

# Reorganization of the Human Somatosensory Cortex in Hand Dystonia

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**Background and Purpose:** Abnormalities of finger representations in the somatosensory cortex have been identified in patients with focal hand dystonia. Measuring blood flow with positron emission tomography (PET) can be used to demonstrate functional localization of receptive fields. **Methods:** A vibratory stimulus was applied to the right thumb and little finger of six healthy volunteers and six patients with focal hand dystonia to map their receptive fields using  $H_2^{15}O$  PET. **Results:** The cortical finger representations in the primary somatosensory cortex were closer to each other in patients than in normal subjects. No abnormalities were found in secondary somatosensory cortex, but the somatotopy there is less well distinguished. **Conclusions:** These data confirm prior electrophysiological and functional neuroimaging observations showing abnormalities of finger representations in somatosensory cortex of patients with focal hand dystonia.

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**Key Words:** Dystonia, Somatosensory cortex, Receptive field, Cortical representation, Positron emission tomography.

Writer's cramp is a task-specific focal hand dystonia characterized by agonist and antagonist muscle co-contraction causing abnormal posturing. Previous studies have shown abnormal activation of the primary sensorimotor cortex during writing<sup>1</sup> and structural primary somatosensory cortex (SI) involvement.<sup>2</sup> There is considerable evidence of sensory involvement in writer's cramp.<sup>3-7</sup> In the present study we mapped the finger representations in somatosensory cortices [SI and secondary somatosensory cortex (SII)] in writer's cramp patients using  $H_2^{15}O$  positron emission tomography (PET).

## Methods

We studied 6 patients (2 males and 4 females) with writer's cramp of their right hands. Mean age was 46.5 (range from 26 to 59). The diagnosis of idiopathic hand dystonia was based on the medical history, physical and neurological examinations, and after excluding other diseases by laboratory tests and magnetic resonance imaging (MRI) scans. All patients were studied after at least 1 year without any botulinum toxin injections. Control subjects consisted of 6 normal volunteers, 2 males and 4 females, mean age 47.5, range 28 to 60. They had no history of neurological disease and no abnormalities on physical and neurological examinations. All subjects were right-handed by the Edinburgh Inventory.<sup>8</sup> The protocol was approved by the Institutional Review Board, and all the subjects gave written informed consent for the study.

For each subject, PET scans of regional cerebral blood flow (rCBF) were performed using  $H_2^{15}O$  as a tracer. The experimental paradigm consisted of three conditions: vibratory stimulation on right thumb (D1), vibratory stimulation on right little finger (D5), and rest. Each condition was repeated five times.

Subjects lay in a supine position. The right arm was lying on a support to maintain a constant arm position. Each subject underwent 15 consecutive scans at 10-minute intervals. Vibratory stimulation on each individual finger was started 20 seconds before injection and con-

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tinued during the whole scan. The subjects were instructed to pay attention to the stimulation site. Surface electromyography from right flexor and extensor carpi radialis was recorded during the study to see whether dystonia was induced. For the rest scan, subjects lay quietly. The vibrator (Brüel and Kjaer, Mini-Shaker type 4810) had two different frequencies, fast (100 Hz) and slow (25 Hz). The stimulus was delivered using these two different frequencies alternating in a random order.

The PET scans were performed using a GE Advance system (General Electric, Schenectady, NY, USA). Data were acquired in 3D mode and reconstructed into 35 contiguous transaxial planes separated by 4.25 mm (center-to-center). In-plane and axial resolution were 5.2 mm and 4.6 mm full-width half-maximum (FWHM) respectively, after reconstruction. Emission scans were attenuation corrected with a transmission scan collected before each session during exposure of a Germanium-68/Gallium-68 external rotating source. Reconstructed images were obtained by summing the activity during the 60 second period following the first detection of an increase in cerebral radioactivity after the intravenous bolus injection of 10 mCi of  $^{15}\text{O}$ -water. Magnetic resonance images were obtained using a General Electric scanner (1.5 T). For each subject a Sagittal T1-weighted, matrix  $256 \times 256$ , 124 contiguous sagittal slices with 1.5 mm thickness were collected. After reconstruction, the MR images were aligned parallel with the intercommissural line, and interpolated to yield a cubic voxel size of  $0.938 \text{ mm}^3$ , which permitted coregistration with the PET.

