

A Pilot Study of Somatotopic Mapping After Cortical Infarct

Steven C. Cramer, MD; Christopher I. Moore, PhD;
Seth P. Finklestein, MD; Bruce R. Rosen, MD, PhD

Background and Purpose—Animal studies have described remodeling of sensory and motor representational maps after cortical infarct. These changes may contribute to return of function after stroke.

Methods—Functional MRI was used to compare sensory and motor maps obtained in 35 normal control subjects with results from 2 patients with good recovery 6 months after a cortical stroke.

Results—During finger tapping in controls, precentral gyrus activation exceeded or matched postcentral gyrus activation in 40 of 42 cases. Patient 1 had a small infarct limited to precentral gyrus. Finger tapping activated only postcentral gyrus, a pattern not seen in any control subject. During tactile stimulation of a finger or hand in controls, postcentral gyrus activation exceeded or matched precentral gyrus activation in 11 of 14 cases. Patient 2 had a small infarct limited to postcentral gyrus and superior parietal lobule. Tactile stimulation of the finger activated only precentral gyrus, a pattern not seen in any control. In both patients, activation during pectoralis contraction was medial to the site activated during finger tapping.

Conclusions—Results during finger tapping (patient 1) and finger stimulation (patient 2) may reflect amplification of a preserved component of normal sensorimotor function, a shift in the cortical site of finger representation, or both. Cortical map reorganization along the infarct rim may be an important contributor to recovery of motor and sensory function after stroke. Functional MRI is useful for assessing motor and sensory representational maps. (*Stroke*. 2000;31:668-671.)

Key Words: magnetic resonance imaging ■ neuronal plasticity ■ stroke recovery

Animal studies suggest that intact cortical regions surrounding an infarct may contribute to return of function. Potentially relevant changes that have been described within peri-infarct cortex include an increase in dendrites, synapses, and levels of proteins related to axonal outgrowth.¹⁻³ Pharmacological interventions that amplify these cellular events, such as amphetamine,¹ basic fibroblast growth factor,² or nerve growth factor,³ have been associated with improved outcome. In association with these cellular events, studies of animals recovered from a cortical stroke show reorganization of motor and sensory representational maps along the infarct rim.^{4,5}

Functional imaging studies in patients recovering from hemiparetic stroke have described a number of changes in cortical function. In the nonstroke hemisphere, increased cerebral blood flow (CBF) and enlarged activation volume have been described in several areas, including sensorimotor cortex and premotor cortex.⁶⁻⁹ Similar changes have been described in the infarct hemisphere, with concordant results from studies using transcranial magnetic stimulation.¹⁰ Most of these studies have used a single task to activate the brain. Seitz et al⁹ evaluated recovered stroke patients with 2

different tasks, but both entailed movement of the same body region. Some studies have identified a shift in the site of contralateral sensorimotor cortex activation during a motor task by the recovered hand^{6,8,11}; however, each assessed only a single element within the cortical representational map.

Reorganization of cortical representational maps likely contributes to stroke recovery. Better insights into stroke recovery might be facilitated by the development of techniques that noninvasively measure reorganization of multiple cortical map elements along the infarct rim. In this pilot study, functional MRI (fMRI) was used to evaluate sensory and motor activation in 2 patients recovered from a small peri-Rolandic cortical infarct. Results were compared with findings in control subjects.

Subjects and Methods

Stroke Patients

Echo-planar (EPI) and conventional images were obtained using a 1.5-T General Electric Signa modified by Advanced NMR Systems. A 5-inch surface coil was placed on the scalp over the region of the central sulcus; use of this coil improved signal in the stroke hemisphere at the expense of signal from the contralesional hemisphere. Foam rubber pads and a restraining hook-and-loop fastener tape (Velcro, Velcro USA Inc) band

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From the Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, Mass (S.C.C., S.P.F.); the MGH-NMR Center, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Charlestown, Mass (S.C.C., C.I.M., B.R.R.); and the Clinical Investigator Training Program, Harvard-MIT Division of Health Sciences and Technology and Beth Israel-Deaconess Medical Center (in collaboration with Pfizer Inc) (S.C.C.).

