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RESEARCH ARTICLE

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Somatotopy and movement representation sites following cortical stroke

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Stroke has been associated with many changes in motor system function, but there has been limited study of changes in somatotopic organization. This was examined in a group of patients with cortical stroke affecting primary sensorimotor cortex. In 17 patients with good outcome after cortical stroke involving precentral and/or postcentral gyri, plus 14 controls, four functional MRI evaluations of brain activity were obtained: finger, shoulder, and face motor tasks plus a sensory task, passive finger motion. For each, coordinates for contralateral primary sensorimotor cortex activation site were determined, as was a measure of inter-hemispheric balance. The normal motor somatotopy measured in controls was largely preserved after stroke. The main difference found between controls and patients was that the face was lateral to finger motor activation in all controls, but face was centered medial to finger in 43% of patients. Among patients, smaller infarct volume was associated with more ventral, and larger infarct with more dorsal, contralateral primary sensorimotor cortex activation. On the other hand, better behavioral outcome was associated with a more posterior, and poorer outcome with more anterior, activation. Larger infarct and poorer behavioral outcome were each associated with a change in inter-hemispheric balance towards the non-stroke hemisphere. Shifts in contralateral movement representation site did not correlate with changes in inter-hemispheric balance. Motor somatotopy is generally preserved after injury to primary sensorimotor cortex. Greater injury and larger behavioral deficits are associated with distinct effects on movement representation sites. Changes in motor organization within and between hemispheres arise independently after stroke.

Keywords Somatotopy · Motor system · Plasticity · Stroke · Functional MRI

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The motor system is affected in approximately 80% of acute strokes, making motor deficits among the most common post-stroke impairments and contributions to disability. A growing body of knowledge has described changes in motor system function after stroke, and the relationship between these changes and behavioral outcome (Calautti and Baron 2003).

Somatotopic organization after stroke, however, has received limited attention to date. Somatotopic organization of motor cortex refers to the spatial relationships of movement representation sites for different body segments. This subject has received considerable study in normal human subjects, where face movement has been found to be centered lateral, ventral, and anterior to hand, which is lateral, ventral and anterior to shoulder (Penfield and Boldrey 1937; Colebatch et al. 1991; Nakamura et al. 1998; Milliken et al. 1999; Lotze et al. 2000; Alkadhi et al. 2002; Stippich et al. 2002). Though brain mapping studies after stroke have described shifts in the site of movement representation (Weiller et al. 1993; Traversa et al. 1997; Rossini et al. 1998; Green et al. 1999; Cramer et al. 2000; Byrnes et al. 2001; Rijntjes and Weiller 2002; Calautti and Baron 2003; Calautti et al. 2003), each has generally focused on 1–2 body regions or tasks for brain activation, and thus the extent to which somatotopic organization of motor cortex is modified by stroke remains unclear. The main hypothesis addressed in the current study was that injury to cortical maps by stroke, while associated with spatial shifts in movement representation sites, does not affect motor cortex somatotopic organization. An improved understanding of somatotopic inter-relationships after central nervous system injury is important given the

therapeutic potential of interventions that target specific cortical representational sites (Brown et al. 2003; Belci et al. 2004; Martin et al. 2004).

A secondary aim of the current study was to determine whether shifts in contralateral movement representation site are correlated with changes in inter-hemispheric balance of the motor system after cortical stroke. A number of stroke studies have found that movement of a stroke-affected limb is associated with a lower laterality index, i.e., a change in inter-hemispheric balance towards the motor system of the non-affected hemisphere, particularly with larger injury and more severe deficits (Calautti et al. 2001; Dijkhuizen et al. 2003; Fujii and Nakada 2003). The current hypothesis was that the extent of shift in movement representation site is independent from extent of change in inter-hemispheric balance because each process arises in part from separate cortical events (Sanes and Donoghue 2000; Shimizu et al. 2002; Nudo 2003).

Materials and methods

Subject selection and evaluation

Entry criteria were unilateral ischemic cortical stroke that (1) had been radiologically verified, (2) involved precentral and/or postcentral gyri, (3) was associated with arm sensorimotor deficits at stroke onset, and (4) had reached a plateau in motor recovery. Control subjects with no stroke and no active neurological disease were also enrolled. Consent was obtained in accordance with local Human Subjects Committee.

