

● IMAGING IN NEURAL REGENERATION

Changes in cortical activation patterns accompanying somatosensory recovery in a stroke patient: a functional magnetic resonance imaging study

The somatosensory system plays a crucial role in executing precise movements by providing sensory feedback (Farrer et al., 2003; Rabin and Gordon, 2004). Somatosensory dysfunction is a common problem following stroke. In particular, somatosensory impairments, such as impairment in touch, proprioception, light touch, and vibration have been frequently observed (Carey et al., 1993; Sullivan and Hedman, 2008; Tyson et al., 2008). Patients with somatosensory dysfunction show negative effects on motor control, and it sometimes becomes difficult to perform daily activities independently. In addition, these patients require more time to recover functions compared with those without somatosensory deficits (Doyle et al., 2010; Sommerfeld and von Arbin, 2004; Sullivan and Hedman, 2008). Therefore, a better understanding of the recovery mechanism underlying somatosensory dysfunction is necessary for a successful neurorehabilitation outcome.

The neural mechanism of somatosensory recovery after stroke has been relatively less investigated compared with motor recovery (Wikstrom et al., 2000; Gallien et al., 2003; Tecchio et al., 2006; Roiha et al., 2011). Previous studies have studied the mechanism underlying somatosensory recovery, which is related to reorganization of the ipsilesional primary and bilateral secondary somatosensory cortices. Perilesional reorganization in the same hemisphere or contralesional somatosensory activation is also involved in somatosensory recovery (Carey et al., 1993, 2002; Cramer et al., 2000; Jang et al., 2010, 2011, 2013). However, the neural mechanism underlying the recovery of somatosensory function following stroke is unclear.

In the current study, we report a stroke patient with severe somatosensory dysfunction showing changes in cortical activation patterns following somatosensory recovery using functional magnetic resonance imaging (fMRI).

A 47-year-old, right-handed patient with brain infarction presented with severe somatosensory dysfunction of the right hand was admitted to the local hospital for rehabilitative treatment. T2-weighted MR images, which were taken at 5 weeks after onset, displayed lesions in the left primary somatosensory cortex (S1), insula, corona radiata, and frontotemporo-parietal (F-T-P) lobe (**Figure 1**). Starting from 2 weeks after onset, the patient underwent rehabilitative treatment at the rehabilitation department of the hospital. The subscale for tactile sensation (full mark: 20 points) of the Nottingham Sensory Assessment (NSA) was used to determine the somatosensory function (Lincoln et al., 1998).

Tactile sensation was scored as follows: 0 (absent – fails to identify the test sensation on three occasions), 1 (impaired – identifies the test sensation, but not on all three occasions in each region of the body), 2 (normal – correctly identifies the test sensation on all three occasions). The reliability and validity of the NSA are well-established (Lincoln et al., 1998).

Ten right-handed normal control subjects (five males; mean ages: 27.1 ± 3.6 years) with no history of neurological disease were enrolled in this study *via* a notice about recruitment for study.

fMRI: (1) Task performance: The subject was examined in a supine position with eyes closed and was firmly secured with forearm pronated. The task consisted of two conditions using a block paradigm: stimulated condition (21 seconds) and baseline rest condition (21 seconds). During stimulated condition, tactile stimulation was applied on the dorsum of the hand distal to the metacarpophalangeal joint using a rubber brush at a frequency of 1 Hz. Two alternative cycles were repeated three times. fMRI and T2-weighted MR images were conducted at 5 weeks and 6 months after onset. (2) Scan acquisition and data analysis: Blood oxygenation level dependent (BOLD) fMRI was measured at 4 years after onset using the Echo Planar Imaging (EPI) technique using a 1.5-T Philips Gyroscan Intera scanner (Hoffman-LaRoche, Ltd., Best, the Netherlands) with a standard head coil. For functional imaging, BOLD-weighted EPI image parameters consisted of repetition time/echo time = 2 s/60 ms, field of view (FOV) = 210 mm, flip angle = 90°, matrix size = 64 × 64, and slice thickness = 5 mm. For anatomical reference image, 20 axial, 5-mm thick, T1-weighted spin echo images were obtained with a matrix size of 128 × 128 and an FOV of 210 mm, parallel to the bicommissure line of the anterior commissure–posterior commissure. We acquired a total of 2,400 images for each subject.