Correspondence to Steven C. Cramer, MD, University of Washington, Department of Neurology, 1959 NE Pacific St, Box 356465, Seattle, WA 98195. E-mail: cramers@u.washington.edu

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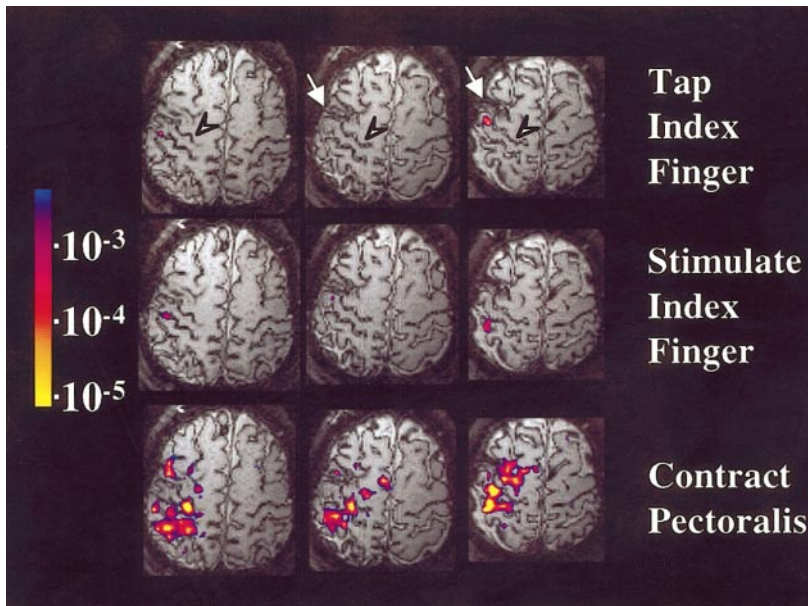


Figure 1. Three contiguous 4-mm axial brain slices are shown for patient 1. A surface coil was placed over the area of the central sulcus of the infarct hemisphere, improving signal locally with a loss of signal over the contralateral (nonstroke) hemisphere. For each task, functional activation maps have been superimposed on anatomic images. The color bar on the left encodes probability value, ie, the probability that a given pixel showed activation by chance. Arrowheads indicate the central sulcus; arrows, the location of the stroke. Patient 1 had an infarct in the right precentral gyrus. Activation during left finger tapping was restricted to the right postcentral gyrus, on the posterior rim of the infarct. No control subject showed this pattern during finger tapping.

across the forehead were used to reduce head motion and hold the surface coil in place. Body movement was limited by placement of bilateral proximal arm straps. Each scanning session included (1) high-resolution volumetric gradient echo images, 2.8 mm thickness, (2) high-resolution EPI anatomic images in plane with functional images, (3) a measurement of relative CBF, and (4) 6 runs of blood oxygenation level-dependent (BOLD) contrast functional images, consisting of asymmetric spin-echo images for T2* signal change, with TR of 2 seconds, TE of 70 ms, effective field of view of 20×20 cm, and in-plane resolution of 3.1 mm². Each run contained 15 contiguous 4-mm axial brain slices, with 100 images per slice obtained over 3.3 minutes. The first 2 runs examined 2-Hz tapping by the recovered index finger; the second 2 runs examined 4-Hz tactile stimulation of the distal palmar surface of the same index finger using a 5.88 log₁₀mg von Frey filament; and the third pair of runs examined contraction of the pectoralis on the same body side, during which the medial epicondyle of the patient's supinated and extended forearm was isometrically pressed against the ribcage at 1 Hz. The extended forearm was pronated for tapping studies and supinated for sensory studies. During each run, the patient alternated between 20-second epochs of rest and stimulus. For the motor tasks, the cue to begin and to cease movements was a light tap on the knee; all movements were driven by an auditory metronome presented through headphones. Patients kept eyes closed at all times. All movements were monitored for accurate performance by one of the experimenters standing in the scanner room at the subject's side.

