

Segregation of Somatosensory Activation in the Human Rolandic Cortex Using fMRI

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Segregation of somatosensory activation in the human Rolandic cortex using fMRI. *J Neurophysiol* 84: 558–569, 2000. The segregation of sensory information into distinct cortical areas is an important organizational feature of mammalian sensory systems. Here, we provide functional magnetic resonance imaging (fMRI) evidence for the functional delineation of somatosensory representations in the human central sulcus region. Data were collected with a 3-Tesla scanner during two stimulation protocols, a punctate tactile condition without a kinesthetic/motor component, and a kinesthetic/motor condition without a punctate tactile component. With three-dimensional (3-D) anatomical reconstruction techniques, we analyzed data in individual subjects, using the pattern of activation and the anatomical position of specific cortical areas to guide the analysis. As a complimentary analysis, we used a brain averaging technique that emphasized the similarity of cortical features in the morphing of individual subjects and thereby minimized the distortion of the location of cortical activation sites across individuals. A primary finding of this study was differential activation of the cortex on the fundus of the central sulcus, the position of area 3a, during the two tasks. Punctate tactile stimulation of the palm, administered at 3 Hz with a 5.88_{log10.mg} von Frey filament, activated discrete regions within the precentral (PreCG) and postcentral (PoCG) gyri, corresponding to areas 6, 3b, 1, and 2, but did not activate area 3a. Conversely, kinesthetic/motor stimulation, 3-Hz flexion and extension of the digits, activated area 3a, the PreCG (areas 6 and 4), and the PoCG (areas 3b, 1, and 2). These activation patterns were observed in individual subjects and in the averaged data, providing strong evidence for the existence of a distinct representation within area 3a in humans. The percentage signal changes in the PreCG and PoCG regions activated by tactile stimulation, and in the intervening gap region, support this functional dissociation. In addition to this distinction within the fundus of the central sulcus, the combination of high-resolution imaging and 3-D analysis techniques permitted localization of activation within areas 6, 4, 3a, 3b, 1, and 2 in the human. With the exception of area 4, which showed inconsistent activation during punctate tactile stimulation, activation in these areas in the human consistently paralleled the pattern of activity observed in previous studies of monkey cortex.

INTRODUCTION

A consistent feature of mammalian sensory systems is the rerepresentation of the sensory periphery in distinct cortical areas.

Sensory cortical areas are defined by several criteria, including their cytoarchitecture, pattern of connectivity, neuronal response properties, receptive field size, and the effect of lesions on perceptual capability (Kaas 1983). Over 30 areas have been delineated within the monkey visual system (Kaas 1989; Van Essen et al. 1992), and several regions, with similar response properties, have been defined recently in the human cortex (DeYoe et al. 1996; Engel 1996; Sereno et al. 1995; Tootell et al. 1995, 1997). Multiple auditory areas, segregated by the pattern of responsiveness in tonotopic space, have been isolated in monkey (Merzenich and Kaas 1980; Morel et al. 1993; Rauschauer et al. 1995) and human cortex (Talavage et al. 1996).

In the somatosensory system, numerous anatomical and physiological studies in monkeys support the existence of four distinct cortical areas within the central sulcus and postcentral gyrus (PoCG), areas 3a, 3b, 1, and 2 (Brodmann 1994; Iwamura et al. 1985, 1993; Jones 1985; Jones and Porter 1980; Kaas et al. 1979; Merzenich and Kaas 1980; Merzenich et al. 1978; Nelson et al. 1980; Paul et al. 1972; Sur et al. 1980; Tommerdahl et al. 1996). Neurons in areas 3b and 1 in the monkey possess discrete tactile receptive fields (DiCarlo et al. 1998; Mountcastle and Powell 1959; Pons et al. 1987; Sur et al. 1980) that are organized into mirror representations of the tactile body surface along the area 3b and 1 border (Kaas et al. 1979; Merzenich et al. 1978). In the unanesthetized animal, a subset of neurons in these areas also respond to deep and proprioceptive input (Iwamura et al. 1993; Taoka et al. 1998), and responses in these areas are modulated by motor activity (Lebedev et al. 1994; Nelson 1996; Nelson et al. 1991; Prud'homme et al. 1994). Area 2 contains neurons responsive to tactile and proprioceptive stimulation (Hyvarinen and Poranen 1978; Iwamura et al. 1993). These neurons demonstrate complex receptive field properties, including the integration of multimodal inputs and an increased concentration of direction-selective neurons (Ageranioti-Belanger and Chapman 1992; Constanza and Gardener 1980; Hyvarinen and Poranen 1978; Iwamura and Tanaka 1996; Iwamura et al. 1985; Whitsel et al. 1972). Neurons in area 3a, located in the cortex in the fundus of the central sulcus, are responsive to deep receptor and proprioceptive stimulation (Iwamura et al. 1993; Jones and

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Porter 1980; Recanzone et al. 1992; Taoka et al. 1998). This area also possesses a minority of neurons with tactile receptive fields (Iwamura et al. 1993; Strick and Preston 1982; Tanji and Wise 1981; Taoka et al. 1998), and recent optical imaging studies have demonstrated cutaneous nociceptive activation of this region (Tommerdahl et al. 1996, 1998).