The primary motor assessment was the Purdue pegboard performance over 30 sec. In addition, clinical characterization included NIH Stroke Scale, arm motor Fugl–Meyer score, and index finger proprioception at the metacarpophalangeal (MCP) joint.

Immediately prior to scanning, subjects rehearsed functional MRI (fMRI) tasks while surface electromyography (EMG) was recorded, as described previously (Crafton et al. 2003), from bipolar leads over 14 muscles: lower face (mentalis) and upper face (corrugator supercilii); plus right and left pectoralis, biceps brachii, wrist flexors, wrist extensors, first dorsal interosseus (FDI), and tibialis anterior.

MRI acquisition

In all subjects, a volumetric anatomical MRI (1.5 Tesla, GE) scan was followed by a T_1-weighted anatomical MRI, in-plane resolution 0.94 mm^2, 7 mm-thickness. Fourteen axial slices were obtained ventral to brain vertex that included the entire infarct.

Next, 4 fMRI runs were acquired, each contrasting rest with a single unilateral task as described previously (Crafton et al. 2003; Cramer et al. 2003): (1) finger motor, in which index finger tapped 25° at metacarpophalangeal joint; (2) shoulder motor, in which hand atop mid-abdomen moved to externally rotate the shoulder across 20°; (3) lower face motor, in which the corner of the mouth contracted at 1 Hz via risorius, mentalis, and zygomaticus major muscles; and (4) finger sensory, in which index finger was passively moved 25° at metacarpophalangeal joint. The finger motor task was 2/3rd maximum tapping rate, no faster than 2 Hz and the finger sensory task was at 2 Hz. The face and shoulder tasks were performed at 1 Hz because pilot studies in control subjects disclosed that faster movement rates for these tasks induced excess fatigue. In patients, the affected body side was tested; in controls, the right side. An examiner at the subject's side during scanning observed and verified task performance. Blood oxygenation level dependent contrast fMRI employed TR = 2000, TE = 50, in-plane resolution 3.75×3.75 mm, 14 axial brain slices of 7 mm thickness with either 100 images/slice (5 rest-active cycles, for the 3 motor tasks) or 200 images/slice (10 rest-active cycles, the sensory task).

Data analysis

Functional images were analyzed as described previously (Crafton et al. 2003; Cramer et al. 2003). In sum, motion correction of all tasks' images to a single volume was followed by linear detrending and a voxelwise *t*-test contrasting each task's active and rest states, with results expressed as a Z-map. Studies with excess head motion, evident as a circumferential ring of activation or total absence of any activated voxels, were excluded.

The volume of activation within right sensorimotor cortex (SMC) and left SMC was measured to generate a SMC laterality index (LI-SMC). SMC was defined as precentral plus postcentral gyri from vertex to 7 mm above the Sylvian fissure, and excluded infarcted tissue. A whole brain analysis identified activation clusters with size greater than that expected by chance ($Z > 3$, $P < .05$) (Friston et al. 1994). Voxels that were within these significant clusters and were within right SMC were then counted; this was repeated for left SMC. LI-SMC, defined as (contralateral−ipsilateral)/(contralateral + ipsilateral) SMC activation, was then derived from these data. Note that ipsi- and contralateral are relative to the moving limb.

Activation maps were spatially smoothed (4 mm filter) and converted to stereotaxic space (Talairach and Tournoux 1988) using FLIRT (FSL). The largest activation ($Z > 4.2$) cluster on precentral gyrus contralateral to movement was identified. The coordinates for its center of activation were noted, with absolute value used in the × (medial-lateral) coordinate.

EMG data were analyzed as described previously (Cramer et al. 2002), with the ratio of (active/rest) EMG root mean square signal calculated for each muscle during each task.