fMRI data process and analysis were accomplished using Statistical Parametric Mapping (SPM 8, Wellcome Department of Cognitive Neurology, London, UK) running in an MATLAB environment (The Mathworks, Natick, MA, USA). All images were realigned, co-registered, and spatially normalized. Then, data were spatially smoothed with an 8-mm isotropic Gaussian kernel to reduce anatomical and functional variability between subjects. For changes in BOLD signal, rest condition data were subtracted from the stimulated condition data. Next, images were averaged across all normal control subjects using group analysis. SPM *t*-maps were computed, and voxels were considered significant at a threshold of $P < 0.05$, uncorrected. Activations were based on the extent of the size of five contiguous voxels. Regions of interest (ROIs) were drawn around the primary sensory-motor cortex (SM1) and supplementary motor area (SMA).

For the tactile sensation score of the NSA, the patient showed improvement from 2 points (5 weeks after onset) to 10 points (6 months after onset). In the results of the fMRI analysis, we found different activated brain areas between the two tasks in response to tactile stimulation. At 5 weeks after onset, cortical activation was observed on the ipsile-

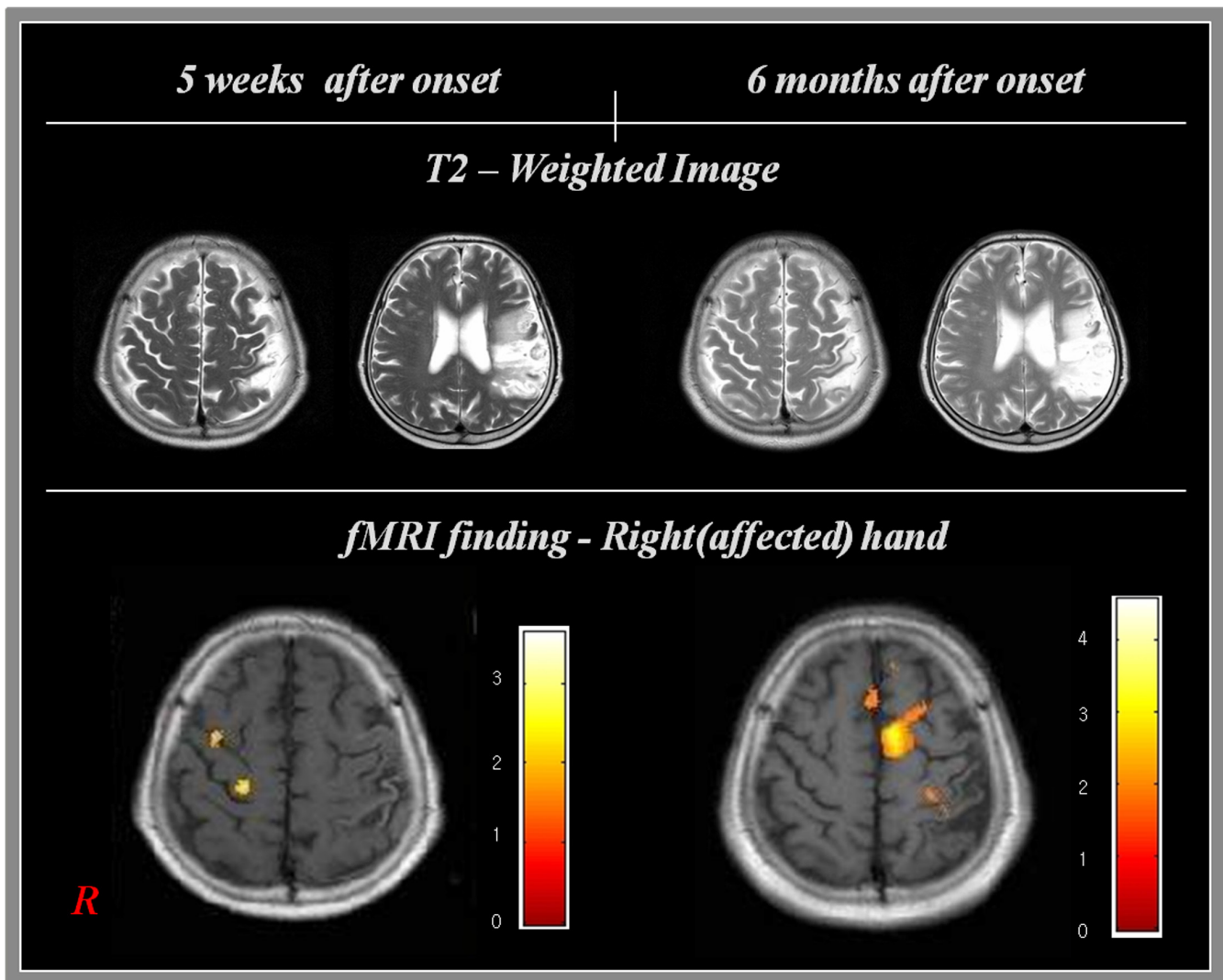


Figure 1 T2-weighted brain magnetic resonance images (above) and functional magnetic resonance images (below) of a 47-year-old patient with stroke were taken at 5 weeks and 6 months after stroke onset. T2-weighted brain magnetic resonance images display lesions in the left primary somatosensory cortex (S1), insula, corona radiata, and fronto-temporoparietal (F-T-P) lobe. Functional magnetic resonance images show changes in cortical activation patterns on the ipsilesional primary sensory-motor cortex (SM1) and contralateral SM1 as well as the supplementary motor area (SMA). The gradient of color indicates statistical value, such as *t*-value. R: Right.

Table 1 Talairach coordinates and *t*-value for peak activation in the activated clusters during tactile stimulation in the stroke patient and healthy controls

Tactile sensation (NAS score)	Brain region (Talairach coordinate (x, y, z, [mm]); <i>t</i> -value)