In addition to the well-documented motor representations within the precentral gyrus (PreCG) of the human and monkey, the PreCG also receives somatosensory input. Distinct tactile and proprioceptive maps have been reported in the anterior bank of the central sulcus, areas 4p and 4a, respectively (Geyer et al. 1995; Strick and Preston 1982; Tanji and Wise 1981). Further, the crown and anterior wall of the PreCG, Brodmann area 6, also possesses a tactile map (Gentilucci et al. 1988; Penfield and Rasmussen 1950). The importance of these regions to tactile perception is potentially significant: following lesions of the PoCG, PreCG stimulation can evoke tactile sensations (e.g., Penfield and Rasmussen 1950), and lesions of the PreCG in monkeys can lead to somatosensory neglect (Rizzolatti et al. 1983).

To investigate the organization of these representations in the hand area of the human central sulcus region, we imaged subjects during two protocols: punctate tactile stimulation and a kinesthetic/motor task. To localize activation, we employed high-resolution functional magnetic resonance imaging (fMRI) and whole-brain three-dimensional (3-D) visualization techniques. High-resolution imaging was necessary to localize precisely activation patterns within this region, because cortical areas in the human can span less than a centimeter in the anterior-posterior plane (White et al. 1997). The 3-D reconstruction of the data provided further practical advantages, offsetting the inherent ambiguity introduced by the curved path of the central sulcus and neighboring gyri, which penetrate 2-D slice planes at a variety of angles, and make the precise assignment of activation to specific sulcal and gyral regions difficult (Gelnar et al. 1998; Sastre-Janer et al. 1998; Sobel et al. 1993).

METHODS

Imaging techniques

Right-handed subjects ($n = 5$, age 20–31 yr, 2 women) were scanned in a 3-Tesla General Electric scanner with a birdcage head coil. Data were sampled from 16 coronal oblique slices oriented approximately parallel to the course of the central sulcus. Before and after functional scanning, a high resolution T1-weighted anatomical scan of these slice positions was taken (voxel size = $1.56 \text{ mm} \times 1.56 \text{ mm} \times 4.0 \text{ mm}$; TE = 57 ms). Functional runs were obtained using a gradient echo pulse sequence (voxel size = $3.125 \text{ mm} \times 3.125 \text{ mm} \times 4 \text{ mm}$; TR = 2,000 ms, TE = 50 ms). A total of 128 images per slice were taken for each 4:16 min functional run. Subjects received a minimum of four functional runs, two each for the tactile and kinesthetic/motor stimulation conditions; each subject's data were averaged within stimulation conditions.

Stimulation parameters

A functional run consisted of periods of stimulation (16 s) alternated with periods of no stimulation (16 s), for a total of eight ON/OFF cycles. The initial 16-s period was a period of no stimulation. During tactile runs, subjects were contacted with a $5.88_{\log 10 \text{ mg}}$ von Frey hair at a rate of 3 Hz. Within an epoch of stimulation, the position of

contact varied over the glabrous surface of the palm, excluding the thenar eminence. Delivery of stimulation by the experimenter was timed to a metronome. During stimulation, the subject's hand was supported with firm but deformable foam cushions. In addition, two subjects also received von Frey stimulation of the third digit of the hand. The site of contact varied over all three segments of the glabrous surface of the finger (2 runs per subject). Subjects were instructed to keep their eyes closed during functional imaging, to attend to the stimulus during presentation, and to keep their eyes open between runs.

Kinesthetic/motor stimulation occurred at the same alternating cycle as the tactile runs. Subjects held their right arm flexed at the elbow with the hand above the chest. They flexed and extended their fingers around the metacarpal and interphalangeal joints of the fingers and thumb of the right hand at a rate of 3 Hz (Rao et al. 1996; Schlaug et al. 1996), as if squeezing an imaginary tennis ball. They did not touch their fingers either to neighboring digits or to the palm surface. Prior to scanning, subjects practiced squeezing at a 3 Hz rate. During scanning, subjects heard a metronome set at 3 Hz and instructions every 16 s to "stop" and "go." Subjects also received this auditory stimulation during the tactile runs. All subjects were monitored visually for compliance with squeezing rate during the scanning session. Due to the noise generated by the scanner, one subject was unable to discriminate the metronome consistently, and squeezed at a self-paced rate of 2–5 Hz; this subject was able to detect the go and stop commands at the beginning and end of each epoch.