Image analysis was performed on Sun SPARC workstations. Head motion was detected and corrected with image registration software adapted for fMRI.¹² For each task, the second run was normalized to the first; the 2 runs for a given stimulus were then averaged. Statistical maps were generated voxel-by-voxel using a Kolmogorov-Smirnov (KS) test, contrasting images taken during stimulus with those taken at rest. Identification of images as active stimulus or rest was shifted 4 seconds to account for the delay normally seen in the rise of CBF after neuronal activation. To improve the signal-to-noise ratio, statistical maps underwent mild spatial smoothing with a Hanning filter.

To identify the site of activation, the precentral, central, and postcentral sulci were identified on the EPI high-resolution images based on sulcal landmarks¹³ and simultaneous review of the volumetric images reformatted in the 3 cardinal planes. This allowed identification of precentral and postcentral gyri. For each task, the spatial extent of significant ($P<0.001$) activation was noted with respect to these gyri.

Control Subjects

Index finger tapping was studied in 27 normal subjects. Each was studied during 2-Hz index finger tapping by the right hand, then during

tapping by the left hand. Two subjects were imaged with a surface coil and the remainder with a quadrature head coil, using a TR between 1.5 and 2.5 seconds, slice thickness 4 to 7 mm, and 100 to 128 images per slice. Each study was motion corrected, analyzed with a KS test, and smoothed as above. Sites of activation ($P<0.001$) were determined as above.

Tactile stimulation of the right index finger, thumb, or palm during 4-Hz stimulation by a 5.88 log₁₀mg von Frey filament was studied in 8 subjects. Studies used a surface coil placed over the region of the central sulcus, a TR of 2, 4 to 7 mm thick slices, and 128 images per slice. Each study was motion corrected, analyzed with a KS test, smoothed as above, and analyzed with a threshold of $P<0.001$.

Results

Three patients remote from cortical infarction were studied. One had excessive head motion artifact that rendered his statistical maps unusable; his results were excluded from further analysis.

Patient 1 (Figure 1) was a 61-year-old right-handed male. At the time of stroke, 6 months before fMRI scanning, examination showed mild weakness of left face and left hand interossei, with normal sensory examination. MRI revealed an acute right precentral gyrus infarct and a right occipital lobe infarct. Intracranial and extracranial cerebral arteries were normal. He received a brief course of occupational therapy. On the day of fMRI, the patient reported no symptoms. Examination documented only mild hyperreflexia of the left upper extremity and trace weakness of the left hand interossei, with normal sensory examination. The Fugl-Meyer arm motor score was 64 (normal score, 66).

For patient 1, the largest focus of significant activation during left index finger tapping was restricted to the right postcentral gyrus, immediately posterior to the infarct. The largest activation focus during left index finger tactile stimulation was on the superior parietal lobule, directly posterior to the motor activation focus; a small focus was seen on postcentral gyrus inferiorly. The largest activation during pectoralis contraction was on precentral gyrus, medial to the infarct and medial to the postcentral gyrus site activated during finger tapping. Relative perfusion¹⁴ in a single suprasylvian axial slice inferior to the infarct showed no hemispheric asymmetries.