Patient	
2 points at 5 weeks after onset	Ipsilesional SM1 (20, -24, 62; 2.56)
10 points at 6 months after onset	Contralateral SM1 (-30, -26, 60; 2.26); contralateral SMA (-10, 6, 54; 3.82)
Controls	Contralateral SM1 (-40, -22, 56; 16.61); contralateral SMA (-2, -16, 52; 3.06)

NAS: the Nottingham Sensory Assessment; SM1: primary sensory-motor cortex; SMA: supplementary motor area.

sional SM1 (voxel count: 159) during tactile stimulation on the affected (right) hand. The Talairach coordinate (mm) and *t*-value for peak activation were located at right M1 ($x = 20, y = -24, z = 62; 2.56$). At 6 months after onset, cortical activated clusters were observed on the contralateral SM1 (voxel count: 87) and SMA (voxel count: 1,148). The Talairach

coordinates and *t*-value were located at left M1 ($x = -30, y = -26, z = 60; 2.26$) and SMA ($x = -10, y = 6, z = 54; 3.82$).

For the results of the group analysis for control subjects, cortical activated clusters were observed around the contralateral SM1 (voxel count: 9,950) and SMA (voxel count: 132) during right hand stimulation. The Talairach coordinates

(mm) and *t*-value for peak activation on the activated clusters were located at contralateral S1 ($x = -40, y = -22, z = 56; 16.61$) and SMA ($x = -2, y = -16, z = 52; 3.06$). The results are summarized in **Table 1**.

We measured changes in brain activation patterns in response to tactile stimulation on the affected hand of a patient using fMRI scans at 5 weeks and 6 months after stroke onset. Regarding changes in brain activation patterns between the two fMRI measurements, SM1 ipsilesional to the affected hand in the pre-fMRI scans disappeared, whereas activation of the contralateral SM1 and SMA was newly observed in the post-fMRI scans. These fMRI findings were equivalent to the brain activation patterns of our normal subjects, which received the same tactile sensory stimulation. In addition to brain activation changes in the neuroimaging findings, tactile sensory function of the patient prominently improved during the NSA test. These results suggest that brain activation patterns similar to the control subjects showed a tendency to be normalized according to improvement of actual sensory function.