Statistical analyses

A Fourier analysis was performed on the activation in each voxel over the full functional scan period. An f test was then conducted, comparing the ratio of the power of the fMRI signal at the stimulus frequency with those at all other frequencies, excluding harmonics. To confirm the localization of activation patterns achieved with the f test, and to permit use of the averaging software, a t -test analysis was also conducted. The t -test analysis pooled signals across stimulation epochs and compared it with the pooled signal from nonstimulation epochs, with a 2-s interval introduced to account for hemodynamic delay. Activation patterns generated by these two statistics were well aligned (for example, compare the activation patterns in individuals in Figs. 1 and 4B), with a more restricted extent of activation identified by the t -test. Analysis of the volume of the cortical area in the PreCG and PoCG region in three subjects (Cardviews) (Kennedy et al. 1998) recommended a Bonferroni correction for the analysis of ~2,000 pixels. After making this correction, we employed a statistical threshold for significant activation of $P < 0.01$ for individual subject and average activation patterns.

Anatomical analyses

The position of the central sulcus is variable among human subjects (White et al. 1997). Because of this variability, morphing brains into Talairach space, a coordinate system that does not account for the position of cortical landmarks in the reconstruction of individual brains, "blurs" central sulcus borders when subjects are averaged (Woods 1996). Therefore in addition to analyzing our data in Talairach space to allow for comparison with previous reports, we have addressed the anatomical variability of the central sulcus in two ways. First, we analyzed the position of activation in each subject relative to his or her specific anatomy, an approach made possible through use of a high field-strength fMRI scanner. This strategy allowed us to account for inter-subject variability in the gross anatomy of the central sulcus region during activation localization, and these anatomically specific analyses could then be combined across subjects to record probabilistic activation maps. Second, we placed brains in a common coordinate space using a technique that maximizes sulcal similarity (Fischl et al. 1998, 2000). This transformation allowed us to take

