release movements at a fixed rate. The laterality index was calculated from the fMRI to assess the relative activity of the ipsilateral versus the contralateral primary sensorimotor cortex. [Results] There were significant improvements in motor function tests and the laterality index between the first and second fMRI. However, the interval changes of motor function tests were not significantly correlated with those of the laterality index of the affected hemisphere. [Conclusion] The patients who showed mild weakness at onset and excellent recovery had cortical activation that changed towards contralateral motor cortex activation from bilateral motor cortex activation during the recovery phase. This finding has important clinical implications with regard to the motor recovery mechanism and the scientific rehabilitation of stroke patients.

Key words: Functional MRI, Stroke, Motor recovery, Cortical reorganization

INTRODUCTION

Elucidation of the changes in cortical activation with motor recovery is important for stroke rehabilitation because such information can be used to develop treatment methods or rehabilitative strategies for hemiparetic stroke patients. It is well known that, in stroke patients, cortical activities change according to motor recovery from activation of the bilateral motor cortex following onset, to activation of the contralateral (ipsi-lesional) motor cortex1–7). Because the persistence of the ipsilateral motor cortex activity is related to poor motor function8–10), the inhibition of ipsilateral motor cortex activity and facilitation of contralateral motor cortex activity during the motor recovery phase could be an important strategy for good motor recovery in hemiparetic stroke patients.

Many studies have reported on the changes in cortical activity with motor recovery in stroke patients1–7,11). However, most of the previous studies have focused on stroke patients with severe
weakness. Therefore, little is known as to whether this principle can be applied to patients that show mild weakness at the time of onset. This type of patient was frequently observed in clinical settings, but they may be neglected in terms of rehabilitative management\textsuperscript{2,11}).

In the current study, using functional MRI (fMRI), we attempted to demonstrate the changes in cortical activation with motor recovery in hemiparetic patients with corona radiata infarct who showed mild weakness at onset and excellent recovery.

**METHODS**

We recruited ten consecutive hemiparetic patients with cerebral infarct on the corona radiata. Six patients completed this study (four males, mean age 49.83 ± 8.75, range 39–64). They were confirmed to have no neurological or psychiatric history before stroke attack by analysis of their medical records and brain MRI. All of the enrolled patients gave their written informed consent prior to this experiment, in accordance with the ethical standards of the Declaration of Helsinki. Inclusive criteria were as followings, (1) Medical Research Council (MRC) scale of all affected upper extremity muscles, except the hand, were above 3 (movement with gravity), and the motor function of the hand was above modified Brunnstrom classification (MBC) 4 (able to grasp a card between thumb and medial side of index finger, able to extend fingers slightly) at onset; (2) MRC scores of all affected upper extremity muscles were 5 (movement against a resistance equal to the maximum resistance overcome by the healthy side) at the second fMRI; (3) an infarct confirmed by a neuroradiologist at the level of the corona radiata which explained the upper extremity weakness\textsuperscript{12,13}). (4) no severe spasticity (modified Ashworth’s scale < 2) or tremor of the affected upper extremity; and (5) no evidence of other serious associated problems (aphasia, attention deficits, Mini-Mental State Examination < 25, or visual neglect). Three of the six patients had left hemiparesis.

The motricity index (MI) for the upper extremity, the MRC for finger extensors, and the MBC were used to determine the motor function for the affected hand\textsuperscript{14–17}). The reliability and validity of MI, MRC, and MBC are well-established\textsuperscript{14–17}). Mirror movement (MM) in this study was defined as unintentional movement in the unaffected hand evoked by intentional movement of the affected hand. The severity of MM was scored at the time of the fMRI scanning according to Woods and Teuber’s criteria\textsuperscript{18}).

The patients were examined supine with their eyes closed, and were secured firmly with the forearm in pronation using an immobilizing frame to minimize the effects of body movement. For the motor task paradigm, finger flexion-extension movements were performed at a frequency of 1 Hz for stimulation, guided by a metronome, over a repeated cycle of 20 seconds of control and 20 seconds of stimulation. Each task paradigm of alternating control-stimulation (40 seconds) was repeated three times. In order to make exact comparisons of interval changes accompanying motor recovery, we performed fMRI at the same rate during the motor task paradigm, and analyzed the fMRI data using the same method. We compared cortical activation of the affected and unaffected hand movements. For each patient, the undamaged hemisphere was used as the control.

