

Somatotopic Organization of Cortical Fields in the Lateral Sulcus of *Homo sapiens*: Evidence for SII and PV

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ABSTRACT

The human somatosensory cortex in the Sylvian fissure was examined using functional magnetic resonance imaging to describe the number and internal organization of cortical fields present. Somatic stimuli were applied to the lips, face, hand, trunk, and foot of 18 human subjects. Activity patterns were transposed onto three-dimensional magnetic resonance images of the brain so that the location of activity associated with the different stimuli could be related to specific regions of the cortex. There were several consistent findings. First, there were three regions of activity in the lateral sulcus associated with stimulation of the contralateral body. The most consistent locus of activation was on the upper bank of the lateral sulcus, continuing onto the operculum. The other two areas, one rostral and one caudal to this large central area, were smaller and were activated less consistently. Second, when activity patterns in the large central area resulting from stimulation of all body parts were considered, this region appeared to contain two fields that corresponded in location and somatotopic organization to the second somatosensory area (SII) and the parietal ventral area (PV). Finally, patterns of activation within SII and PV were somewhat variable across subjects. Repeated within-subject stimulus presentation indicated that differences across subjects were not due to inconsistent stimulus presentation. Comparisons with other mammals suggest that some features of organization are found only in primates. It is hypothesized that these features may be associated with manual dexterity and coordination of the hands, a characteristic generally restricted to the primate lineage. *J. Comp. Neurol.* 418:1-21, 2000. © 2000 Wiley-Liss, Inc.

Indexing terms: somatosensory cortex; second somatosensory area; parietal ventral area; functional magnetic resonance imaging

Until recently, investigations directly examining the functional organization of human cortex have been limited to lesion studies and postmortem analysis. Unfortunately, these types of studies provide only limited information, and they lack specificity in terms of the site of the lesion or damage. Thus, we rely on studies of nonhuman primates to understand basic sensory processing strategies and details of the underlying anatomical networks that generate perceptual abilities and motor output. Indeed, much of our understanding of basic sensory processing in humans comes from comparative work in a variety of other mammals.

The advent of new techniques, such as positron emission tomography (PET), magnetoencephalography (MEG), and functional magnetic resonance imaging (fMRI), has

allowed us to study human brains directly (for review, see Kwong, 1995) and to test our hypotheses generated from work on nonhuman primates. Although progress has been made in describing the regions of the brain involved in complex abilities, such as language, cognition, attention, and memory (Stern et al., 1996; O'Craven et al., 1997; Clark et al., 1998; Neville et al., 1998), and these nonin-

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vative techniques have been used to explore sensory representations in the neocortex (Sereno et al., 1995; Roberts and Poeppel, 1996; Tootell et al., 1996; Morris et al., 1998), very few studies have used these techniques to determine the number of cortical sensory fields present and their topographic organization (Tootell et al., 1997). Furthermore, few studies have been guided by what is known about the organization of neocortex in other mammals.

Now that we can examine human cortical organization noninvasively, comparative studies play a new role in directing the questions we ask about the organization of neocortex in humans and in helping us to interpret the results from imaging studies. In addition, animal studies can provide information about the detailed connections of neocortical fields by using neuroanatomical tracing methods that cannot be used in humans. The present investigation was designed to increase our understanding of the organization of somatosensory cortex in humans. We specifically were interested in examining the organization of fields in the lateral sulcus that are associated with processing somatic inputs.

The number and internal organization of anterior parietal fields have been well described in monkeys (Merzenich et al., 1978; Kaas et al., 1979; Nelson et al., 1980; Sur et al., 1980, 1984; Carlson et al., 1986), area 2 (Phillips et al., 1971; Yumiya et al., 1974; Pons et al., 1985; Recanzone et al., 1992b; Iwamura et al., 1994; Huffman et al., 1996; for reviews, see Kaas, 1983; Kaas and Pons, 1988; and Johnson, 1990). In humans, the topographic organization of the postcentral gyrus has been appreciated for over 50 years (Penfield and Boldrey, 1937; Penfield and Jasper, 1954; Penfield and Rasmussen, 1968b). Functional MRI and PET techniques have been used successfully to demonstrate activation of the postcentral gyrus (peri-Rolandic cortex) resulting from tactile stimulation (Roland, 1981; Fox et al., 1987; Hammeke et al., 1994; O'Sullivan et al., 1994; Yetkin et al., 1995; Lin et al., 1996; Gelnar et al., 1998; Moore et al., 1998), and some studies (e.g., Fox et al., 1987) support the mediolateral organization of anterior parietal fields first described in the pioneering work of Penfield and colleagues. Furthermore, architectonic distinctions of these fields in humans have been appreciated since the beginning of this century (Brodmann, 1909) and correspond to architectonic/physiological features in monkeys. Thus, it is likely that these fields are similar in organization and function to those described in monkeys (Fig. 1A).

Only recently have cortical areas lateral to anterior parietal fields been examined in detail in nonhuman primates. In monkeys, electrophysiological techniques have been used to demonstrate that the lateral sulcus contains multiple fields (Robinson and Burton, 1980a,b; Burton and Robinson, 1981). At least two of these fields contain a complete map of the sensory epithelium, the second somatosensory area (SII) and the parietal ventral area (PV; Krubitzer and Kaas, 1990; Krubitzer et al., 1995; or areas SIIr and SIIc of Whitsel et al., 1969). These two representations are mirror symmetric maps of the body surface and share a common boundary at the representation of the face, hands, and feet. PV is located rostral to SII and corresponds to SIIr of a recent neuroanatomical tracing study (Burton et al., 1995). These fields have a mediolateral organization in which the face is represented most laterally, near the lip of the lateral sulcus, followed in a lateromedial sequence by a large hand representation and

a foot representation (Fig. 1B). The lateral sulcus of nonhuman primates has been shown to contain additional areas, such as the ventral somatosensory area (VS), the retroinsular area (Ri), and area 7b (see, e.g., Robinson and Burton, 1980a,b; Cusick et al., 1989; Krubitzer and Kaas, 1990; Krubitzer et al., 1995). However, the details of organization of these fields have yet to be described.

Most data in nonhuman primates indicate that cortical fields residing in the lateral sulcus are involved in complex functions, such as intramanual dexterity and bilateral coordination of the hands (for review, see Krubitzer, 1996). Connections of this region of cortex with posterior parietal cortex (Cavada and Goldman-Rakic, 1989; Disbrow et al., 1998) and lesions along this pathway indicate that these areas may be involved in tactile recognition and memory (Mishkin, 1979; Murray and Mishkin, 1984). Electrophysiological recording studies have demonstrated that some neurons in the lateral sulcus have bilateral receptive fields (Whitsel et al., 1969; Robinson and Burton, 1980a,b; Burton and Carlson, 1986; Cusick et al., 1989; Schneider et al., 1993) and complex response properties (Burton and Sinclair, 1990; Hsiao et al., 1993; Sinclair and Burton, 1993; R. Burton et al., 1997). For these reasons, exploring this region in humans is particularly interesting, because one might expect that the areas of the neocortex involved in intramanual dexterity and bilateral coordination of the hands to be particularly well developed in our species.

Despite the advances in understanding nonhuman primate somatosensory cortex organization and function, relatively little is known about the topographic organization and function of the lateral sulcus in humans. The focal stimulation studies of Penfield and colleagues (Penfield and Boldrey, 1937; Penfield and Jasper, 1954; Penfield and Rasmussen, 1968a) were limited in their descriptions of SII, because this field lies in the depths of the Sylvian fissure, and the resolution of the technique was not sufficient to describe the organization of SII in any detail. There have been a few functional imaging studies that have demonstrated areas that are activated differentially during tactile stimulation (Burton et al., 1993) and during the discrimination of microgeometric (roughness) and macrogeometric (shape) stimuli (Ledberg et al., 1995). However, the number of fields present, their internal organization, and their correlation to cortical fields identified in the lateral sulcus of monkeys are not known.

Our goal was to examine the organization of the lateral sulcus in humans using fMRI techniques in an effort to determine the number of fields present as well as the topographic organization of fields. We then compared the organization of this region in human and nonhuman primates with that of other mammals to determine whether there is a basic pattern of organization that may be common to all mammals. We hypothesize that additional fields exist in some lineages, such as primates, possibly associated with complex manual abilities and bilateral coordination of the hands. Portions of this work have been presented briefly elsewhere (Disbrow et al., 1997).

MATERIALS AND METHODS

In the current investigation, we used fMRI to examine the neocortex in the lateral sulcus of 18 human subjects in an effort to determine the number and internal organization of somatosensory cortical fields in this region. In two

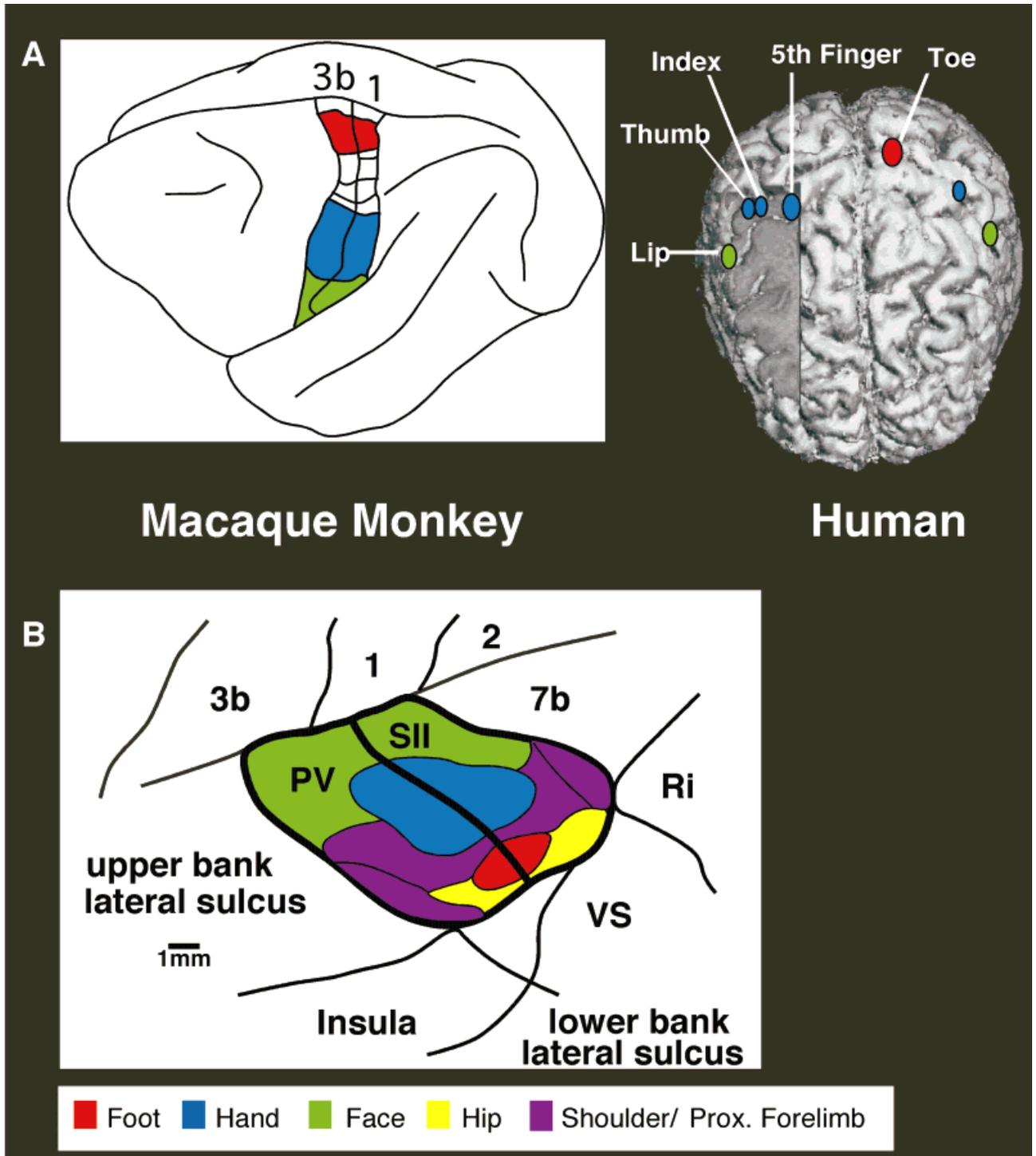


Fig. 1. **A:** The somatotopic organization of the postcentral gyrus in a macaque monkey determined by using electrophysiological recording techniques (from Nelson et al., 1978). **Top right:** Dorsal view of the human brain showing the somatotopic organization of cortex on the postcentral gyrus (determined by using magnetoencephalography). In both of these primates, the foot is represented most medially in the cortex (red) followed by representations of the hand (blue) and the face (green) more laterally. **B:** The somatotopic organization of the second somatosensory area (SII) and the parietal ventral area (PV) on the upper bank and parietal operculum of the lateral sulcus of the macaque monkey, as described by Krubitzer et al., 1995. The lateral-most portion of the sulcus is adjacent to anterior parietal fields 3b, 1, and 2; and the medialmost portion is adjacent to the insula. In these