Consistent with the findings of our study, many previous investigations have suggested converging evidence clarifying the neural mechanism of sensory reorganization concomitant with somatosensory recovery in stroke patients (Cramer et al., 2000; Ward et al., 2006; Jang et al., 2010; Roiha et al., 2011). Perilesional reorganization, secondary somatosensory cortex, recovery of injured somatosensory pathway, and contribution of unaffected somatosensory cortex have been generally accepted as the possible mechanisms of somatosensory reorganization (Carey and Seitz, 2007; Johansen-Berg, 2007; Rossini et al., 2007; Buma et al., 2010; Jang, 2013). Based on our findings of the pre-fMRI scans, we are convinced that contralesional SM1 activation was due to an unaffected somatosensory cortex. Several studies have reported that stroke patients presenting with activation of the unaffected sensory cortex by stimulation of the affected corresponding body area also show poor improvement in somatosensory function (Weder et al., 1994; Taskin et al., 2006; Jang, 2013). Our case also demonstrates poor somatosensory function similar to these previous reports.

However, alteration of brain activation patterns relevant to the same tactile sensory stimulation was observed in our post-fMRI scan findings, accompanied by improvement in sensory perception. Ipsilesional activation is already known as a positive predictor of improved sensory function (Carey et al., 2002; Staines et al., 2002; Rossini et al., 2007; Jang, 2011). According to previous studies (Carey et al., 2002, 2011; Staines et al., 2002; Rossini et al., 2007), activation of the ipsilesional SM1 is associated with sensory recovery, and preservation of this region results in relatively mild impairment. In addition, Weder et al. (1994) suggested that bilateral SM1 activation or distributed cortical activation induces more severe impairment in somatosensory perception.

This case study provides insights into the recovery mechanism of somatosensory function in stroke patient. Brain activation pattern responding to tactile sensory stimulation showed a tendency toward normalization of neural activity

in a stroke patient with cortical and subcortical lesions accompanying recovery of somatosensory function. In addition, this study is limited to a single case report, and further studies including a larger sample size need to be performed.

Yong Hyun Kwon¹, Mi Young Lee²

1 Department of Physical Therapy, Yeungnam University College, Namgu, Daegu, 705-703, Republic of Korea

2 Department of Physical Therapy, College of Health and Therapy, Daegu Haany University, Gyeongsan-si, Gyeongsangbuk-do, 712-715, Republic of Korea

Corresponding author: Mi Young Lee, Ph.D., Department of Physical Therapy, College of Health and Therapy, Daegu Haany University, 1, Haanyaero, Gyeongsan-si, Gyeongsangbuk-do, 712-715, Republic of Korea, mykawai@hanmail.net.

Funding: This study was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning, No. 2013R1A1A3007734.

Author contributions: Lee MY designed this study and collected experimental data. Kwon YH provided technical assistance and supervised the study. Both of these two authors wrote the manuscript, provided critical revision of the manuscript for intellectual content and approved the final version of the paper.

Conflicts of interest: None declared.

doi:10.4103/1673-5374.139468 <http://www.nrronline.org/>

Accepted: 2014-07-06

Kwon YH, Lee MY. Changes in cortical activation patterns accompanying somatosensory recovery in a stroke patient: a functional magnetic resonance imaging study. *Neural Regen Res.* 2014;9(15):1485-1488.

References

- Buma FE, Lindeman E, Ramsey NF, Kwakkel G (2010) Functional neuroimaging studies of early upper limb recovery after stroke: a systematic review of the literature. *Neurorehabil Neural Repair* 24:589-608.
- Carey LM, Matyas TA, Oke LE (1993) Sensory loss in stroke patients: effective training of tactile and proprioceptive discrimination. *Arch Phys Med Rehabil* 74:602-611.
- Carey LM, Abbott DF, Puce A, Jackson GD, Syngeniotis A, Donnan GA (2002) Reemergence of activation with poststroke somatosensory recovery: a serial fMRI case study. *Neurology* 59:749-752.
- Carey LM, Seitz RJ (2007) Functional neuroimaging in stroke recovery and neurorehabilitation: conceptual issues and perspectives. *Int J Stroke* 2:245-264.
- Carey LM, Abbott DF, Harvey MR, Puce A, Seitz RJ, Donnan GA (2011) Relationship between touch impairment and brain activation after lesions of subcortical and cortical somatosensory regions. *Neurorehabil Neural Repair* 25:443-457.
- Cramer SC, Moore CI, Finklestein SP, Rosen BR (2000) A pilot study of somatotopic mapping after cortical infarct. *Stroke* 31:668-671.
- Doyle S, Bennett S, Fasoli SE, McKenna KT (2010) Interventions for sensory impairment in the upper limb after stroke. *Cochrane Database Syst Rev* (6):CD006331.
- Farrer C, Franck N, Paillard J, Jeannerod M (2003) The role of proprioception in action recognition. *Conscious Cogn* 12:609-619.
- Gallien P, Aghulon C, Durufle A, Petrilli S, de Crouy AC, Carsin M, Toulouse P (2003) Magnetoencephalography in stroke: a 1-year follow-up study. *Eur J Neurol* 10:373-382.
- Jang SH (2011) Contra-lesional somatosensory cortex activity and somatosensory recovery in two stroke patients. *J Rehabil Med* 43:268-270.
- Jang SH (2013) Recovery mechanisms of somatosensory function in stroke patients: implications of brain imaging studies. *Neurosci Bull* 29:366-372.