Table 1 Values are mean (SD), otherwise median. Pegboard scores are paretic side for patients; mean of left and right for controls

	Patients	Controls	*P*
n	17	14	
Age	57 (16)	51 (19)	NS
Gender	10F/7M	6F/8M	NS
Fugl-Meyer arm motor score	64	66	< .005
NIHSS score	1	0	< .005
Purdue Pegboard, pegs/30 sec	9 (4.4)	14 (2.5)	< .005
Months, stroke to fMRI	4.4		
Side of stroke	9R/8L		
Infarct volume (cc)	29 (44)		

Statistics

Two-tailed, non-parametric statistics were used at alpha = 0.05, without correction for multiple comparisons. Multiple linear regression was used to determine whether side affected by stroke was a significant explanatory variable,

Results

The 14 controls and 17 stroke patients were right-handed except one patient. Six patients had a prior stroke that in each case spared peri-Rolandic gyri. Deficits varied from mild to severe initially and were mild at fMRI (Table 1, Fig. 1). All patients received post-stroke physiotherapy. Three patients, all with stroke affecting the left arm, had unilateral cervical internal carotid artery occlusion ipsilateral to stroke. More patients than controls had a 10-pack-year smoking history (10/17 vs. 1/14, $P < 0.01$). Index finger proprioception was normal in 14/14 controls and in 15/17 patients (P = NS), with mild deficits in 2/17.

Technical errors, subject preference, and excess head motion reduced the number of maps available for analysis to 90 (Table 2), 10 of which showed minimal deviations in task performance. Movement rate during the finger motor or finger sensory tasks was 2 Hz in 52/56 scans, 1–1.4 Hz in 4/56. All shoulder and face scans were 1 Hz. Differences between patients and controls in EMG (Fig. 2) were rare and trivial.

Somatotopy

Among control subjects, an orderly spatial distribution of sensorimotor representation sites was consistently present. For controls, there was a significant ($P <$ .0005, Wilcoxon test) difference overall for Tal-x according to task, as well as for Tal-y ($P <$ .005), and for Tal-z ($P <$ .00001, Table 2). Subsequently, the relationship between individual tasks within subject was evaluated on a pairwise basis. For Tal-x, face motor was significantly ($P < 0.05$) lateral to the two finger tasks, which were significantly lateral to shoulder motor; for Tal-y, face motor was significantly more anterior to the three others; and for Tal-z, face motor task was significantly more ventral to the two finger motor tasks, which were significantly ventral to shoulder motor. Comparison of maps within each individual subject found that these same lateral/anterior/ventral somatotopic relationships were present in every instance. Some Tal-xyz control data have been previously reported (Cramer et al. 2003).

Among patients, the motor somatotopy findings in controls were preserved in most, but not all, instances. Among all 17 patients, there was a significant difference in Tal-x across the 4 tasks, as well as for Tal-y, and Tal-z (Table 2, Fig. 3). Results of subsequent pairwise testing of the relationship between individual tasks within subject were identical to findings in con-

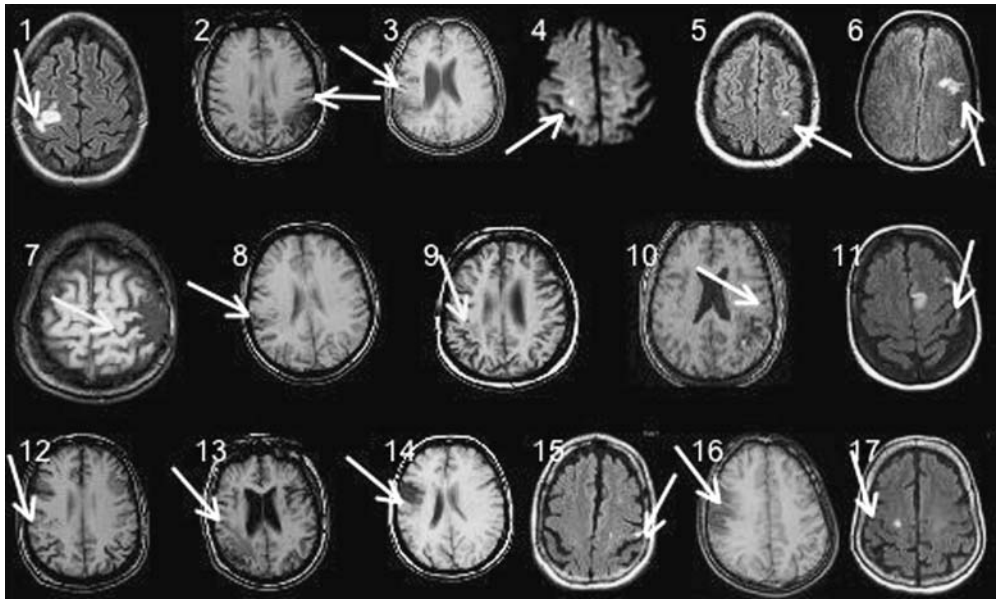

Fig. 1 For each of the 17 patients, infarct affected precentral and/or postcentral gyrus. The MRI image best depicting stroke injury, from acute stroke or fMRI evaluation, is presented. White arrow = central sulcus