regions, the face is represented most laterally (green) followed by the representation of the hand (blue) and the foot (red) more medially. The representations of distal body parts in SII and PV are adjacent to one another, whereas the proximal portions of the body, such as the shoulder (purple) and hip (yellow), are represented rostrally in SII and caudally in PV. These fields have mirror-symmetric representations of the body surface. Ri, retroinsular area; VS, ventral somatosensory area; 1, 2, and 3b, somatosensory areas of the anterior parietal cortex; 7b, somatosensory area of the lateral sulcus. In A and B, rostral is to the left. In the magnetic resonance image (MRI; top right), rostral is to the bottom, and lateral is to the right and left of the midsagittal sulcus.

TABLE 1. Stimulation Presentation to Different Body Parts in All Subjects¹

Subject	Hand	Face	Foot	Shoulder	Hip	Other
AO	X	—	X	X	X	—
DMS	X	X	—	—	—	Reproducibility vF
DS	X	—	—	X	X	—
EC	X	Motion	X	X	Motion	—
ED	X	X	X	—	X	—
HR	X	—	X	X	—	Fingertip vF
JO	X	—	X	X	X	—
KA	X	X	X	—	—	—
LK	X (vF)	Motion	X (vF)	—	—	—
PS	X	X	—	—	—	—
RT	X	X	X	No activation	—	Direction
SC	X	X	—	—	—	—
SS	X	X	X	—	—	—
TB	X	—	X	Motion	—	Direction
VC	X	No activation	X	—	—	Reproducibility
SP	X	—	—	—	4/5	Reproducibility
Scans used/total scans	16/16	7/10	11/11	5/7	4/5	6/6
PF	No activation	—				
SB	No activation	No activation	No activation	No activation	—	—

¹Summary of the different body parts stimulated in all of the subjects that participated in the present investigation. The columns denote the body parts that were stimulated for an individual subject. Each cell contains the result of a particular scan for that given body part. An X indicates a successful scan that was described in our results. "No activation" indicates that the scan yielded no activation for stimulation of a particular body part. "Motion" indicates that the scan could not be used because of motion artifact. "Reproducibility" denotes the subjects that were used to examine the consistency of our stimulus application. "vF" indicates scans in which a von Frey hair was used to stimulate the subject. "Direction" denotes scans in which the hand was stimulated with the sponge moving in one direction. In all other scans of sponge stimulation of the hand, the sponge was moved back and forth in two directions. All successful scans indicated with an X were generated by stimulating the body part with a sponge. The two rows at the bottom of the table summarize the scans done on the two subjects who were excluded from the analysis.

of these subjects, no activity was generated under any of our stimulus conditions; thus, these subjects are not part of this report. One of the 18 subjects was used only to test the reproducibility of our stimulus presentation. The other 15 subjects were used to examine topographic organization and, in some cases, stimulus preference and reproducibility (Table 1). Our somatosensory stimuli elicited activation in cortex that resides on the upper bank of the Sylvian fissure or lateral sulcus at an anterior/posterior location just caudal to the central sulcus. Anterior parietal areas located on the postcentral gyrus were examined to a limited extent in an effort to compare the types of stimuli required to elicit a response in this region with the types of stimuli needed to generate activity in areas in the lateral sulcus.

fMRI acquisition

Imaging was performed by using a standard clinical General Electric 1.5 Tesla Signa scanner equipped with 5.6 software and the sr120 gradient system. Three head coils, produced by General Electric, were used: a standard whole-head coil, a 5-inch surface coil, and a 3-inch surface coil. First, an anatomical high-resolution, three-dimensional (3D) steady precession gradient-recalled (3D-SPGR) series [acquisition: axial, interleaved, 256×256 matrix; field of view (FOV), $40 \text{ cm} \times 40 \text{ cm}$; 124 slices, 1-mm slice thickness; repetition time = 35 msec; echo time = 6 msec; flip angle = 30° ; 1 excitation (NEX) with fat saturation] was collected for use in overlay. Then, a gradient-echo, echo-planar imaging sequence designed to detect variations in local $T2^*$ (repetition time = 2 seconds; echo time = 69 msec; flip angle = 60°) was used. For all coils, a 256×128 matrix was used with a rectangular FOV of $40 \text{ cm} \times 20 \text{ cm}$ and a slice thickness of 5 mm (0.5-mm gap), yielding a true voxel (3D pixel) size of $3.0 \text{ mm} \times 3.0 \text{ mm} \times 5 \text{ mm}$. To view the region of interest in a tangential plane, axial slices of the brain were acquired. Five or six slices were obtained, depending on the size of the brain. The block of slices was centered over the Sylvian fissure on a coronal image and covered from just above the lateral ventricles to the middle temporal sulcus.

Seventy sequential multislice image sets were acquired at 2-second intervals over a 2-minute and 20-second period. Stimuli were presented in a block design with alternating 20-second blocks of stimulation and rest (4 blocks off, 3 blocks on).

During scanning, each subject's head was held securely in position. A plastic pillow (Olympic Vac-Pac; Olympic Medical, Seattle WA) filled with Styrofoam packing beads was fitted around the head, and the air was removed from the pillow so that it became rigid, conforming to the contours of the head. Subjects were instructed to remain still, keeping their eyes closed during each scan. Gross translational motion was determined during analysis of the variance of image center of mass. If motion artifact was noted ($> 3 \text{ mm}$), then data from that scan were excluded from further analysis. Fifty-five scans were done on 16 subjects, and 4 of these scans were discarded due to motion artifact. Two of these discarded scans were collected for stimulation of the face: one for stimulation of the shoulder and one for stimulation of the hip (Table 1). Two scans (one for stimulation of the face and one for stimulation of the shoulder) resulted in no activation in the cortex. Our study of human subjects was approved by the Human Subjects Committee at the University of California, Davis and by the Committee of Human Research at the University of California, San Francisco.

Stimuli

The stimuli used in this investigation were based on those that most effectively activated neurons in the lateral sulcus areas in monkeys (Robinson and Burton, 1980a; Krubitzer and Kaas, 1990; Krubitzer et al., 1995; Disbrow et al., 1998). In monkeys, cells in this region have large receptive fields; therefore, we used broad stimuli covering a large portion of the skin. A sponge rubbed in two directions across a large area of the skin was most effective in eliciting activation in the lateral sulcus (Fig. 2A,C–F). For example, stimulation of the hand consisted of rubbing both the glabrous and hairy surfaces of the hand at the same time with two sponges

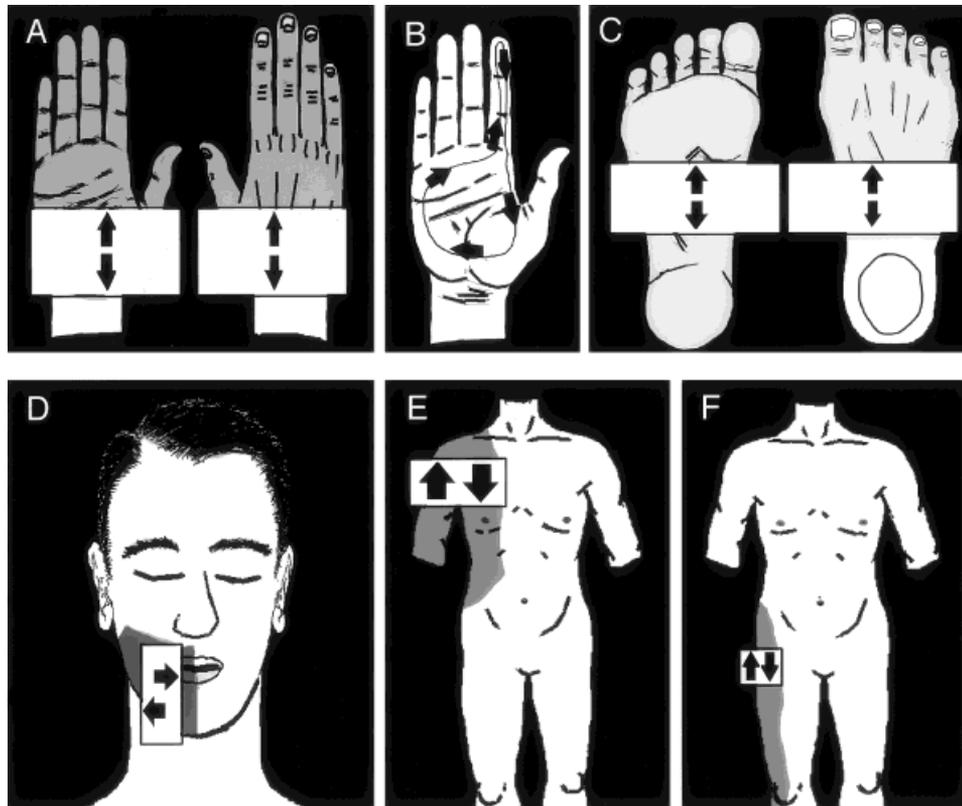


Fig. 2. **A-F:** The stimuli applied to the different body parts in the 16 human subjects used in this study. In A and C, the distal limbs were stimulated by rubbing two sponges back and forth across the dorsal and ventral surfaces of the hand or foot. In some of the cases, a von Frey hair was rubbed along the glabrous surface of the hand in a manner illustrated in B. For the face, a sponge was rubbed in a back-and-forth motion in a mediolateral direction (D). For the trunk/

shoulder and proximal arm (E), two sponges were rubbed in a rostral-caudal direction on the ventral surface of the body, and, for the trunk/hip and proximal leg (F), two sponges were rubbed along the ventral surface in a rostral-to-caudal-to-rostral direction. Shaded areas represent the portions of the body that were stimulated in these experiments.

(rate, 0.2 Hz; Fig. 2A). The stimuli were moved back and forth from proximal to distal. The method of stimulation of the foot was identical to that described for the hand (Fig. 2C). For stimulation of the face, the lips, cheek, and jaw were rubbed in a medial-to-lateral direction from the nose to the lateral edge of the cheek with a sponge attached to a 3-inch plastic rod (Fig. 2D). Stimulation of the shoulder/trunk included skin on the proximal, ventral forearm as well as the adjacent ventral upper trunk. A large sponge with a surface area that covered the entire mediolateral area to be stimulated was rubbed back and forth along a large rostrocaudal extent of the skin (Fig. 2E). Stimulation of the hip and thigh was similar to that described for the shoulder and included a large portion of skin (Fig. 2F).