Data analysis was performed with statistical parametric mapping 96 (SPM96 from the Wellcome Dept. of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc., Natick, MA, USA). The scans from each subject were realigned and normalized to Montreal Neurological Institute template. Following realignment, the mean image was used to coregister PET data onto the same individual's MRI scan. Afterwards the MRI image was normalized using the same parameters. Each image was smoothed using a Gaussian filter (FWHM = 8 mm for all direction). In the stereotaxic standard space, each voxel was  $2 \times 2 \times 2 \text{ mm}$  in size.

After the appropriate design matrix was specified, the condition effects were estimated according to the general linear model at each and every voxel. Differences in global cerebral blood flow between scans were removed by proportional scaling with global flow as a confounding variable.<sup>9</sup> To test the hypothesis about the specific regional effects of the condition, the estimates were compared using linear contrasts. Analysis of data was performed as single subject analysis. Because the hypothesis was somatotopic organization in the somatosensory cortices, we restricted the cortical areas for the analysis to the somatosensory cortices. Although the images were normalized to standard space, the exact anatomic locations of the local maxima were identified for each individual with

reference to the gyral anatomy identified on each individual MRI. The location of each finger in SI was determined by the highest change in rCBF posterior to the central sulcus. The location of each finger in SII was determined by looking at the highest change in rCBF in insula and operculum.

The Mann-Whitney-Wilcoxon test was used for statistical comparison of the distances between the finger representations, and the level of significance was  $p < 0.05$ .

## Results

Vibratory stimulation of each finger evoked increase in rCBF in the contralateral postcentral sulcus. The location of D1 in relation to D5 in normal subjects was located in a homuncular fashion in SI: inferior (6 of 6 subjects), anterior (5/6) and lateral (5/6). Similarly, for hand dystonia patients, the location of D1 in relation to D5 was inferior (5/6), anterior (6/6), and lateral (4/6). Only one patient showed inferior-to-superior topography inverted (D1 superior to D5).

Patients with hand dystonia showed some degradation of the homuncular S1 organization, with changes in the relative positions of D1 and D5. The unidirectional distances between D1 and D5 in the control subjects and patients were, respectively, 15.3 mm and 8.0 mm in the x axis; 7.3 mm and 5.0 mm in the y axis; and 15.7 mm and 8.7 mm in the z axis, showing that the distance between fingers 1 and 5 was decreased. There were no significant difference in the horizontal (x, y) plane (17.6 mm vs. 10.5 mm,  $p = 0.3$ ), and sagittal (y, z) plane (18.0 mm vs. 10.1 mm,  $p = 0.1$ ). However, there was significant difference in the coronal (x, z) plane (24.0 mm vs. 12.9 mm,  $p = 0.009$ ). The mean three-dimensional distance between fingers 1 to 5 representations was significantly decreased, 25.3 mm for controls vs. 14.1 mm for dystonia ( $p = 0.02$ ).

Individual finger representations could be identified in SII in all control subjects and dystonia patients, for both insula and operculum. In the insula, the location of D1 in relation to D5 was inferior (4/6), anterior (4/6) and lateral (3/6) for control subjects, and inferior (5/6), anterior (6/6) and lateral (1/6) for dystonia patients. Location in the operculum showed more variability in both groups. The mean coordinates for each region are in Table 1. There were no significant differences in distance between fingers 1 and 5 for the two groups (Table 2).

## Discussion

Focal hand dystonia occurs in persons experiencing repetitive movements and sensory inputs and these might induce plastic changes of SI and contribute to the pathology.<sup>3,4,10-12</sup> The motor system is driven by the sensory system. The functional sensory and motor maps in the cortex are plastic and the topographic organization of the sensory and motor corti-

**Table 1.** Mean coordinates for peak delta ( $\Delta$ ) rCBF in each somatosensory cortical region (SI and SII), for control subjects and dystonia patients

	Subjects	Task	X	Y	Z	$\Delta$ rCBF	Position 1-5
Primary sensory (SI)	Control	Finger 1	-51.7	-21.7	49.3	11.7	I, A, L
		Finger 5	-36.3	-26.3	65	11.1	
	Dystonia	Finger 1	-44.3	-22.7	49.3	11.1	I, A, L
		Finger 5	-39	-27.7	56	9.9	
Insula	Control	Finger 1	-43.7	-21	13	9.0	I, A, L
		Finger 5	-40.7	-24	17	8.5	
	Dystonia	Finger 1	-39.3	-22.3	10	7.6	I, A, M
		Finger 5	-42.3	-29	16	9.4	
Operculum	Control	Finger 1	-60.3	-21.3	17	8.8	I, M
		Finger 5	-61	-21.3	17.7	8.1	
	Dystonia	Finger 1	-57.7	-27.7	19.3	7.8	I, P, L
		Finger 5	-57.3	-26.3	20	8.9	

Mean  $\Delta$  rCBF (mL/min/100 mL). Relative position of finger 1 relative to finger 5. rCBF: regional cerebral blood flow, SI: primary somatosensory cortex, SII: secondary somatosensory cortex, I: inferior, A: anterior, P: posterior, L: lateral, M: medial.