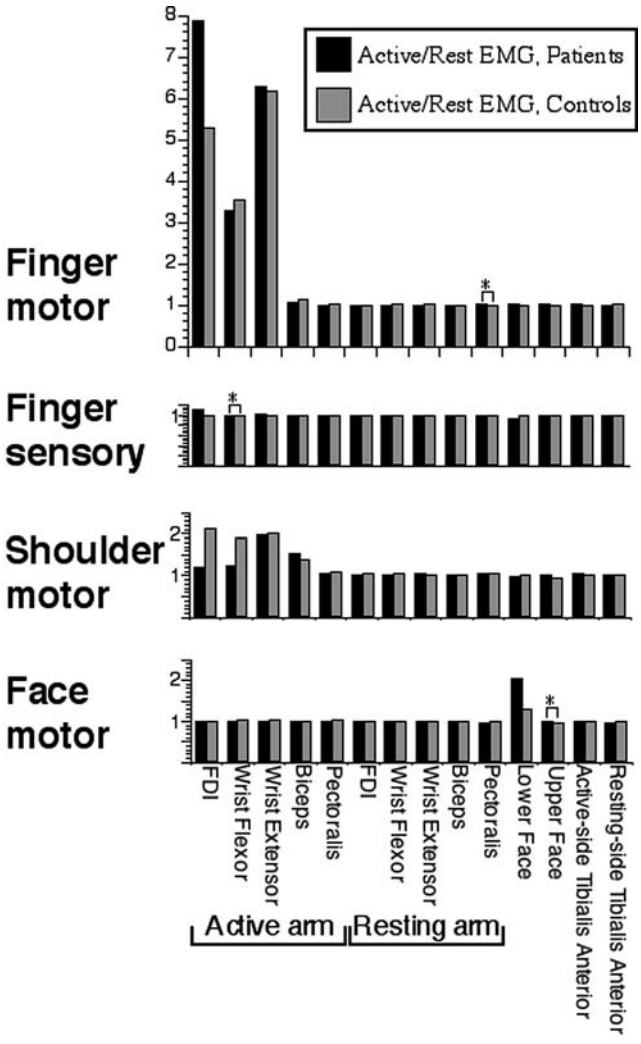

Fig. 2 Median EMG values (task performance/rest) are presented. Each task showed a unique profile of muscle activity appropriate to task content: distal arm for finger motor; quiescence for finger sensory; proximal + distal arm for shoulder motor; and face muscles for face motor. EMG in leg and in muscles intended to be at rest did not change with task performance. *$p < 0.05$, patients vs. controls

trols except that shoulder-finger motor differences did not reach significance for Tal-x and Tal-z. For the eight patients with stroke affecting the right arm, a significant difference across the 4 tasks for Tal-x, Tal-y, and Tal-z was present, but none of these three was significant for the nine patients with stroke affecting the left arm. Comparison of maps within each individual patient found the same results as in controls in all but one instance. The exception was that, whereas face motor activation was lateral to finger motor activation in each individual control subject, face movement was centered *medial* to finger in three of the seven (43%) patients who had both maps available for comparison. Two of these patients had left arm affected and one had right arm affected. Features of injury and behavioral status did not vary according to whether face was represented medial or lateral to finger.

Patients with right body side affected by stroke had no significant differences in fMRI results when compared with control subjects. Both subject groups moved right body side during fMRI. Patients with right body side affected by stroke, when compared with patients with left body side affected by stroke, had activation that was significantly more medial (shoulder motor and both finger tasks), more ventral (face motor), and more bilaterally organized (face motor, Table 2). Note that somatotopy results did not differ between patients according to presence or absence of involvement within precentral gyrus, postcentral gyrus, ventral premotor cortex, or dorsal premotor cortex.

Overlap of maps

Among all subjects, map overlap varied from a maximum of 32% (shoulder-finger movement) to a minimum of 7% (shoulder-face), with no significant patient-control differences. Extent of map overlap did not correlate with dorsal-ventral coordinate (Tal-z).