Due to scanning time constraints, not all subjects underwent stimulation of all five body parts. The hand was stimulated in all 15 subjects who showed activation (Table 1), because it was expected to have the largest representation due to the cortical magnification observed for the hand in both human and nonhuman primates in the first somatosensory area (SI; Penfield and Boldrey, 1937; Penfield and Rasmussen, 1968b) and in nonhuman primates for SII and PV (Robinson and Burton, 1980a; Burton and

Carlson, 1986; Krubitzer and Kaas, 1990; Krubitzer et al., 1995). The hand representation also was used as a reference point for comparison with activation generated by stimulating other body parts. Ten subjects underwent stimulation of the face, 11 underwent stimulation of the foot, 7 received stimulation of the shoulder and trunk, and 5 received stimulation of the hip (Table 1).

Reproducibility was examined in three subjects (DMS, VC, and SP; see Table 1). In two of these subjects (VC and SP), a sponge rubbed back and forth across the hand was used in two separate trials. In one subject (DMS), we examined the difference in activity generated from stimulating the hand with a sponge versus a von Frey hair dragged across a large portion of the glabrous hand (compare Fig. 2A with Fig. 2B; see below). Stimulus preference for fields in the anterior parietal cortex compared with the lateral somatosensory areas was examined in one subject (HR; Table 1, Fig. 3). A punctate stimulus was applied to the tip of the finger with a von Frey hair (0.711-mm diameter; 0.74 Newtons of force; Fig. 3A). In two subjects (RT and TB), we compared activity that resulted from moving the sponges across the hand in one direction versus two directions (Fig. 4).

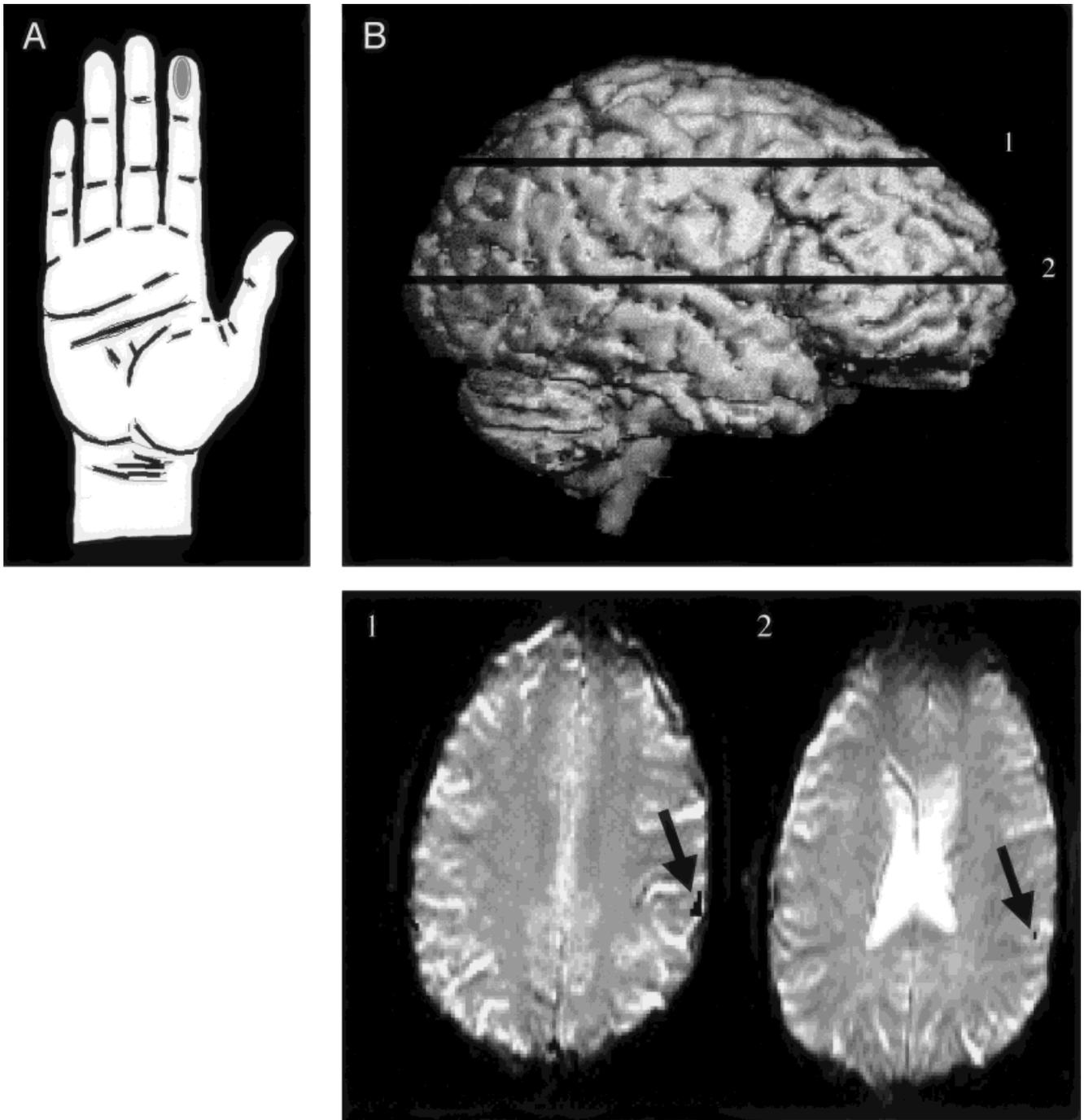


Fig. 3. **A:** A small, punctate stimulus applied to the tip of the finger with a von Frey hair (0.74 Newtons of force) resulted in a relatively large focus of activity on the postcentral gyrus (bottom, 1) and only in a very small focus of activity in the lateral sulcus (bottom, 2). **B:** The regions of the cortex from which the slice of the brain was taken shown in a dorsolateral view of the brain. The locations of the

cut are approximated from the dorsoventral location from which the axial slice was taken. **Bottom:** Arrows in slices 1 and 2 indicate areas of activation (black) in anterior parietal cortex (slice 1) and the lateral sulcus (slice 2) generated by stimulating distal D2 (A), as described in the legend to Figure 2.

In an attempt to grossly quantify our large moving-sponge stimulus, a von Frey hair also was used to stimulate the hand (Semmes-Weinstein monofilaments; Stolting Co., Wood Dale, IL; Fig. 2B). A monofilament with a

0.711-mm diameter that exerted a force of 0.74 Newtons was dragged lightly across the surface of the glabrous palm and index finger (Fig. 2B). The monofilament was dragged at approximately 10 cm/second, with the circuit

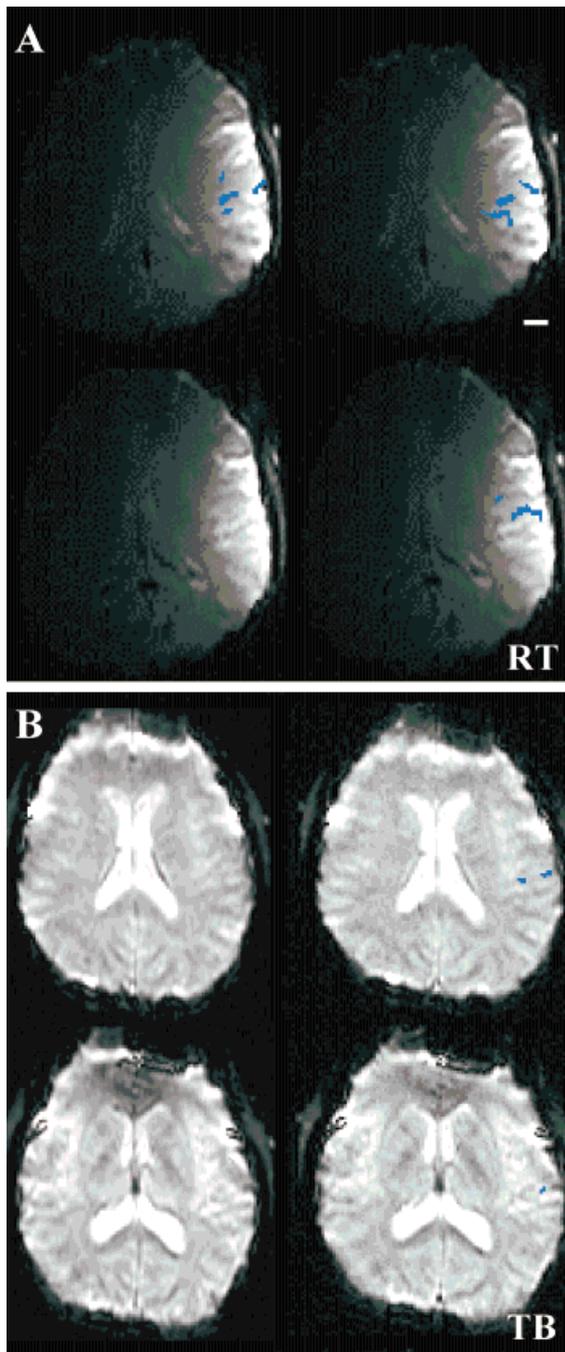


Fig. 4. **A,B:** Axial slices through the upper bank of the lateral sulcus and parietal operculum in two subjects in which the hand was stimulated. In one instance, the hand was stimulated with a sponge rubbed in one direction (A and B, scans on left). In another scan, the sponge was rubbed back and forth in two opposite directions (A and B, scans on right). The scans in which the hand was stimulated in only one direction are markedly reduced (A, left) or absent (B, left) compared with the scans in which the hand was stimulated in two directions. RT and TB indicate the individual subject from whom these scans were taken. For conventions, see Figures 1–3. Scale bar = 1.5 cm

TABLE 2. Talairach Coordinates for the Center of Mass of Cortical Fields and Body Part Representations in the Parietal Ventral Area and the Second Somatosensory Area¹

Area	Mean (S.D.) Talairach coordinates		
	ML (X)	AP (Y)	SI (Z)
RL	49.6 (11.4)	-15.0 (5.4)*	-17.2 (4.4)
SII/PV	50.8 (8.9)	-24.4 (8.0)*	-14.7 (5.3)
C	50.4 (7.4)	-26.1 (13.9)	-12.6 (1.1)
SII/PV body part representation			
Face	59.8 (3.6)*	-23.8 (2.3)	-9.8 (4.0)
Rostral shoulder (PV)	40.3 (9.7)	-15.8 (7.5)*	-15.4 (6.8)
Hand	51.1 (0.84)*	-23.3 (7.8)	-13.3 (5.9)
Caudal shoulder (SII)	41.2 (7.8)	-30.3 (15.3)*	-15.9 (5.8)
Rostral hip (PV)	49.8 (21.5)	-14.3 (1.8)	-13.6 (0.8)
Foot	48.0 (7.6)*	-16.3 (6.7)	-13.6 (5.5)
Caudal hip (SII)	48.7 (17.9)	-20.0 (14.1)	-15.9 (4.4)

¹Talairach coordinates for the center of mass of cortical fields (based on the representation of the hand) and body part representations in the second somatosensory area (SII) and the parietal ventral area (PV). Means and standard deviation (S.D.) of coordinates in the medial-lateral (ML or X), anterior-posterior (AP or Y), and superior-inferior (SI or Z) planes are listed.

*Significant differences in location for the centers of mass were found for activation of RL and SII/PV in the AP plane, for the shoulder representation in SII and PV in the AP plane, and for the face, hand, and foot representations in the ML plane.

around the palm and index finger made 5 times in one 20-second stimulus period. This method worked well for stimulation of the hand, but it did not yield consistent activation when applied to other body parts.