The blood oxygenation level dependent (BOLD) fMRI measurement, which employs the Echo Planar Imaging (EPI) technique, was performed using a 1.5T MR scanner (Vision, Siemens, Erlangen, Germany) with a standard head coil. For the anatomic base images, 13 axial, 5-mm thick, T1-weighted, conventional, spin echo images were obtained with a matrix size of 128 × 128 and a field of view (FOV) of 210 mm, parallel to the bicommissure line of the anterior commissure-posterior commissure (AC-PC). The EPI BOLD images were acquired over the same 13 axial sections for each epoch, producing a total of 780 images for each subject. The imaging parameters for each experiment consisted of TR/TE = 2 sec/60 msec, FOV = 210 mm, matrix size = 64 × 64, and slice thickness = 5 mm. fMRI data were analyzed using SPM-99 software (Wellcome Department of Cognitive Neurology, London, UK) running under the MATLAB environment (The Mathworks, Inc., Natick, Ma, USA). The images were then smoothed with an 8-mm isotropic Gaussian kernel. Statistical parametric maps were obtained, and voxels were considered significant at a threshold of p<0.001, uncorrected.

Regions of interest were drawn around the primary sensorimotor cortex (SM1). The SM1 centered to the precentral knob extended from the
precentral to the postcentral gyrus. The laterality index (LI) for the SM1 was calculated in order to compare the relative activity in the ipsilateral SM1 versus the contralateral SM1. LI was defined using the equation below.

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\text{Laterality Index} = \frac{(\text{contralateral SM1 voxel count} - \text{ipsilateral SM1 voxel count})}{(\text{contralateral SM1 voxel count} + \text{ipsilateral SM1 voxel count})}
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Where the contralateral SM1 voxel is the active voxel count for the ROIs in the hemisphere contralateral to the hand performing the movement and the ipsilateral SM1 voxel is the active voxel count for the corresponding region in the hemisphere ipsilateral to the performing hand. The possible range of the LI is from 1.0 (all activity in the contralateral hemisphere) to –1.0 (all activity in the ipsilateral hemisphere).

The second fMRI evaluation was performed when patients’ motor function in MI, MRC, MBC, and LI for the affected SM1 increased up to the maximum grade, except LI for the affected SM1 (0.93) in patient 2, and the scores for MM decreased. The interval changes in all variables showed significant differences (p<0.05). Spearman’s non-parametric test showed that interval changes of motor function tests (MI, MRC, MM, and MBC) were not significantly correlated with those of LI for the affected SM1 (p>0.05).

The findings of fMRI indicate that the bilateral sensorimotor cortex was activated in all of our patients during their affected hand movements at the first scanning. However, at the second scanning, only the contralateral sensorimotor cortex was focally activated in all patients, except patient 2, who showed bilateral sensorimotor cortex activation that had shifted from the bilateral to contralateral hemisphere in the interval between the first and the second scans.

### RESULTS

For all of our patients, the scores for MI, MRC, MBC, and LI for the affected SM1 increased up to the maximum grade, except LI for the affected SM1 (0.93) in patient 2, and the scores for MM decreased. The interval changes in all variables showed significant differences (p<0.05). Spearman’s non-parametric test showed that interval changes of motor function tests (MI, MRC, MM, and MBC) were not significantly correlated with those of LI for the affected SM1 (p>0.05).