Inter-hemispheric balance

In control subjects, LI-SMC was significantly different across tasks. Subsequent testing across each pair of tasks found significantly lower LI-SMC (more bilaterally distributed) for face motor task as vs. each of the other three tasks. The same results were found across patients.

Correlation with injury

Smaller infarct volume correlated with (1) more ventral movement representation site for shoulder, face (both $P < .05$), and finger ($P = .07$) movement, the extent of which did not correlate with decreased proximal arm EMG or increased distal arm EMG; and (2) greater balance ($P < .05$) of SMC activation towards stroke hemisphere (higher LI-SMC), for finger sensory and face motor. Note that finger sensory LI-SMC results were due to increased stroke SMC activation plus decreased non-stroke hemisphere SMC activation, while face motor LI-SMC results reflected decreased non-stroke hemisphere SMC activation.

Correlation with post-stroke behavior

Higher pegboard performance correlated significantly ($P < .05$) with (1) more posterior location (higher Tal-y, Fig. 4) for shoulder movement, which did not correlate with either EMG increases in proximal arm muscles or

Table 2 Features of motor system activation are presented for somatotopy within hemisphere and for interhemispheric balance (LI-SMC)

Measure	Patients: Left arm affected	Patients: Right arm affected	All Patients	Controls
Total n studied	9	8	17	14
Number of available studies				
Finger motor	8	7	15	12
Finger sensory	9	7	16	13
Shoulder motor	7	5	12	6
Face motor	5	4	9	7
Talairach coordinates				
Shoulder motor				
Tal-x	35* (8)	23 (3)	30** (9)	22 (2)
Tal-y	−21 (9)	−27 (4)	−24 (7)	−27 (5)
Tal-z	53 (5)	52 (5)	53 (5)	57 (2)
Finger motor				
Tal-x	37* (4)	29 (5)	33** (6)	30 (2)
Tal-y	−21 (5)	−22 (5)	−22 (4)	−21 (5)
Tal-z	50 (6)	51 (4)	51 (5)	51 (4)
Finger sensory				
Tal-x	41* (5)	33 (4)	37 (6)	31 (5)
Tal-y	−23 (8)	−23 (7)	−23 (7)	−21 (7)
Tal-z	47 (4)	49 (4)	48 (4)	49 (4)
Face motor				
Tal-x	41 (10)	39 (5)	40 (8)	40 (5)
Tal-y	−14 (5)	−15 (4)	−14 (4)	−9 (6)
Tal-z	43* (7)	36 (2)	40 (6)	35 (5)
LI-SMC				
Shoulder motor	0.23 (.7)	0.73 (.18)	0.44 (.56)	0.80 (.20)
Finger motor	0.28 (.74)	0.70 (.30)	0.47 (.60)	0.79 (.16)
Finger sensory	0.58 (.88)	0.63 (.44)	0.60 (.66)	0.86 (.17)
Face motor	−0.70* (.31)	0.10 (.52)	−0.34 (.57)	0.10 (.42)

Mean (SD) values shown. Tal-x are absolute values. ** $p < .05$, patients vs. controls; * $p < .05$ patients with left vs. right arm affected