Data analysis

Data analysis and display were performed by using the Stimulate software package (Strupp, 1996). Cross-correlation analysis was used to determine significantly active voxels in the entire data set. A correlation threshold of $r = 0.3$ was used with a cluster threshold of 4 voxels. All active voxels were displayed with the exception of voxels in the sagittal sinus along the rostral and caudal midline. These voxels often were outside the brain. Furthermore, a similar pattern of activation has been seen in our laboratory in response to a variety of stimuli (motor, visual, auditory, picture naming). We therefore are confident that these active voxels are not related specifically to the stimulus but, rather, are an artifact of the blood oxygenation level dependent (BOLD) technique. To determine the effect of different thresholds of analysis on the pattern of activation, correlation thresholds of $r = 0.3$ and $r = 0.4$ were compared in two subjects.

By using the Stimulate software package (Strupp, 1996), the center of mass was calculated for each cortical field and for the individual body part representations within a field. Activation patterns were superimposed on the high-resolution 3D images. These brains were warped to Talairach space, and the standardized stereotaxic coordinates of these points were determined (Talairach and Tournoux, 1993). These values were then compared by using a paired *t* test to determine whether cortical field or body part representation locations were significantly different (Table 2).

In a second analysis to compare further activity patterns between subjects, all brains were stretched to the same anterior-posterior (AP) and mediolateral (ML) space by matching major landmarks, such as sulci, the lateral ventricle, and the outline of the section or slice. In this analysis, we used coordinates such as the distance between the anterior horn and occipital horn of the lateral

TABLE 3. Topographic Relationships Between Body Part Representations in the Second Somatosensory and Parietal Ventral Areas in Humans Based on Expected Relationships in Monkeys¹

Subject	Mediolateral			Rostrocaudal		Total
	Hand/ face	Hand/ foot	Face/ foot	Hand/ shoulder	Foot/ hip	
AO	—	1/1	—	1/1	1/1	3/3
DMS	0/1	—	—	—	—	0/1
DS	—	—	—	1/1	—	1/1
EC	—	1/1	—	1/1	—	2/2
ED	0/1	1/1	1/1	—	0/1	2/4
HR	—	1/1	—	1/1	—	2/2
JO	—	1/1	—	0/1	1/1	2/3
KA	1/1	1/1	1/1	—	—	3/3
LK	—	1/1	—	—	—	1/1
PS	0/1	—	—	—	—	0/1
RT	0/1	1/1	1/1	—	—	2/3
SC	0/1	—	—	—	—	0/1
SS	1/1	1/1	1/1	—	—	3/3
TB	—	1/1	—	—	—	1/1
VC	—	0/1	—	—	—	0/1
Total	2/7	10/11	4/4	4/5	2/3	22/30

¹Classification of the relationship between body part representations for each subject. The fractions in each cell represent the number of observed relationships that correspond to those described in monkeys (numerator) over the total number of possible relationships for a given body part (denominator). The fractions in the column at the far right indicate the number of observed relationships over the total number of possible relationships that could be obtained for each case.

ventricle, the ML distance between the midline and the lateral edge of the brain at the AP level of the central sulcus, and the AP distance between the rostral and occipital poles of the cerebral cortex. Modern software packages use similar coordinate systems to align activity patterns across subjects.

Separate regions of activation were then encircled. We considered a region to be separate if one or more of the following conditions were met: 1) it was more than a centimeter away from another region activated by stimulation to the same body part, 2) it rerepresented a body part activated in an additional region, and 3) it exhibited a similar consistency (across subjects) in activating a particular region of cortex. For instance, some regions always were activated; however, under similar stimulus conditions, others were activated only some of the time. By using the landmarks noted above, the regions of activation were collapsed across slices in an individual case so that they could be viewed on a single section (Figs. 7–9). By matching major landmarks, each case was superimposed onto a single drawing, and the regions of activation were drawn in different colors so that they could be distinguished from one another.

To determine the topographic organization of fields in the lateral sulcus, the activity patterns from stimulation of each of the body parts were collapsed across sections for an individual case (as described above) and viewed on a single section. The patterns of activity were then evaluated for mediolateral progressions of body part representations as well as for anteroposterior progressions of activation within the central region of activation.

To evaluate of the consistency of the topography, we devised a system in which the topographic order was expressed as a fraction (Table 3). The denominator contained the number of possible topographic relationships. The expected relationships in the denominator were based on the organization of similar fields in monkey cortex (Krubitzer et al., 1995; see Fig. 1B). The numerator contained the number of these relationships that corresponded to the expectation. For instance, if the face and

the hand were stimulated and resulted in a pattern of activation in which the face activation was located lateral to the hand (as expected), then the fraction shown in Table 3 is 1/1. If the topography is reversed from what normally would be expected, then the fraction would be 0/1. If the foot, hand, and face were stimulated and the pattern of activation was medial to lateral, respectively (as expected), then the subject would be given a 3/3, because the foot is medial to the hand (1/1), the foot is medial to the face (1/1), and the hand is medial to the face (1/1). In this way, both the number of body parts stimulated and the extent to which topographic relationships are maintained are indicated. We then ran a Monte Carlo analysis to determine whether the topographic relationships that we observed were significantly different from chance.

RESULTS

Effective stimuli

Stimuli with a large surface area, such as a sponge moved across the skin, proved to be the most effective for eliciting a cortical response. The two key parameters of the stimulus were its large surface area and its movement. The amount of skin stimulated in the fashion described above varied with the portion of the body being stimulated. For instance, stimulation of the hand produced a larger cortical activation than stimulation of the shoulder and trunk, which included a larger surface area of the skin.

It is important to note that there were some stimuli that were not effective in eliciting significant cortical activation in areas in the lateral sulcus. Significant activation is defined as a cluster of ≥ 4 voxels that have a correlation coefficient of $r \geq 0.3$ (see Materials and Methods). First, when only a small portion of the finger, such as the distal pad, was stimulated at a low frequency (≈ 1 Hz) with a von Frey hair, very little or no activation was generated in the lateral sulcus (Fig. 3A). Stimulation of the entire glabrous surface of the hand, which consisted of moving a sponge in two directions, consistently (14 subjects, 1 was von Frey hair only) elicited activation in at least one of the regions in the lateral sulcus (Fig. 4). In this condition, the sponge was in constant contact with the hand during the 20-second stimulation period. In two cases (Table 1), moving the sponge in only one direction across the glabrous hand did not elicit a robust response compared with the response elicited by moving the sponge in two directions (Fig. 4). In both subjects, more voxels were significantly active for two directions versus one direction. In one subject (Fig. 4B, left scan), no voxels were significantly active in the one-direction condition. In this condition, the sponge was moved across the hand from the palm to the distal tips of the fingers, lifted from the tips, and placed back at the palm to be moved again. The sponge was in contact with the skin for about half of the 20-second stimulation period.

Even when stimulus parameters that elicited maximal activity were applied, stimulation did not always elicit detectable activation for all body parts. Again, significant activation is defined as a cluster of ≥ 4 voxels that have a correlation coefficient of $r \geq 0.3$. Of the original 18 subjects, 2 showed no activation for stimulation of any body part (Table 1). All 16 subjects showed significant activation for stimulation of the hand. Seven of the 10 subjects

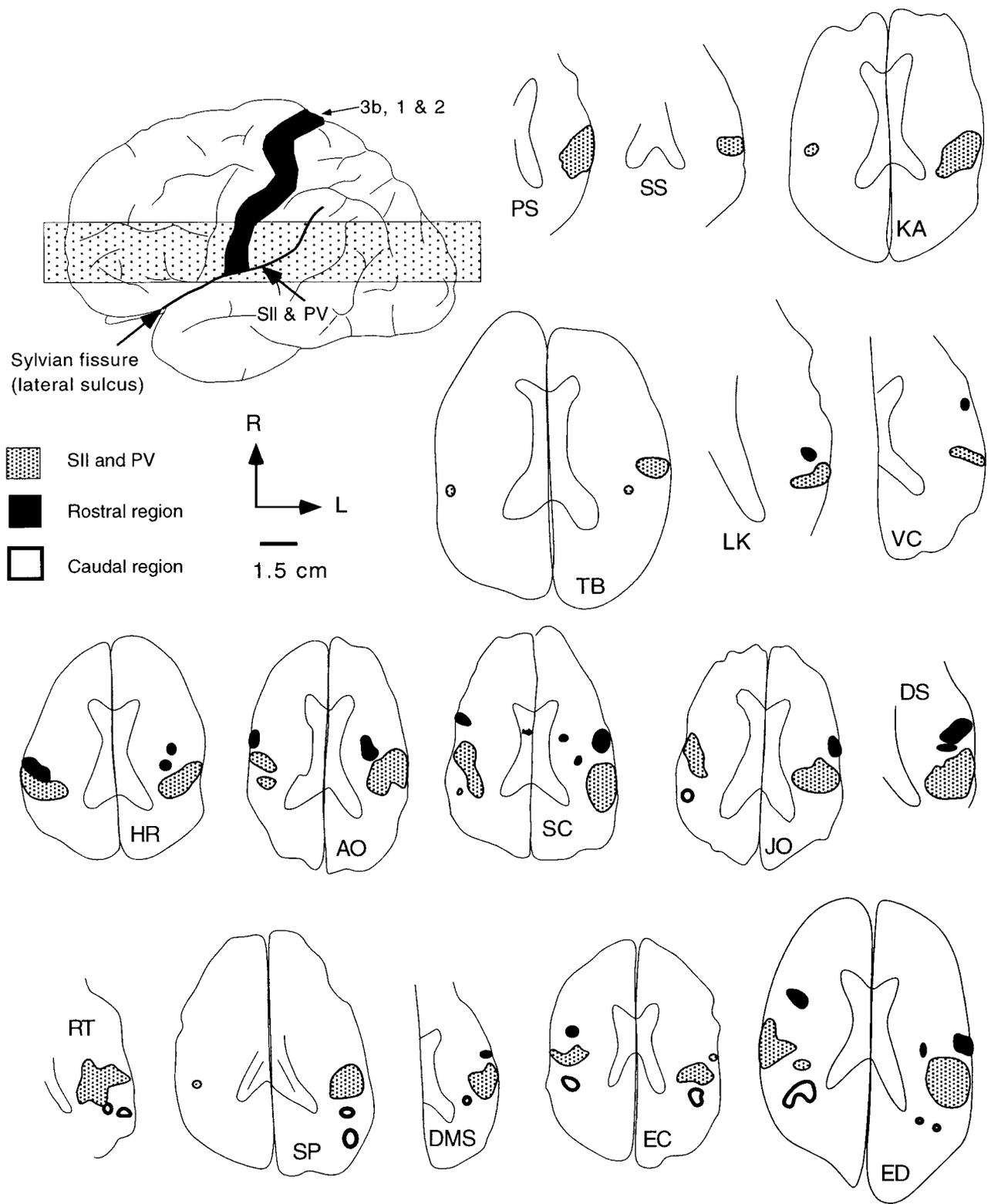


Fig. 5. Reconstructions of axial slices of the brain drawn from each of the subjects. In all cases, the activity patterns were collapsed across one to three slices (in one case, four slices) in the different subjects in the region of the brain denoted in the shaded box in the upper left figure. Each brain is drawn to the same scale, and major landmarks were matched, such as portions of the lateral ventricle, the midline, major sulci, and the lateral edge of the brain (see Materials and Methods). Areas of activity are encircled. If regions of activity were ≥ 1 cm apart and/or rerepresented body parts of another region, then they were considered as a separate area of the somatosensory cortex. Our data indicate that one region (gray areas) was activated consistently in all subjects and that this region was activated bilaterally in

all of the subjects in which a whole head coil was used. This region was the combined areas SII and PV. A second region (black areas), whose center of mass was rostral to this region (> 1 cm), was activated contralateral to the site of stimulation in 11 of the 15 cases and bilaterally in 5 of the 7 cases in which a whole head coil was used. A small region caudal to SII and PV (open encircled areas) was activated in cortex contralateral to the side of stimulation in only 4 of the 15 cases and bilaterally in 4 of the 7 cases in which a whole head coil was used. Thus, the only areas that were activated consistently both contralaterally and bilaterally were SII and PV. L, lateral; R, rostral. For conventions, see Figures 1–3.