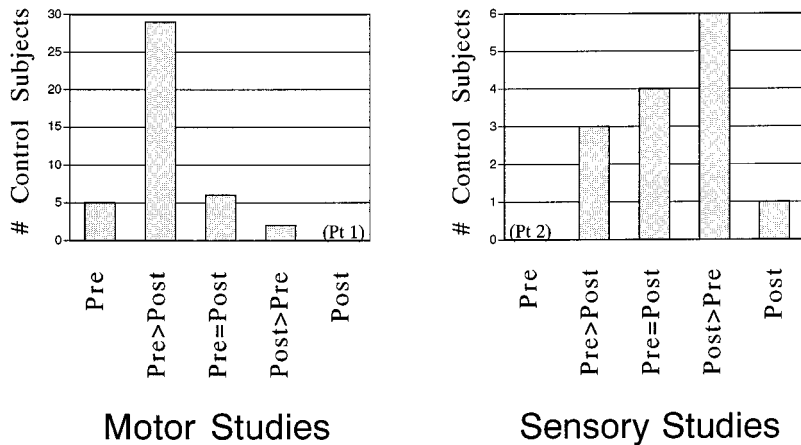


Figure 2. Distributions for the largest focus of significant activation during motor and sensory studies. The y axis describes the number of control subjects with the largest activation focus at each site. Left, Among the control motor studies ($n=42$), the most common pattern seen was an activation focus in precentral gyrus with a small extension into the postcentral gyrus ($n=29$). Patient 1 activated postcentral gyrus only, a pattern not seen in any of the control studies. Right, Among the control sensory studies ($n=14$), the most common pattern seen was an activation focus in postcentral gyrus with a small extension into the precentral gyrus ($n=6$). Patient 2 activated precentral gyrus only, a pattern not seen in any of the control studies. Pre indicates precentral gyrus; post, postcentral gyrus.

Patient 2 was a 67-year-old right-handed male. At the time of stroke onset, 6 months before fMRI scanning, examination showed slight weakness of the right wrist extensors and right hand interossei, plus a moderate deficit in right hand tactile and position sensation. MRI showed an acute stroke limited to the left postcentral gyrus plus anterior aspect of the superior parietal lobule. An old lacune was noted in the left parieto-occipital white matter. Intracranial and extracranial cerebral arteries were normal. He received 3 weeks of outpatient occupational therapy. Subsequently, quantitative monofilament testing documented substantial improvement in right-hand sensory function. On the day of fMRI, the patient felt sensory and motor symptoms were improved but still present. Examination documented mild hyperreflexia and increased tone in the right upper extremity without weakness. Pinprick, light touch, and position sense were decreased in all fingers; stereognosis was normal. The Fugl-Meyer arm motor score was very mildly decreased at 62.

For patient 2, the largest focus of significant activation during right index finger tapping was on the left precentral gyrus. The largest activation focus during right index finger tactile stimulation was also on the left precentral gyrus, anterosuperior to the infarct and largely inferior to the finger tapping activation site. During pectoralis contraction, the largest activation focus was on the precentral>postcentral gyrus; it overlapped with the finger-tapping activation site and extended more medially. Relative perfusion in 10 contiguous axial slices using a rapid intravenous injection of gadolinium showed no abnormalities outside the area of infarct.

The mean age of the 27 control subjects studied during index finger tapping was 46 years (range 25 to 76 years). All but 1 were right-handed. Two subjects were studied during right index finger tapping only, 1 study was excluded because of head motion, and 9 studies showed no activation. In 40 of the 42 remaining studies, the spatial extent of precentral gyrus activation exceeded or matched postcentral gyrus activation (Figure 2, left). None of the control studies showed activation restricted to postcentral gyrus, a finding significantly different from results in patient 1 ($P<0.03$, Fisher's exact test).

The median age of the 8 control subjects studied during tactile stimulation was 33 years (range 20 to 64 years). All were right-handed. Seven studies evaluated stimulation of the palm; 3 the thumb; and 4 the index finger. In 11 of these 14 studies, the spatial extent of postcentral gyrus exceeded or matched pre-

central gyrus activation (Figure 2, right). None of the control studies showed activation restricted to precentral gyrus, a finding different from results in patient 2 ($P<0.07$, Fisher's exact test).