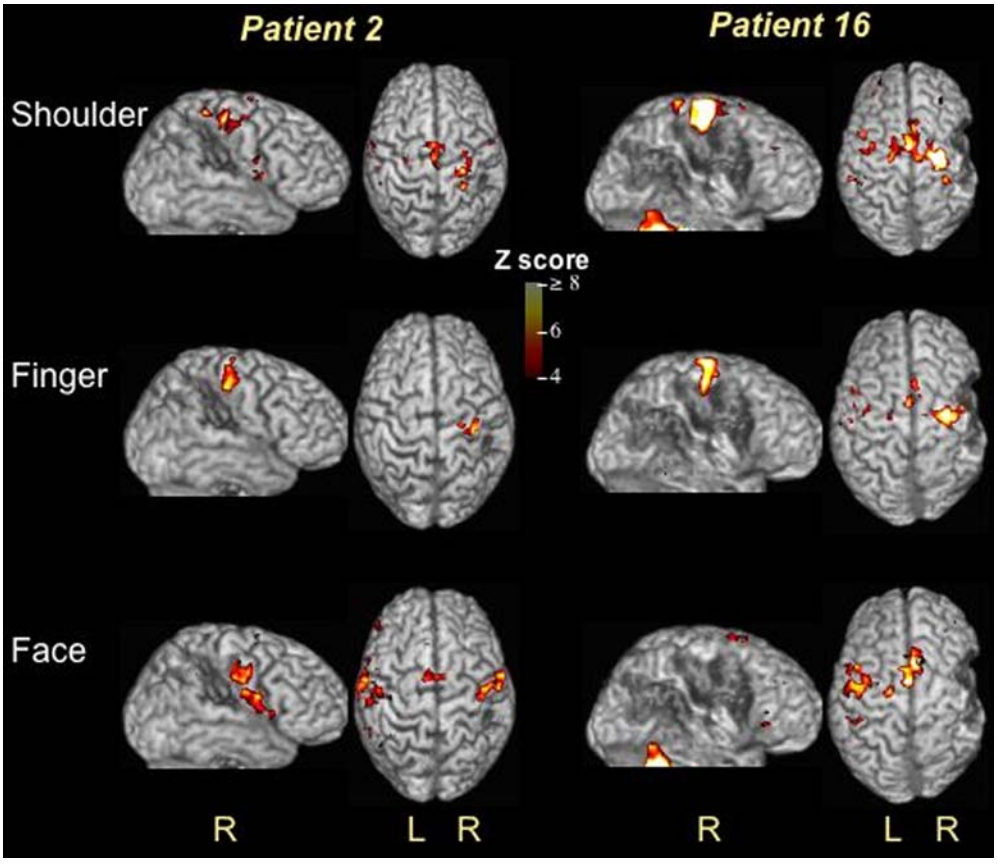

Fig. 3 Activation during performance of three motor tasks is shown for two patients with chronic cortical stroke. Somatotopic organization is preserved. With larger volume of injury, activation is more dorsal. Thus, the infarct volume for patients 2 and 16 respectively was 33 vs. 155 cm^3, and Tal-z was 52 vs. 57 for the finger motor task. The face motor task was the most bilaterally organized task in controls, a finding that is duplicated in patient 2 and exaggerated in patient 16–where all activation was ipsilateral to movement. The stroke for patient 2 was in left hemisphere but has been flipped in this figure for illustrative purposes

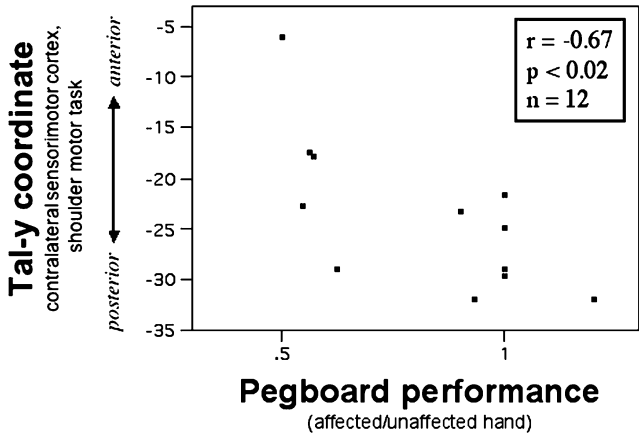

Fig. 4 In patients, more posterior movement representation site during the shoulder motor task correlated with better hand dexterity on pegboard testing

EMG decreases in distal arm muscles; and (2) greater balance of SMC activation towards the stroke hemisphere (higher LI-SMC) for finger sensory task and shoulder movement. Note that in both cases, higher LI-SMC reflected reduced non-stroke hemisphere SMC activation.

In multiple regression analysis, side affected by stroke was not a significant covariate for any of the injury- or behavior-fMRI correlations.

Patients, parallel motor system changes

For each of the 4 tasks, there was no significant correlations between LI-SMC and contralateral Tal-x, Tal-y, or Tal–z.

Discussion

The current study evaluated somatotopy and movement representation sites in 17 well-recovered patients with a cortical stroke that affected peri-Rolandic gyri. Normal motor somatotopy was largely preserved after stroke affecting SMC. Smaller infarct volume was associated with more ventral, and better behavioral outcome with posterior, movement representation sites. A shift in inter-hemispheric balance towards non-stroke hemisphere SMC was found for both larger infarct and poorer behavioral outcome, which arose independently of contralateral movement representation site changes.