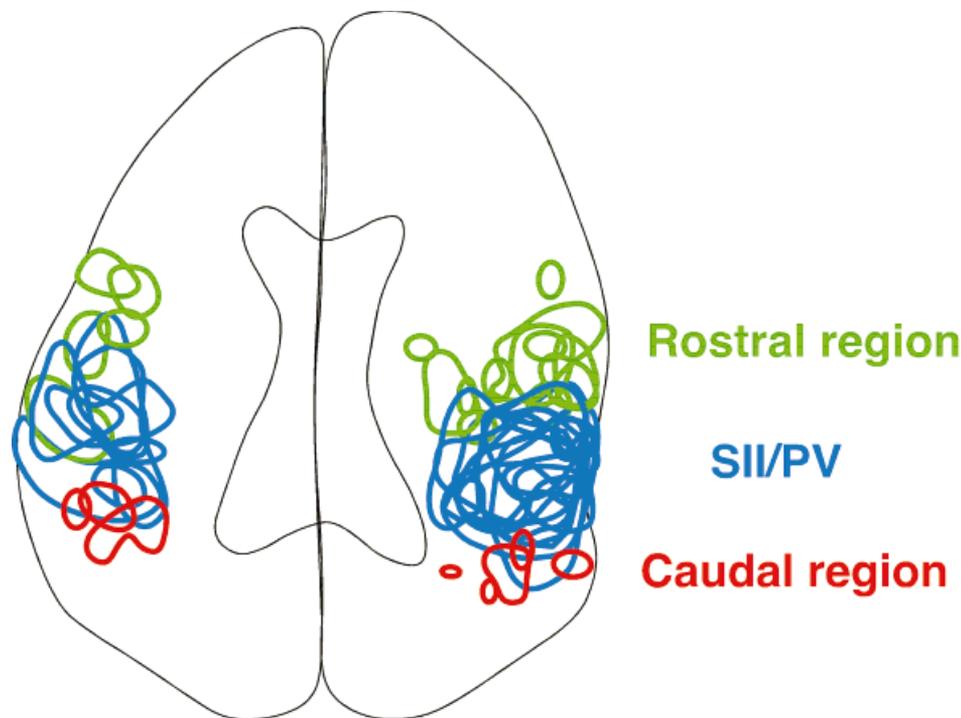


Fig. 6. Reconstruction of an axial slice through the lateral sulcus with the activity patterns from all 16 cases collapsed onto a single drawing. The patterns were collapsed by matching all major features of the brains drawn in Figure 5 and encircling major areas of activation. All of the blue encircled areas denote the SII/PV region from all

of the cases, the green denotes the rostral field, and the red denotes the caudal field. This illustration demonstrates that the major regions of activation are in only slightly variable locations across cases. Also, when all patterns are coregistered, three separate regions are seen clearly.

scanned during facial stimulation had significant activation in the lateral sulcus cortex. All 11 subjects who were scanned during stimulation of the foot showed significant activation. Of the seven subjects who underwent stimulation of the shoulder and trunk, five showed significant activation. For the five subjects who received hip stimulation, four showed significant activation (Table 1).

Anteroposterior axis—Evidence for three regions of activation

An important observation of the present investigation was that there were three regions of activation along the anterior posterior axis of the lateral sulcus and adjacent operculum (Figs. 5, 6). Axial slices taken from the upper bank of the Sylvian sulcus allowed the cortex to be viewed from a tangential plane and enabled the identification of the three separate regions of activation: the most rostral region of activation, the rostral lateral region (RL); the middle region of activation, termed SII/PV for reasons described below; and the caudal region (C). The center of mass for these regions usually was separated spatially by a distance of 1 cm (Table 2, Fig. 5). For the largest region (SII/PV), a topographic organization could be determined (see below).

It should be noted that there often were multiple sites of activation (more than three) in the cortex for stimulation of a single body part (Figs. 7, 8). In many instances, these separate foci were clustered closely in what we consider to be a single region. For several reasons, we did not consider

every separate voxel cluster of cortical activation for stimulation of a single body part to be a distinct cortical area. First, clustered foci were not seen for every individual, and only a single focus within a given region was identified (e.g., subject SS in Fig. 7A [foot] and Fig. 7B [foot and face]). Second, separate foci often overlapped somewhat with foci of activation resulting from stimulation to other body parts (e.g., Fig. 7A,B, subject KA; Fig. 7E,F, subject RT). For example, stimulation of the foot in one subject (AO; Fig. 8A) resulted in one large area of activation in the hemisphere contralateral to the foot that was stimulated. Stimulation of the hip/thigh resulted in several small foci of activation. One group of foci generated by stimulating the hip/thigh was clustered and overlapped the foot activation zone to a large extent (Fig. 8B). Only two of the foci generated from stimulation of the hip did not overlap the activation from stimulation of the foot but were located immediately adjacent to the representation of the foot. This indicated to us that the region in question contained neurons with very large receptive fields that often encompassed much of the body (e.g., the foot and hip and lower trunk). This group of foci was considered to be located in the same region and not located in four separate somatosensory areas. In the same subject, there was another area of activation (≈ 1.5 cm) rostral to this first region of activation. For stimulation to the foot, one small focus was seen, and, for stimulation of the hip, a small focus was observed in this same location slightly overlapping the area of activation of the foot. This region of activation was

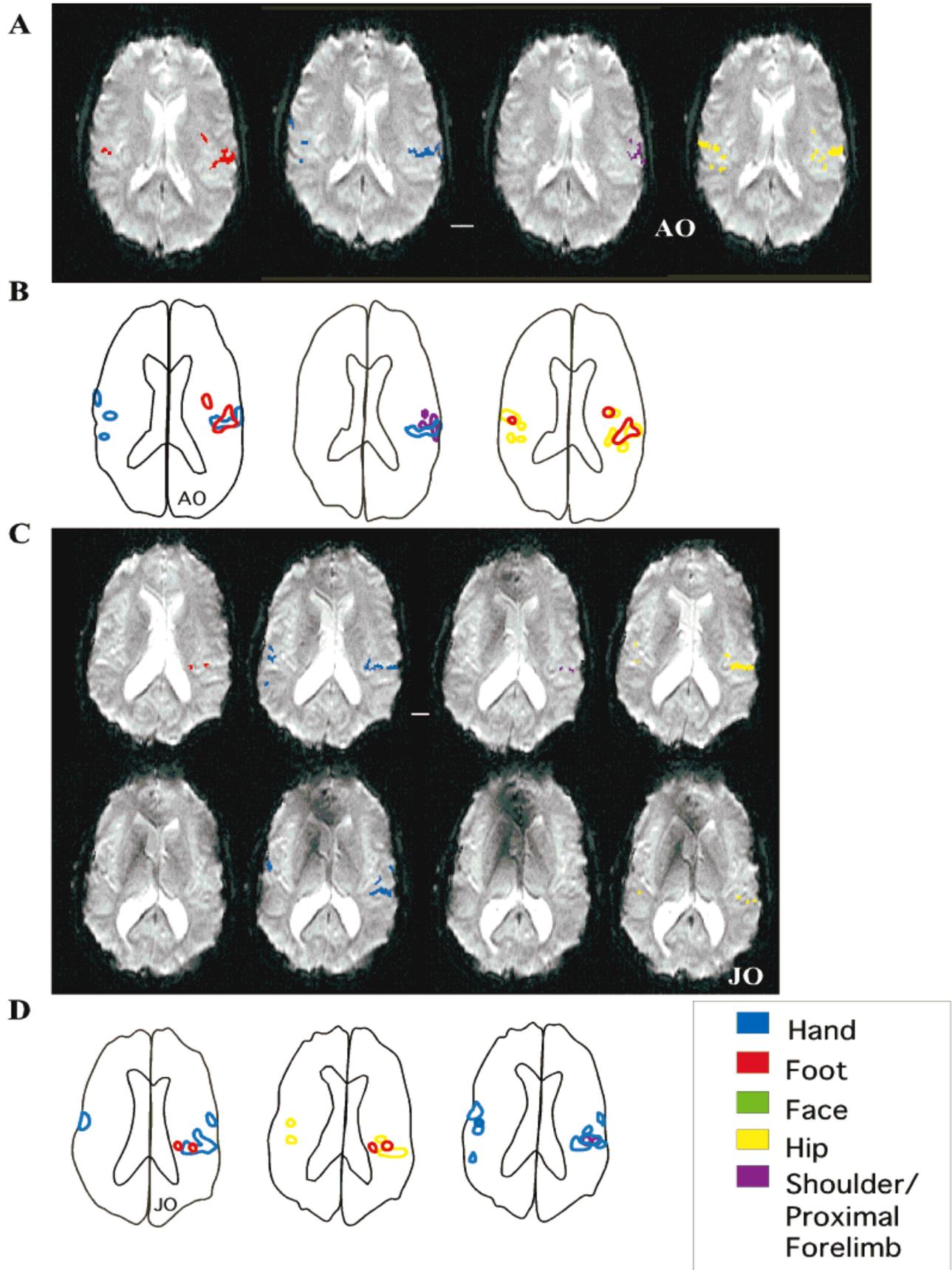


Fig. 8. **A-D**: Echo-planar axial slices through the upper bank of the lateral sulcus and parietal operculum depicting the activity generated from stimulating the foot, hand, hip, and shoulder (A,C) from two of the six subjects who underwent stimulation of proximal body parts. These cases demonstrate the rostrocaudal organization of SII and PV. B and D show reconstructions of data that demonstrate the correlation between body parts, specifically, from left to right, be-

tween the hand and foot, the foot and hip, and the hand and shoulder. In five of six subjects, the activity generated from stimulating the shoulder and hip clearly flanks both rostrally and caudally the activity generated from stimulating the hand and foot. Thus, two mirror-symmetric representations that adjoin at the representations of the hand and foot are demonstrated. In all of these cases, a sponge was used to stimulate the body part. For conventions, see Figures 1-4.

considered to be separate from the region described previously.

A third reason why these areas were considered separate representations was the consistency with which they could be activated. One large region just lateral to the occipital horn of the lateral ventricle was activated in all cases under our stimulus conditions (area SII/PV). A second region $\approx 1\text{--}2$ cm rostral to the first region was activated in ten cases. A third region, just caudal to the first region, was activated in only five cases (Figs. 5, 6).

Once the boundaries of the three fields were determined for each subject, the center of gravity was calculated for each field. The average Tailarach coordinates (Tailarach and Tournoux, 1993) for the three fields are listed in Table 2. A paired *t* test was used to compare these values in the anterior-posterior of rostral-caudal plane for SII/PV versus RL and SII/PV versus C. The difference between SII/PV and RL was statistically significant ($P < 0.05$), whereas the difference between SII/PV and C was not. The location of C was relatively variable (Table 2).

Examination of the ipsilateral hemisphere also indicated a separation of these regions (Figs. 7, 8), although this hemisphere was not examined systematically in all subjects. Eight subjects were scanned using a whole-head coil, allowing for examination of the ipsilateral hemisphere (see, e.g., Figs. 7A, 8A,B). All subjects showed bilateral activation in response to hand stimulation. One of the two subjects with face stimulation showed bilateral activation. Seven subjects underwent foot stimulation, and four of these showed bilateral activation. Four subjects underwent trunk stimulation, and two of these showed bilateral activation. Three subjects underwent hip stimulation, and all showed bilateral activation (Figs. 7, 8).