Discussion

Penfield and Boldrey¹⁵ described an orderly but overlapping representation of body regions along both precentral and postcentral gyri, observations supported by functional imaging studies. The effect of cortical injury on these representations has been studied in primate^{4,16} and rat¹⁷ models, but little such data exists for humans. The current study compared 3 sensorimotor map activations from 2 stroke patients with findings from 35 control subjects.

Though precentral gyrus is normally associated with movement and postcentral gyrus with sensory function, movement is also accompanied by activation of the postcentral gyrus and somatosensory stimuli also activate the precentral gyrus. For most body regions, motor responses have been described upon direct stimulation of the postcentral gyrus. The postcentral gyrus is the second largest source of corticospinal tract axons after the precentral gyrus,¹⁸ and its motor representation is more extensive for the hand than for any other segment of the upper or lower extremities.¹⁹ Sensory inputs reach the precentral gyrus independent of postcentral gyrus, as well as via the postcentral gyrus.²⁰ Sensory responses are frequently found during cortical stimulation of the precentral gyrus.²¹ The current results from control subjects (Figure 2), that a motor task also activates postcentral gyrus and a sensory stimulus also activates precentral gyrus, are consistent with these observations and are similar to findings from numerous previous functional imaging studies.

In the current study, patient 1 activated only postcentral gyrus during finger tapping, a pattern not seen in 42 control studies, whereas patient 2 activated only the precentral gyrus during tactile finger stimulation, a pattern not seen in 14 control studies. Maps were not obtained in the patients before infarct, so it is impossible to establish that cortical organization changed subsequent to the stroke. Minor differences exist between stroke patients and some of the control subjects in the methods used for data acquisition. However, the methods used with the stroke patients should increase sensitivity to the presence of activation.

The findings in these 2 patients may reflect preservation of cortical processing regions or may indicate a shift in repre-

sensation site. For example, in patient 1, postcentral gyrus activation after a motor strip infarct could be an exaggeration of the postcentral gyrus activation seen in 37 of 42 control subjects. Alternatively, a shift in hand motor representation has been described in association with several forms of nervous system pathology and may be medial,¹⁶ anterolateral,⁴ ventral,⁶ or posterior.^{11,22} Studies by Bornschlegl and Asanuma²³ also support a potential role of postcentral gyrus in motor recovery; motor improvement in monkeys recovered from a thalamic lesion could be reversed by removing postcentral gyrus. Similarly, an anterior displacement of activation to the precentral gyrus has been described during sensory stimulation in some patients after stroke.²⁴

Previous functional imaging studies have demonstrated a shift in cortical activation site in association with stroke recovery. Four of the patients reported by Weiller et al,⁶ as well as patient 1 of Cao et al,⁸ showed a ventral shift in the activation site within sensorimotor cortex of the infarct hemisphere during a recovered-hand motor task. The patient reported by Rossini et al¹¹ showed a posterior shift in sensorimotor cortex activation during motor task performance. In the current study, multiple cortical representational maps were acquired, providing an additional level of information. In patient 1, finger movement activated postcentral gyrus, while sensory stimulation activated superior parietal lobule, which suggests a generalized posterior translocation of finger representational maps. In both patients, activation during pectoralis contraction was medial compared with that observed during finger tapping, which suggests preservation of the medial-lateral relationship identified in previous studies comparing shoulder and hand representation sites in human sensory and motor cortex.^{19,25}

The relationship between shifts in cortical activation sites and clinical outcome requires further study in patients with a wide range of infarct sizes and clinical outcomes. Both patients described in this report were clinically improved by the time of fMRI, and initial deficits were mild. Changes in the organization of peri-infarct tissue are important to stroke recovery.^{1-3,26} Future treatments targeting the period of stroke recovery may be guided by an improved understanding of poststroke changes in the peri-infarct region, possibly at the individual level. Establishing tools to measure these processes will contribute to this goal. Functional MRI with BOLD contrast is able to map multiple sensory and motor map elements and may be of value for imaging reorganization of cortical representational maps after stroke.

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