The motor somatotopy findings in control subjects are largely concordant with prior human studies (Penfield and Boldrey 1937; Colebatch et al. 1991; Nakamura et al. 1998; Milliken et al. 1999; Lotze et al. 2000; Alkadhi et al. 2002). Normal motor representation maps shift location in response to a number of peripheral and central influences (Sanes and Donoghue 2000; Nudo 2003), including experimental infarct affecting SMC (Nudo et al. 1996; Xerri et al. 1998). However, there has been limited study of motor somatotopic organization in humans after stroke. The current study suggests that injury to these maps is associated with limited change to the fundamental somatotopic organization of the motor strip, at least for face, proximal arm, and distal arm.

One exception to this, unique to patients, was reversal of the normal finger-face relationship, with finger movement becoming centered *lateral* to face. Face-hand representational relationships may be among the most plastic in motor cortex, a finding that is supported by reports of invasion of hand motor representation into face motor area (Kew et al. 1994; Rijntjes et al. 1997) and face into hand (Elbert et al. 1994; Lotze et al. 2001; Blake et al. 2002; Corbetta et al. 2002). The anatomical basis for such plasticity may be the overlap between horizontal connections that have been described between hand and lower face areas (Manger et al. 1997). Further study is needed to understand which features of injury or of behavior influence the likelihood of this reversal.

Increased SMC injury volume was associated with a dorsal shift for the three motor tasks. The data suggest that this was a multi-map shift without a change in interrelationships of maps, as for these three maps, extent of dorsal shift was not associated with change in either degree of map overlap or in relevant EMG measures. The basis for a dorsal shift might reflect topography of injury or surviving white matter. Reports of a dorsal shift for hand movement representation in patients with upper extremity amputation (Elbert et al. 1994; Lotze et al. 2001) suggests underlying anatomy might be conducive for this event.

Greater behavioral deficits also correlated with changes in movement representation site, and did so in a manner that was different from that seen with larger injury, a dissociation described with multiple sclerosis (Reddy et al. 2002). Better dexterity correlated with more posterior location (Figure 4). This correlation reached significance only for shoulder movement, the posterior-most task studied. A posterior shift in movement representation site has been reported after stroke (Rossini et al. 1998; Green et al. 1999; Cramer et al. 2000; Byrnes et al. 2001; Pineiro et al. 2001; Calautti et al. 2003) multiple sclerosis (Lee et al. 2000), and spinal cord injury (Green et al. 1998; Turner et al. 2003). However, these reports did not find that the extent of posterior shift was related to clinical status, possibly because of the task used to activate the brain. A posterior shift might indicate increased reliance on postcentral gyrus, the second largest source of corticospinal tract axons (Galea and Darian-Smith 1994), or increased contribution to motor recovery by postcentral-to-precentral projections (Bornschlegl and Asanuma 1987).

Reduced LI-SMC (change in SMC inter-hemispheric balance towards the non-stroke hemisphere) was found with both increased injury and greater deficits. After stroke or multiple sclerosis, this observation has been reported to be due to both reduced injured-hemisphere activity and increased non-affected hemisphere activity

(Weiller et al. 1993; Cramer et al. 1997; Netz et al. 1997; Traversa et al. 1997; Green et al. 1999; Lee et al. 2000; Calautti and Baron 2003). Reduced laterality index, i.e., a shift towards the non-stroke hemisphere, does not reflect bilateral movement, as evidenced by EMG data (Fig. 2). Current data suggest that, as with many other variables, choice of motor task influences LI-SMC. The task most bilaterally organized in controls (face motor) was also the task most bilaterally organized after stroke, supporting the idea that reorganization after brain injury is best interpreted in the context of normal functional anatomy.

There were several limitations to the current study. The fMRI slices were 7 mm thick, which did shorten scan time per task and thus permit performance of more tasks, but limited Tal-z spatial resolution. A minority of subjects had slight deviations in movement performance. Not all strokes were on the same side of the brain, though this was not a significant covariate when evaluating injury and behavioral correlations. The content of, and time since discharge from, post-stroke physiotherapy varied across patients. A strength of the study was enrollment of a relatively homogenous form of stroke injury, cortical stroke involving the primary sensorimotor cortex maps of peri-Rolandic gyri.

In sum, the current study found that somatotopy is largely preserved after stroke, that injury and behavioral status each correlate with features of movement representation site after stroke but do so in different ways, and that changes in motor organization within and between hemispheres arise independently after stroke.

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