Topography of SII and PV

The topographic organization of SII and PV was examined by using two statistical methods. First, we calculated the center of mass for each body part representation in SII and PV and located these points in Tailarach space (Tailarach and Tournoux, 1993). Mean values for these locations are listed in Table 2. For medial-lateral organization, a paired *t* test was used to compare the locations of the centers of mass for the representations of the hand versus the foot and the hand versus the face. Both comparisons were significant ($P < 0.05$), demonstrating a medial-to-lateral topographic organization of the body part representations at the shared boarder of SII and PV. To examine anteroposterior organization and to distinguish between two mirror-symmetric representations (SII and PV), the two shoulder and two hip locations (one in SII, one in PV) were compared with one another. The SII and PV shoulder representations were significantly different from one another ($P < 0.05$), whereas the hip locations were not ($P = 0.066$). The location of the hip representations was relatively variable (Table 2).

Second, the data from Table 2 were used to determine whether the probability of the resulting relationships between body parts was significantly different from chance. We examined 30 relationships of body part representations (Table 3). The probability of each expected relationship was calculated: for example, 1 in 6, for a score of 3 out of 3 for the mediolateral relationships; 1 in 2 for the hand and trunk relationship. A Monte Carlo analysis was done in which scores (0 or 1) of the topographic relationships

were assigned randomly for each relationship for each subject. A total of 20,000 iterations yielded a $P = 0.0025$, indicating that the consistency of topographic relationships was significantly different from chance (α equals; 0.5).

Twenty-two of the 30 relationships allowed us to determine whether a mediolateral topographic organization was present, and 8 of the 30 relationships allowed us to determine whether an anteroposterior topographic organization was present. Body part representations within the SII/PV region could be ascertained by examining individual slice data in a number of the subjects studied (see, e.g., Fig. 7A, subject KA; Fig. 8A, subject AO). However, it was useful to collapse the data across sections within each subject to appreciate the details of topography from the SII/PV region. Collapsing across the two or three axial slices in which activity was observed affords us a tangential view or flattened map of this region (see Materials and Methods; Figs. 7, 8). Below, we first describe the mediolateral organization of activation by examining patterns of activation generated from stimulation of the foot, hand, and face; then, we describe the rostrocaudal organization of the PV/SII region by examining the activation patterns generated from the foot and hip/thigh or from the hand and shoulder /trunk.

In 22 of the 30 relationships, a topography was present in SII and PV. For 22 possible relationships in which the mediolateral organization could be determined, 16 topographic relationships, similar to those described in non-human primates, were observed. The activation produced by stimulation of the foot was found most medially in the sulcus. The activation produced by stimulation to the hand was lateral to this, and the activation produced by stimulation of the face was the most lateral, at the lip of the upper bank of the lateral sulcus. In some instances, this topography was very distinct (e.g., Fig. 7A–D, subjects KA and SS), and, in some cases, it was less distinct but still present (e.g., Fig. 7E,F, subject RT). Most of the mediolateral correlations that were not topographic (five of seven) were for the face and hand. Activity from stimulation of the face generally spread into regions in which activation resulted from stimulation of the hand (Fig. 7E,F, subject RT). Thus, of the seven possible hand/face relationships, only two resulted in the expected topographic relationship.

There were eight relationships in which the rostrocaudal organization of the SII/PV region was examined (Table 3, Fig. 8). Of these, six relationships demonstrated distinct topographic order. For instance, in two cases in which the foot activation was superimposed on activation generated from stimulation of the hip, it was found that either the foot activity was flanked immediately rostrally and caudally by the hip activity (Fig. 8B,C, subject JO) or that the pattern of activity generated from stimulation of the hip/thigh overlapped that of the foot but spread both rostrally and caudally beyond that of the foot (Fig. 8A,B, subject AO). When activity generated by stimulating the hand was superimposed with the activity generated from stimulating the shoulder/trunk, in most cases, the patterns of activity, although overlapping, showed a distinct spread of the shoulder/trunk activation beyond the rostral and caudal boundaries of the hand activation (Fig. 8A,B).

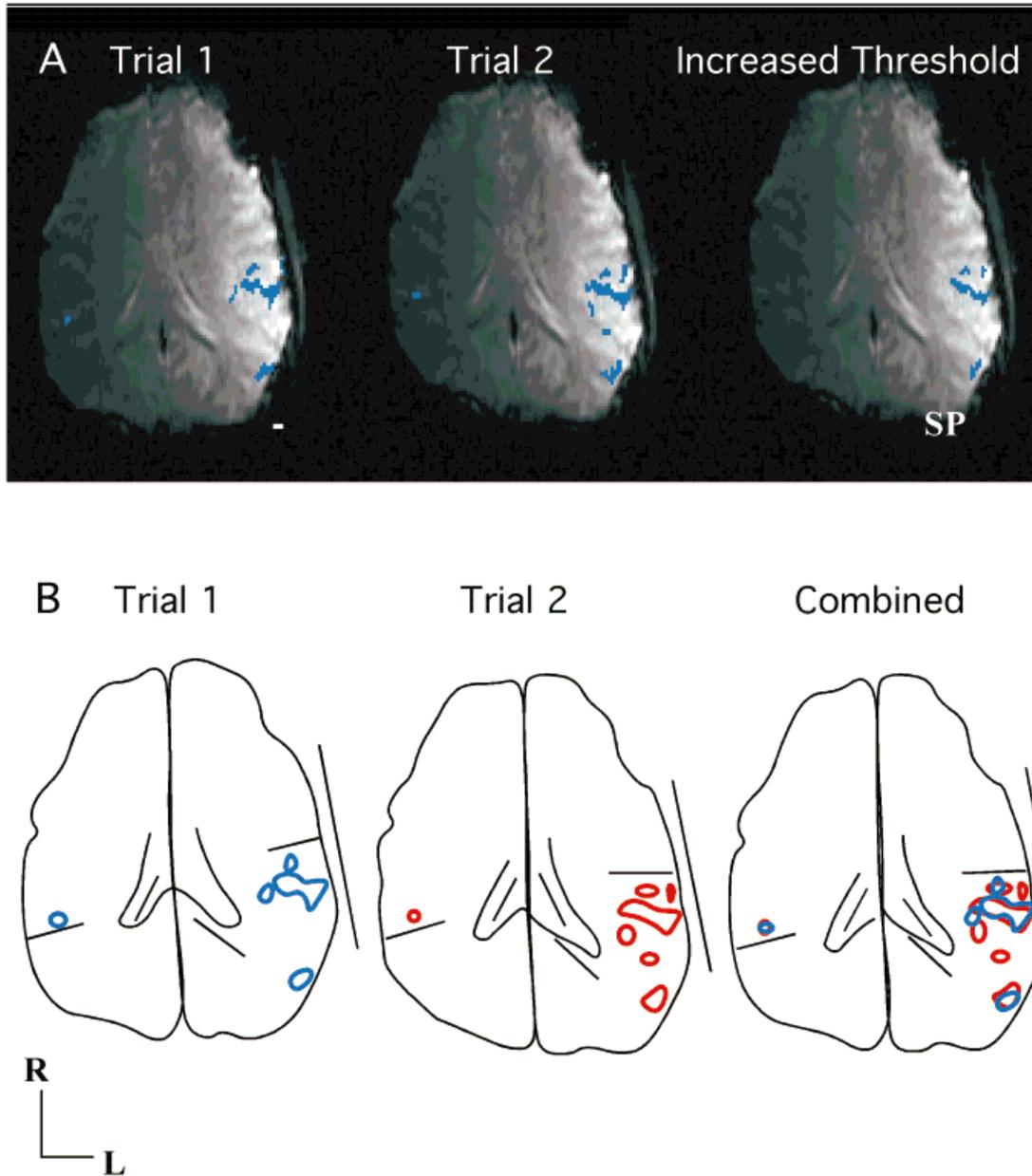


Fig. 9. **A:** Axial slices through the brain from one of three subjects in whom the consistency of response to stimulation was tested. The left and middle scans indicate the activity generated at two separate times during the same scanning session by using a sponge rubbed across the hand in two directions. Data are displayed with a correlation threshold of 0.3. The right scan was generated by using the

stimulus at a correlation threshold of 0.4. The activity patterns under all three conditions are similar. **B:** Reconstruction of the data from the left and middle scans shown in A. The combined reconstruction (right) shows the correspondence of the data from the two trials of in which the same stimulus was used. For conventions, see Figures 1–4.

Within-subject variation and across subject variation

Because of the noted variability between subjects, such as the different number of fields activated, the possibility that the stimulation was delivered inconsistently was considered. To check the consistency of our stimulus application and the patterns of activity that it elicited in a given subject on different trials, we applied

stimulation to the hand on two separate trials in each of three different subjects (see, e.g., Fig. 9, subject SP). Our results demonstrate that the pattern of activation was similar within a subject on separate trials. Although this does indicate that small variation within subjects across trials does occur, this small degree of variation is not enough to account for the differences we observed across subjects.

DISCUSSION

In the discussion below, we first consider the number and internal organization of cortical fields in the lateral sulcus in light of our results. We then compare other work on the organization of cortex in the lateral sulcus of humans with the current investigation. We review studies on the organization of somatosensory cortex in nonhuman primates and other mammals to determine whether they support our contentions that SII and PV exist in humans and that these fields are homologous to those described in other mammals. We discuss the different types of stimuli needed to activate these areas compared with anterior parietal fields, and we propose that the lateral sulcus regions are likely to have functions that differ from those of the anterior parietal fields. We also examine the variability across subjects and discuss the possibility that this variation is the result of differential use of the hands, as studies of cortical plasticity in nonhuman primates have suggested. Finally, we review the methodological issues pertinent to the interpretation of our data.

Number and internal organization of cortical fields in the lateral sulcus

In the current investigation, we provide evidence for four separate somatosensory fields in the lateral sulcus of humans. Two of these fields, SII and PV, are mirror-symmetric representations of the body surface. Statistical analysis of the Talairach coordinates of the center of mass for body part representations indicated a medial-lateral progression from foot, to hand, to face. Flanking these body part representations were areas activated in response to stimulation of the shoulder and hip. Two areas of activation in response to shoulder stimulation flanking the hand representation could be distinguished statistically. However, two hip representations could not be delineated. Our inability to distinguish the two areas of activation for hip stimulation flanking the foot representation may be due to the fact that the hip and foot representations overlap. In the three cases in which the hip/foot comparison could be made, one comparison was not as expected (Table 3). The small sample size (Table 1) and the relatively large variation in location (Table 2) indicate that additional study is needed to examine this correlation. In general, we have shown that SII and PV are two separate fields that are organized topographically in a manner consistent with the organization of SII and PV described in other primates and other mammals.

Two additional fields, RL and C, showed activation in response to somatosensory stimulation that was not consistent (RL = 10 of 16 subjects; C = 5 of 16 subjects). The center-of-mass analysis showed a clear distinction between SII/PV and RL, whereas the difference between SII/PV and C was not significant. Although the difference between SII/PV and C was clear on visual inspection (Fig. 6), the small sample size probably contributed to our inability to distinguish them statistically. Clearly, further investigation is warranted using a stimulus optimized for neurons in C.