- Jang SH, Ahn SH, Lee J, Cho YW, Son SM (2010) Cortical reorganization of sensori-motor function in a patient with cortical infarct. *NeuroRehabilitation* 26:163-166.
- Johansen-Berg H (2007) Functional imaging of stroke recovery: what have we learnt and where do we go from here? *Int J Stroke* 2:7-16.
- Lincoln N Jackson JM, Adams SA (1998) Reliability and revision of the Nottingham Sensory Assessment for stroke patients. *Physiotherapy* 84:358-365
- Rabin E, Gordon AM (2004) Tactile feedback contributes to consistency of finger movements during typing. *Exp Brain Res* 155:362-369.
- Roiha K, Kirveskari E, Kaste M, Mustanoja S, Makela JP, Salonen O, Tatlisumak T, Forss N (2011) Reorganization of the primary somatosensory cortex during stroke recovery. *Clin Neurophysiol* 122:339-345.
- Rossini PM, Altamura C, Ferreri F, Melgari JM, Tecchio F, Tombini M, Pasqualetti P, Vernieri F (2007) Neuroimaging experimental studies on brain plasticity in recovery from stroke. *Eura Medicophys* 43:241-254.
- Sommerfeld DK, von Arbin MH (2004) The impact of somatosensory function on activity performance and length of hospital stay in geriatric patients with stroke. *Clin Rehabil* 18:149-155.
- Staines WR, Black SE, Graham SJ, McIlroy WE (2002) Somatosensory gating and recovery from stroke involving the thalamus. *Stroke* 33:2642-2651.
- Sullivan JE, Hedman LD (2008) Sensory dysfunction following stroke: incidence, significance, examination, and intervention. *Top Stroke Rehabil* 15:200-217.
- Taskin B, Jungehulsing GJ, Ruben J, Brunecker P, Krause T, Blankenburg F, Villringer A (2006) Preserved responsiveness of secondary somatosensory cortex in patients with thalamic stroke. *Cereb Cortex* 16:1431-1439.
- Tecchio F, Zappasodi F, Tombini M, Oliviero A, Pasqualetti P, Vernieri F, Ercolani M, Pizzella V, Rossini PM (2006) Brain plasticity in recovery from stroke: an MEG assessment. *Neuroimage* 32:1326-1334.
- Tyson SF, Hanley M, Chillala J, Selley AB, Tallis RC (2008) Sensory loss in hospital-admitted people with stroke: characteristics, associated factors, and relationship with function. *Neurorehabil Neural Repair* 22:166-172.
- Ward NS, Brown MM, Thompson AJ, Frackowiak RS (2006) Longitudinal changes in cerebral response to proprioceptive input in individual patients after stroke: an fMRI study. *Neurorehabil Neural Repair* 20:398-405.
- Weder B, Knorr U, Herzog H, Nebeling B, Kleinschmidt A, Huang Y, Steinmetz H, Freund HJ, Seitz RJ (1994) Tactile exploration of shape after subcortical ischaemic infarction studied with PET. *Brain* 117:593-605.
- Wikstrom H, Roine RO, Aronen HJ, Salonen O, Sinkkonen J, Ilmoniemi RJ, Huttunen J (2000) Specific changes in somatosensory evoked magnetic fields during recovery from sensorimotor stroke. *Ann Neurol* 47:353-360.

Copyedited by Li CH, Song LP, Zhao M