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### DISCUSSION

This study was designed to investigate the changes of cortical activation due to motor recovery of hemiparetic patients with mild weakness at onset and excellent recovery. We adapted the MI, MRC,
Fig 1. T2-weighted brain MR images (column A). The T2-weighted image shows the ischemic infarction in the corona radiata (arrow). The first (column B) and second functional MRI (column C) show that the activities in the ipsilateral primary sensorimotor cortex disappeared in all of the patients except for one patient (patient 2), in whom the activities in the ipsilateral primary sensorimotor cortex decreased.
MM, and MBC to assess the motor function of the paralyzed limbs at the first and second evaluations, and calculated LI to measure the hemispheric lateralization of hand motor function from functional activation patterns. The cortical activation changed from bilateral motor cortex activation towards contralateral motor cortex activation with motor recovery in all patients with corona radiata infarct. However, the degree of motor function change was not significantly correlated with the LI change of the affected hemisphere. For this reason, we think that the improvements of motor function between the first and second MRI were relatively small, because only patients with mild weakness were recruited, and the sample size was small. We focused on analysis of the primary motor cortex, because many previous fMRI and transcranial magnetic stimulation (TMS) studies have reported that change in the activation of the primary motor cortex among the various cortical areas is closely related with motor recovery irrespective of the other cortical areas\textsuperscript{1–7,11}. The results of the present study are in agreement with those of previous studies, which found that the bihemispheral reorganization mechanism underlying motor recovery evolved from activation of the ipsilateral primary sensorimotor cortex at the subacute stage to activation of the contralateral primary sensorimotor cortex at the chronic stage\textsuperscript{1–7}). However, most previous studies primarily recruited patients with severe weakness and few previous studies included patients with mild motor weakness, while some studies did not provide exact information on the state of motor weakness of each patient\textsuperscript{1–7}). Takeda et al. have reported on the changes in cortical activation of patients with mild motor weakness, although four of five patients had lesions that were not related to the CST injury (for example, thalamic, putaminal, or frontal infarct)\textsuperscript{7}). Recently, Foltys et al. reported that patients with rapid and good recovery showed bilateral motor cortex activation using fMRI, at an early stage after stroke onset but without follow-up fMRI scanning\textsuperscript{11}). In the current study, we recruited only patients who experienced a CST injury at the corona radiata, and we performed follow-up fMRI scanning after excellent recovery.

Mirror movements (MM) are involuntary movements involving one side of the body that occur as mirror reversals of the intended movement on the other side of the body\textsuperscript{18,19}). The decrement in the severity of MM was closely related to the decrement in the ipsilateral motor cortex activity and with motor recovery in this study. These results are also in agreement with those of previous studies, indicating that the underlying pathophysiological mechanism of MM is activity of ipsilateral motor cortex, and that the severity of MM is inversely correlated with the motor function of the affected hand\textsuperscript{6,19}). It seems that the severities of the ipsilateral motor cortex activity, MM, and motor function are closely related, but additional complementary studies involving larger case numbers are warranted.

It is anticipated that the manipulation of brain plasticity will become the main topic of the field of stroke rehabilitation in the near future\textsuperscript{20}). According to previous studies in normal subjects, the activity of the ipsilateral primary motor cortex can be altered using various rehabilitative interventions\textsuperscript{21–28}). More forceful, complex, longer tasks or repetitive TMS (rTMS) can facilitate ipsilateral primary motor cortex activation and, conversely, the ipsilateral primary motor cortex can be inhibited by rTMS or specific motor tasks. Recent rTMS studies have demonstrated that the application of rTMS to the ipsilateral primary motor cortex can improve the motor function of the affected hand in stroke patients\textsuperscript{29,30}). Therefore, it seems that the ipsilateral primary motor pathway can be manipulated by rehabilitative therapies.

The clinical significance of this study would be that stroke patients who show mild weakness at onset and excellent recovery also experience changes in cortical activation similar to those experienced by stroke patients with severe weakness. This means that less severely affected stroke patients should also undergo rehabilitative management to inhibit the ipsilateral primary motor cortex during the motor recovery phase in order to shorten the recovery time or get a better motor outcome. As such, one potentially important topic of study may be when the ipsilateral primary motor cortex activity disappears during the recovery phase. However, little is currently known about this topic. Recently, Takeda et al. suggested that the increase in ipsilateral motor cortex activation may have played an important role within one month after onset in five stroke patients with an infarct\textsuperscript{7}). This period could be the critical period for manipulating the ipsilateral motor cortex activity in hemiparetic stroke patients. Also, this finding has
important implications in terms of motor recovery and scientific rehabilitation of stroke patients. It is a limitation of the present study that the sample size was small. We suggest that further research should focus on the critical period of ipsilateral motor pathway after stroke and rehabilitative intervention for the manipulation of the motor cortex activities, with larger sample populations.

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REFERENCES