Studies on the organization of areas in the Sylvian fissure (lateral sulcus) of humans

There are only a few studies in which the organization of the lateral sulcus was examined by using techniques that measure changes in cerebral blood flow or oxygenen-

ation resulting from peripheral stimulation. These studies demonstrated activity in the lateral sulcus and on the insula with the application of vibration (Burton et al., 1993; Coghill et al., 1994; Gelnar et al., 1998) and/or a tactile stimulation (Seitz and Roland, 1992; Burton et al., 1993; Ledberg et al., 1995; Gelnar et al., 1998). In most of these investigations, the activation was reported to be on the upper bank of the lateral or Sylvian sulcus and on the parietal operculum. This region of cortex is designated as SII. Examination of the patterns of activation from these previous studies reveals that, with respect to major sulcal and ventricular landmarks, the regions of activation in the lateral sulcus and on the parietal operculum that result from tactile stimulation are in the approximate location of our SII/PV activation (e.g., compare Figs. 1 and 2, slice Z18, in Burton et al., 1993, with our Figs. 7 and 8). Further, a comparison of previous studies in which standardized Talairach coordinates were reported for the location of SII (Burton et al., 1993; Gelnar et al., 1998) reveals that our center of mass locations are similar (within 1 cm). Thus, our results are in agreement with previous studies in which activation to tactile stimulation was described in the lateral sulcus of humans.

Only three studies have investigated directly the topographic organization and possible number of fields in the lateral sulcus of humans. In a recent PET study (Burton et al., 1993), the hand and the foot were stimulated passively by using a portable vibrator/massager that delivered vibrations of a high amplitude. The main finding of this investigation was that there were two major regions of activation, SII and a region located rostrally on the insula. Although the SII region appears to be in a similar location in both studies, the rostral region described in the current study was located on the upper bank of the lateral sulcus and did not extend on to the insula. The previous investigators reported that they did not find any of the regions of activation to be topographically organized and that only a single field, SII (rather than SII and PV) could be identified. This, of course, differs from the results of the current study.

One of the reasons why results may differ is that the methods used by Burton et al. (1993) and those used in the current investigation were different. The spatial resolution of PET may not be sufficient to determine differences in location of the two adjoining hand and foot representations in SII and PV. Another reason that the previous study did not observe topographically organized fields in this region may be because the body parts stimulated were limited to the hand and the foot. Because PV and SII form mirror-symmetric representations in the macaque monkey that are adjacent at the representations of the hand and foot (Krubitzer et al., 1995), stimulation of the hand and foot alone would not be sufficient to distinguish them from one another. Thus, it is necessary to stimulate a number of body parts, including proximal parts, to distinguish these fields from one another. Finally, the stimulus was quite different (a broad, slowly moving stimulus in the current study compared with vibration) and may contribute to the differences in active cortical areas. The stimulus preferences of neurons in RL versus a rostral area on the insula may be different, accounting for the difference in the cortical areas activated.

In another PET investigation, Ledberg et al. (1995) demonstrated activation in the lateral sulcus for roughness and length discriminations. Their results indicate

that a large portion of the contralateral and ipsilateral parietal operculum was activated in response to microgeometric or roughness discriminations made with the right hand. This region is in the location of our SII/PV activation. In addition, two regions of the ipsilateral parietal operculum could be described, one of which was activated when cylinders of different lengths were discriminated. Our data demonstrate that, in all cases in which a whole-head coil was used, the SII/PV region was activated on both sides of the brain after unilateral stimulation of the hand. This is in good agreement with the study by Ledberg et al. (1995), although, in their study, the left and right hemispheres were activated differentially for different tasks. Unlike this previous study, our results demonstrate that the contralateral and ipsilateral hemispheres vary in the consistency with which they are activated during the same stimulus application.

In a third study of topography, Gelnar et al. (1998) attempted to examine the topography of different finger representations in SI and SII in humans using fMRI. A vibratory stimulus was presented to the different digits, and the mediolateral patterns of activation and the spatial separation of activity patterns from the different digits were noted. Although a precise topography of SII could not be ascertained, and the information regarding Tailarach coordinates is incomplete, these investigators reported that the spatial separation of activity patterns was greatest for digits 1 and 5. They also reported that the activation from stimulation to digit 5 was lateral to that resulting from stimulation to digit 2. This latter result suggests that the topographic organization for the hand in SII in humans is reversed from the pattern of representation reported for the hand in SII in monkeys (Friedman et al., 1980; Robinson and Burton, 1980a; Pons et al., 1988). However, the data from the Gelnar et al. (1998) study that were used to describe this result were limited. In the current investigation, we did not attempt to differentiate between the different digit representations in the areas in the lateral sulcus; however, the location of the hand representation in the current investigation appears to correspond with that reported by Gelnar and colleagues (1998).

Organization of lateral somatosensory fields in mammals

SII. The organization of areas lateral to anterior parietal fields has been described differently by different investigators. However, a few consistent features of organization emerge when all studies on primates are considered. The first is that this region contains at least one complete representation of the sensory epithelium that is noninverted in organization with respect to the body. This field was described first in the middle of this century by Woolsey and colleagues (1946, 1958) in a variety of mammals, including monkeys, and is termed SII (for reviews, see Johnson, 1990; Krubitzer, 1996). SII has been described in a variety of primates, including macaque monkeys (Whitsel et al., 1969; Friedman et al., 1980; Robinson and Burton, 1980a; Pons et al., 1988; Krubitzer et al., 1995), owl monkeys (Cusick et al., 1989), marmosets (Krubitzer and Kaas, 1990), and galagos (Burton and Carlson, 1986).

There are several features of SII in nonhuman primates that distinguish it from SI. First, SII has dense interconnections with all representations of the opposite hemisphere, including that of the hand (Karol and Pandya,

1971; Manzoni et al., 1984; Krubitzer and Kaas, 1990; for review, see Krubitzer et al., 1998), whereas most anterior parietal fields do not (Pandya and Vignolo, 1968; Jones and Hendry, 1980; Killackey et al., 1983; Krubitzer and Kaas, 1990; Beck and Kaas, 1994; for review, see Krubitzer et al., 1998). Another feature of SII is the presence of neurons with bilateral receptive fields (Whitsel et al., 1969; Robinson and Burton 1980a,b; Burton and Carlson, 1986; Cusick et al., 1989). Finally, receptive fields for neurons in SII are larger than for neurons in anterior parietal fields (Whitsel et al., 1969; Robinson and Burton, 1980a; Krubitzer and Kaas, 1990; Krubitzer et al., 1995).

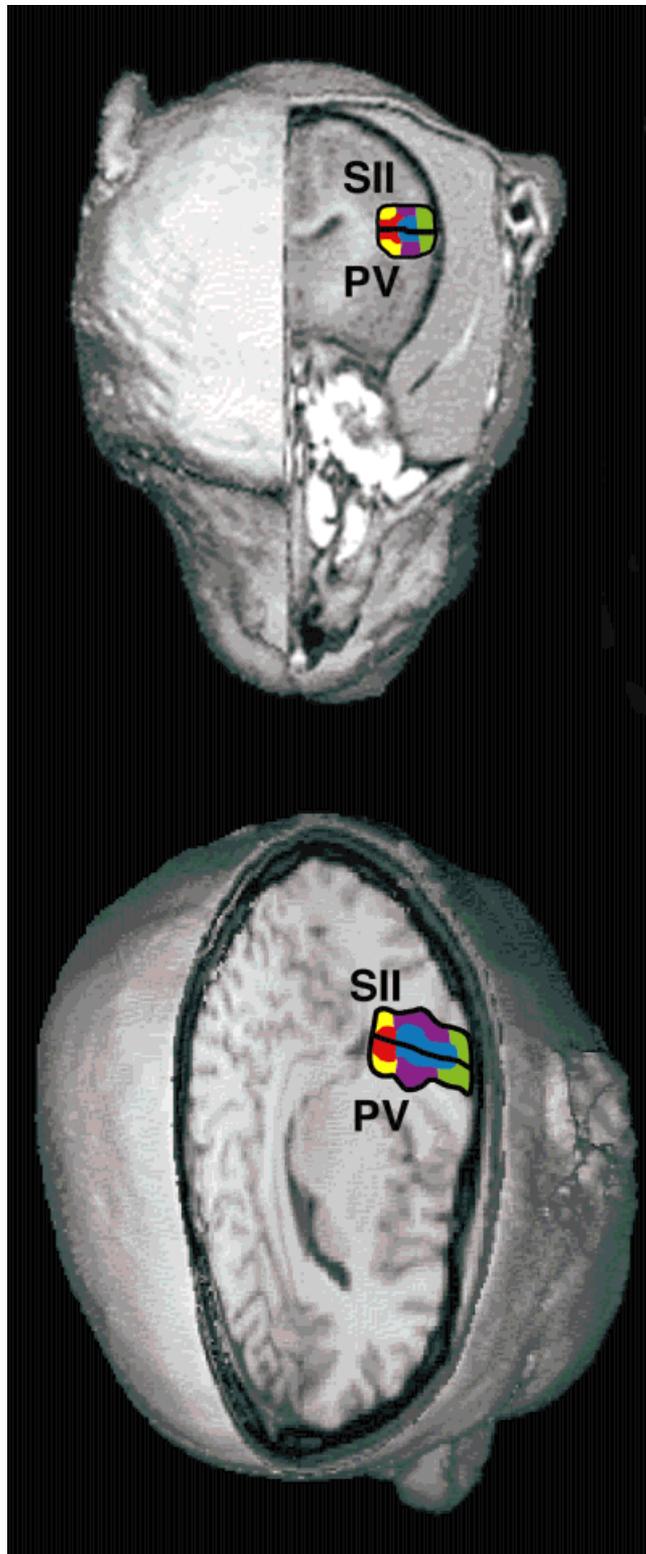
Although the connections of SII with anterior parietal fields have been well documented (Jones and Powell, 1969; Cusick et al., 1985; Friedman et al., 1986; Pons and Kaas, 1986; Cusick et al., 1989; Darian-Smith et al., 1993; Burton et al., 1995; Huffman et al., 1996), there are only a few studies that have examined directly the connections of SII with other cortical fields and thalamic nuclei. Recent work in the macaque monkey from our laboratory demonstrates that SII and PV have distinctly different patterns of connections (Disbrow et al., 1998). SII is densely interconnected with area 3b and, to a lesser extent, with area 1. It projects rostrally to PV and also caudally to area 7b, which is similar in location to the caudal field described in the current report. The thalamic connections of SII are more contentious (Jones, 1985; Friedman and Murray, 1986; Burton and Carlson, 1986; Krubitzer and Kaas, 1992), although we have recently demonstrated that SII and PV share a number of common inputs from the thalamus (Disbrow et al., 1998).

SII has been described in all mammals in which this region of cortex was investigated (for reviews, see Johnson, 1990; Krubitzer, 1996). SII in nonprimate mammals has features of organization, cortical and subcortical connections, and receptive field configurations for neurons therein similar to those described for primates (Nelson et al., 1979; Krubitzer, 1996; Krubitzer et al., 1986; Johnson, 1990). Because SII has been identified in all mammals investigated, including prosimians and Old and New World monkeys, it has been proposed to be inherited from a common ancestor and retained in humans.

The current investigation as well as previous studies in humans provide direct support for this hypothesis by demonstrating that a field in the expected location of SII is activated by cutaneous stimulation. The topographic organization of SII in humans is like that described in other primates and other mammals, and the receptive field size also is similar. Finally, SII in humans is activated bilaterally under unilateral stimulus conditions, and the signal intensity of activation in SII increases when both hands are stimulated simultaneously (Disbrow et al., 1997), suggesting that neurons here have bilateral receptive fields. Thus, like SI, SII is part of a basic processing network shared by all extant mammals. The function of SII is unknown, but hypotheses based on types of stimuli required to elicit a response can be generated (see below).