**Table 2.** Mean distance (SD) between fingers 1 and 5 in control subjects and dystonia patients, in unidimensional (X, Y, Z) bidimensional (X-Y, X-Z, Y-Z) and tridimensional measurements; in SI and SII cortices

	Primary sensory cortex (SI)		Operculum (SII)		Insula (SII)	
	Control	Dystonia	Control	Dystonia	Control	Dystonia
	subjects	patients	subjects	patients	subjects	patients
Left-right direction (X)	15.3 ( $\pm$ 8.7)	8.0 ( $\pm$ 5.2)	4.7 ( $\pm$ 3.0)	3.0 ( $\pm$ 1.7)	5.0 ( $\pm$ 6.8)	6.3 ( $\pm$ 4.3)
Anterior-posterior direction (Y)	7.3 ( $\pm$ 3.0)	5.0 ( $\pm$ 2.4)	4.0 ( $\pm$ 3.3)	5.3 ( $\pm$ 7.3)	10.3 ( $\pm$ 10.5)	6.7 ( $\pm$ 3.5)
Superior-inferior direction (Z)	15.7 ( $\pm$ 7.0)	8.7 ( $\pm$ 3.7)	3.3 ( $\pm$ 4.5)	5.3 ( $\pm$ 6.9)	6.0 ( $\pm$ 4.7)	6.7 ( $\pm$ 4.8)
Horizontal plane (X-Y)	17.6 ( $\pm$ 7.8)	10.5 ( $\pm$ 3.0)	6.4 ( $\pm$ 4.1)	7.0 ( $\pm$ 6.5)	13.5 ( $\pm$ 9.8)	9.6 ( $\pm$ 4.6)
Coronal plane (X-Z)*	24.0 ( $\pm$ 2.8)*	12.9 ( $\pm$ 2.8)*	6.6 ( $\pm$ 4.1)	7.2 ( $\pm$ 5.8)	8.6 ( $\pm$ 7.3)	9.4 ( $\pm$ 6.1)
Sagittal plane (Y-Z)	18.0 ( $\pm$ 5.4)	10.1 ( $\pm$ 4.1)	6.2 ( $\pm$ 4.2)	8.7 ( $\pm$ 8.8)	12.7 ( $\pm$ 10.6)	9.8 ( $\pm$ 5.2)
Tridimensional*	25.3 ( $\pm$ 2.7)*	14.1 ( $\pm$ 2.4)*	8.0 ( $\pm$ 4.7)	9.9 ( $\pm$ 8.1)	14.9 ( $\pm$ 10.7)	11.9 ( $\pm$ 6.2)

\* $p < 0.005$ . SI: primary somatosensory cortex, SII: secondary somatosensory cortex, SD: standard deviation.

ces is modulated based on learning and experience.<sup>13,14</sup>

Our study shows degradation of the normal organization of SI in patients with hand dystonia. The cortical finger representations in SI were closer to each other in patients than in normal subjects, mainly in the coronal plane, but also in the tridimensional distance. Only one patient showed inversion of the finger representation in the superior-inferior topography. The results confirm the previous findings using electroencephalography, magnetoencephalography, functional MRI.<sup>3-5,7</sup> There appears to be an abnormal clustering of digit representations and a disruption of the normal homuncular arrangement in the SI. The explanation for this may be due to expansions of the representations and overlapping, similar to what has been shown in studies of learning-induced cortical remodeling in monkeys.<sup>10,14</sup> This finding appears to be primary because representation of the symptomatic fingers are more affected than asymptomatic ones.<sup>7</sup>

Activation of each individual finger was identified in each subject in both insula and operculum, but there was more topographical variability than in SI. We did not find differences between control and dystonia patients. Our findings in nor-

mal subjects are consistent with previous reports in non-human primates and humans that have shown somatotopic arrangement with large inter-individual differences. The differentiation was not as clear as that seen in the homunculus in the SI.<sup>15-18</sup> It is uncertain whether the failure to find a difference between groups in our work is because of the intrinsic variability or the relatively small number of subjects that we have studied. Current knowledge of SII function is predominantly from animal studies, and role of SII in humans remain unclear. A functional role for SII areas in processing somatosensory stimuli has been implicated as being important for tactile processing, learning and memory.<sup>18-22</sup>

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