PV. Although the organization of fields in the lateral sulcus is still controversial, there is a growing consensus that multiple fields exist in primates and that some of these fields are found in other mammals as well. For instance, early single-unit electrophysiological studies in macaque monkeys demonstrated the presence of a retroinsular area (Ri), a granular insular area (Ig), and area 7b (Robinson and Burton, 1980b). Recent multiunit electro-

physiological recording studies in New and Old World primates (Krubitzer and Kaas, 1990; Krubitzer et al., 1995) have demonstrated that a field just rostral to SII contains a complete representation of the sensory epithe-



lium. This field has been termed PV. Like SII, this field contains neurons with large receptive fields, and the mediolateral organization of the field is similar to that of SII. However, PV forms a mirror image of SII, with the proximal limbs represented at a far rostral location and the distal limbs represented at a caudal location. This is in contrast to SII, in which the distal limbs are represented rostral in the field adjacent to the distal limb representation in PV, and the proximal limbs are represented caudally in the field (Fig. 10).

PV also has been described in a wide variety of mammals, including rodents (in which it was described first; Krubitzer et al., 1986; Fabri and Burton, 1991), marsupials (Beck et al., 1996; Huffman et al., 1999), and flying foxes (Krubitzer and Calford, 1992). Its ubiquity in the majority of mammals investigated suggests that the field was inherited from a common ancestor and is present in all extant mammals, including humans. The current results support this hypothesis directly by demonstrating a field in the location of PV that is organized topographically and forms a mirror-symmetric representation with SII. PV is activated under stimulus conditions similar to those that activate SII and has neurons with receptive fields of a size and configuration similar to those in SII.

The connections of PV have not been described fully in primates; however, limited evidence indicates that it has dense connections with premotor cortex and with regions of posterior parietal cortex, such as area 5 (Krubitzer and Kaas, 1990; Disbrow et al., 1998). PV also projects rostrally to an area that is similar in location (on the upper bank of the lateral sulcus rostral to SII/PV) to the rostral area described in this report. The connections with areas in anterior parietal cortex also exist; however, in the macaque monkey, they are much less dense than with other fields (Disbrow et al., 1998). Like SII, PV has strong homotopic and homoareal callosal connections (Krubitzer et al., 1986, 1998; Krubitzer and Kaas, 1990; Disbrow et al., 1998). The connections of PV with higher order areas of the frontal and parietal lobe suggest that it is involved in more complex processing than SII (see below).

Rostral and caudal regions of activation. There is evidence that additional areas exist in the lateral sulcus of primates (Robinson and Burton, 1980b; Friedman et al., 1986; Krubitzer et al., 1995). In the current study, regions both rostral and caudal to SII and PV were activated inconsistently under our stimulus conditions. The caudal region corresponds (at least in location) to area 7b, whereas the rostral region, which is confined to the upper bank of the lateral sulcus and does not extend on to the insula, has yet to be described. However, there is limited evidence from electrophysiological recording studies in anesthetized macaque monkeys that cells in cortex rostral to SII/PV respond to deep stimulation (Disbrow et al., 1998). In addition, a recent study of the connections of SII

Fig. 10. Summary of the somatotopic organization of SII and PV in the human (**bottom**) and macaque monkey (**top**). The schematic drawings of SII and PV have been superimposed on three-dimensional steady precession gradient-recalled images. The hand representation is shown in blue, the foot is in red, the face is in green, the shoulder is in purple, and the hip is in yellow. These digital images demonstrate that, in both human and nonhuman primates, homologous cortical fields are present.

and PV in the macaque monkey (Disbrow et al., 1998) revealed that SII projects caudally to area 7b, which is located on the upper bank of the lateral sulcus, and that PV projects rostrally to an area on the upper bank of the lateral sulcus similar to the location of RL described here. Thus, there is converging evidence from both humans and macaque monkeys that the upper bank of the lateral sulcus contains two fields in addition to SII and PV: a rostral field (RL) and a caudal field, possibly area 7b.

Function of lateral somatosensory areas

In an effort to determine differences in receptive field size and stimulus preference for groups of neurons in the lateral sulcus and anterior parietal cortex, we used similar types of stimulation and examined the activation patterns in both anterior parietal cortex and areas of the lateral sulcus. The most important result was that small punctate stimuli applied to a very small region of the body surface proved highly effective in eliciting activity in the anterior parietal fields (areas 3b and 1) but either failed to elicit activity or elicited a minimal amount of activity in the lateral sulcus. On the other hand, stimuli that had a large surface area that was moved across the skin proved highly effective in eliciting cortical activation in lateral sulcus areas. Moreover, we observed that regions that were activated by stimulation to the hand often were activated by stimulation to the shoulder as well. These results lead to two conclusions.

First, the receptive fields for neurons in SII and PV may be larger than for neurons in anterior parietal fields, because the same site was activated by stimulating a number of different body parts (e.g., shoulder and hand). Although it is possible that this large activation is due to a fractured topography in which neurons have small receptive fields, such an observation has not been made for any somatosensory area or any sensory area in nonhuman primates. Although we appreciate that the fMRI technique does not allow a direct assessment of receptive field size, the current results and related studies in nonhuman primates in which receptive field size was assessed directly support our contention that the receptive field size of neurons in the lateral sulcus in humans is larger than for neurons in areas 3b and 1.

The second conclusion is that neurons in SII and PV may be selective for a moving stimulus. Our data are limited (direct comparisons were made in only two subjects; Table 1), and further study of stimulus preference is necessary using a calibrated and reproducible stimulus. Nevertheless, the current observation is consistent with a recent electrophysiological study in nonhuman primates (Disbrow et al., 1998) and suggests that a stimulus moving in two directions elicits a larger activated area in SII and PV than a stimulus moving in one direction (Fig. 4).

We have proposed that, in monkeys, regions in the lateral sulcus are involved in integration of somatic inputs across large portions of the hand, sensorimotor integration, and bilateral coordination of the hands (Krubitzer, 1996). This proposition is based on connection studies, single- and multiple-unit mapping studies, and lesion studies (see below). The current results in humans indicate that, unlike SI, SII and PV are activated on both sides of the neocortex under unilateral stimulus conditions of the hand, face, foot, and proximal body parts, suggesting that these regions receive dense callosal input in humans, as in monkeys. Further support for this proposition comes

from a recent MEG and fMRI study of unilateral versus bilateral stimulation of the hands (Disbrow et al., 1997). These data demonstrate an increase in signal intensity in cortex in the lateral sulcus at long latencies for bilateral versus unilateral stimuli. This increase was not observed for anterior parietal fields under bilateral stimulus conditions.

In addition, data from the current study suggest that cells in the lateral sulcus may be involved in the integration of inputs from other functionally related body parts. The hand and face representations overlapped more often than those of any other two body parts stimulated (Table 3). Although the comparison of the centers of mass showed that the center of the face representation was lateral to that of the hand, the face representation often was spread over a large area that overlapped the hand representation (see Fig. 7E,F). Like our previous work on unimanual versus bimanual stimulation using fMRI (Disbrow et al., 1997), this overlap may be involved in the integration of information between two body parts necessary for performing complex behaviors. This relationship between the hand and face representations has not been appreciated previously in studies using electrophysiological techniques that offer a more restricted view of cortical activation.

Studies in which the parietal operculum and insula were ablated in monkeys demonstrated deficits in discrimination of size, texture, and shape of an object (Murray and Mishkin, 1984; Horster and Ettliger, 1987). Deficits in the discrimination of size and shape are consistent with the notion that SII is integrating inputs across the hand, a feature that must be present in order to discriminate the length of an object.

It also has been suggested that SII in primates is involved in tactual memories and tactile learning (Mishkin, 1979). Support for this hypothesis comes from lesion studies in humans in which deficits in tactile recognition tasks are observed when the SII region is ablated (tactile agnosia; Caselli, 1991, 1993). In addition, regional cerebral oxidative metabolic studies in humans have demonstrated increases in oxygenation in SII and insular cortex during tactile recognition and tactile learning tasks (Roland et al., 1988). Taken together, observations in both humans and nonhuman primates support the contention that these regions may be critical for coordinating tasks involving somatic and motor activities of multiple body parts, such as the digits of the hand, the two hands, or the hand and the face.

Variability in activation patterns across subjects

One important observation of the current investigation is that the patterns of activation generated by the same stimulus were highly variable across subjects. Our tests of within-subject variability indicate that the differences in the pattern of activation across subjects are not the result of inconsistent application of the stimulus but represent true variability across subjects. The variation we observed (specifically, the difference in the proportion of representation of different body surfaces and the topographic relationships of different body parts) is consistent with that described for topographic maps in monkeys in which electrophysiological recording techniques were used (Merzenich et al., 1987). Studies of adult plasticity in the primary somatosensory cortex in monkeys and, recently,

in humans (Elbert et al., 1995) indicate that cells in area 3b are capable of a large degree of reorganization that is use-dependent (Jenkins et al., 1990; Recanzone et al., 1992a,b; for review, see Recanzone, 1998) or the result of a peripheral perturbation (Rasmusson, 1982; Merzenich et al., 1983, 1984; Kelahan and Doetsch, 1984; see also Wall, 1988; Kaas, 1995). If regions in the lateral sulcus are involved in more complex somatosensory processing, sensorimotor integration, and intramanual and bimanual dexterity, the latter of which often requires a large learning component, then our demonstration of the variation in patterns of activation in regions in the lateral sulcus across subjects is not surprising. One might expect even greater effects on the organization of these fields with use than regions in anterior parietal cortex. Perhaps a more surprising result is that the patterns across subjects were similar enough to allow us to appreciate the number and location of four of the fields located here and the topographic organization of two of these fields.

Methodological issues

Of the 18 original subjects, two showed no activation to repeated application of any stimulus. Also, within a single-subject stimulation of one body part may not have resulted in significant activation (RT shoulder and VC face), whereas stimulation of other body parts did. Finally, the rostral and caudal areas were not activated consistently with our simple stimuli.

There are several factors that may contribute to the variability in the patterns of activation observed between subjects. First, these differences may be due to methodological problems. Of the 64 scans done for various body part stimulation in the original 18 subjects, 11 of the scans yielded no significant activation. Nine of these scans were from the two subjects from whom the data were discarded, and one scan was from each of two subjects (RT and VC) whose remaining data were included in the analysis. This failure rate of 17% is consistent with, although slightly higher than, previous reports (Roberts and Rowley, 1997). The rate of success may be due to the magnetic field strength, which, in turn, affects the signal-to-noise ratio. To increase the signal-to-noise ratio in the current study, two surface coils were used in several subjects. Although surface coils can be used to image only a restricted portion of the brain, they yield a higher signal-to-noise ratio than a whole-head coil. In both of the cases in which no activation was elicited, as well as in the two cases in which one of the scans showed no significant activation (subjects VC and RT), a surface coil was used. Thus, the lack of activation observed in the current study was unlikely to be the result of a poor signal-to-noise ratio.

Variability in the stimulus may also account for some of the differences in activation between subjects. Insufficient or inconsistent application of pressure, timing of stimulation, or surface area coverage may have resulted in failure of activation. However, our data on reproducibility suggest that this explanation is unlikely.

Finally, differences between subjects may account for the observed variability. Reduced capillary density may explain the lack of activation in some subjects. Furthermore, a relatively small cortical representation of a body part in a given subject may have resulted in a signal that was too small to be detected. Indeed, in the subjects who did show activation, there was a large amount of variation in the extent of activation for the same body part (compare

subjects KA, SS, and RT in Fig. 7). We believe that the anatomical variability in capillary vascularization and the variability in the internal organization of the areas across subjects are likely to account for the rate of success in the activation to somatic stimulation. With respect to areas RL and C, in addition to the two factors noted above, our stimulus may not have been of sufficient complexity to activate these fields consistently.

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