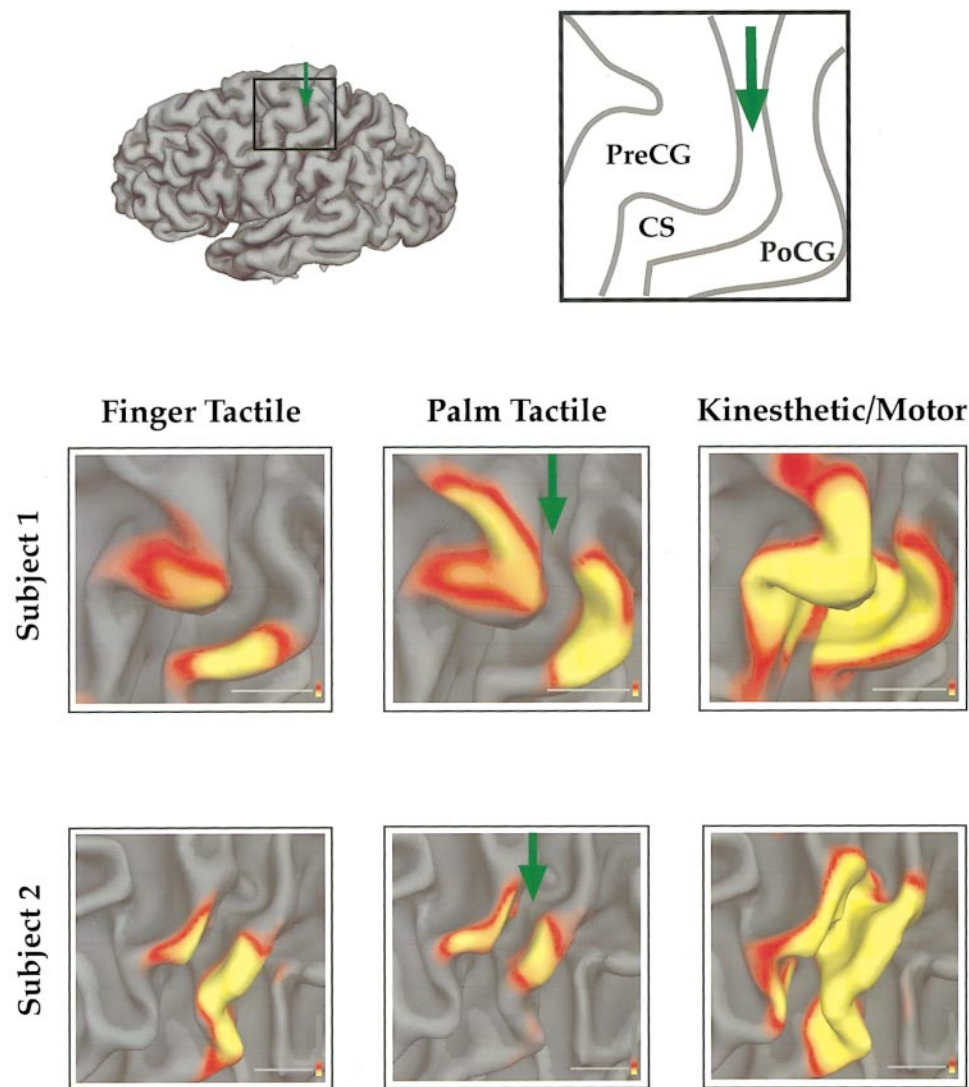


FIG. 1. Activation within the hand area during tactile and kinesthetic/motor protocols was segregated to distinct cortical areas. *Top*: on the gray matter–white matter border model, the position of the hand area in the central sulcus region is marked by the black box. A cartoon of the hand area on the *right* shows the position of the precentral gyrus (PreCG), central sulcus, and postcentral gyrus (PoCG) for the gray matter–white matter magnifications displayed below. The green arrows mark the position of the central sulcus. *Bottom*: activation is shown for 2 subjects during palm tactile, finger tactile, and kinesthetic/motor stimulation (f test). During tactile stimulation, activation was observed in a PreCG and a PoCG region but not in a gap region spanning the central sulcus. During kinesthetic/motor stimulation, all 3 regions defined by tactile stimulation were activated. Scale bar is 1 cm.

advantage of the increased signal-to-noise ratio generated by averaging activation across subjects. In both approaches, the use of whole-brain visualization techniques facilitated individual subject and averaged data analysis.

Anatomical reconstruction

Cortical surface-based analysis techniques were conducted as described in Dale and Sereno (1993), Dale et al. (1998), and Fischl et al. (1998, 2000). Briefly, an initial SPGR high-resolution anatomical scan was taken for each subject (128 slices, 1.0 cubic mm; head coil, 1.5 T GE or Siemens scanner). From this scan, all white matter voxels were labeled, and the gray matter–white matter border was tessellated to form a surface. The surface thus obtained was fitted against MRI data, and surface defects were corrected, if needed, by manual tracing. Following each functional scanning session, the surface was aligned with the high-resolution T1 scan, to correct for differences in the orientation and position of the brain in individual experiments. Functional data were then interpolated onto the surface, and the brain was inflated by an algorithm that employed curvature reduction and local metric-preserving terms (Fischl et al. 1998, 2000). For all anatomical analyses, we examined activity projected onto a 3-D rendering of the gray matter–white matter border of each individual's brain. To minimize the probability of partial volume contamination of signal across the central sulcus, only pixels overlying white matter were included in

the analysis. In all subjects, the position of the gray matter–white matter border of the PreCG wall of the sulcus was ≥ 5 mm from the border of the PoCG wall. This affords a distance of greater than a voxel width between the two regions of interest, decreasing the probability of misattribution.

Localization of the central sulcus and definition of the hand area

The central sulcus was identified using two anatomical landmarks (Kido et al. 1980; Sobel et al. 1993). First, on the lateral view of the reconstructed brain, the central sulcus was defined as the sulcus immediately posterior to the perpendicular intersection of the anterior-posterior oriented superior frontal sulcus and the medial-lateral oriented precentral sulcus. Second, on the medial view, the central sulcus was defined as the small sulcus oriented dorsal-ventral on the dorsal surface of cortex, located anterior to the ascending, marginal branch of the cingulate sulcus. At the midline, the central sulcus was limited in extent, but a few millimeters lateral to the midline view was readily identifiable as a deep sulcus.

The *hand area* was defined as the first posterior convexity of the central sulcus lateral to the midline. This area has been described as an omega-shaped formation in the central sulcus in the axial plane, and a hook-like folding of the cortical mantle in the sagittal plane (White et al. 1997; Yousry et al. 1997). The hand area is readily

visible from the lateral view of the reconstructed cortical surface (Fig. 1). Several studies using intracortical electrical stimulation or functional neuroimaging have confirmed the presence of a motor and/or somatosensory hand representation in this anatomical location either explicitly (Sastre-Janer et al. 1998; Yousry et al. 1997) or through the position of the hand representation in their illustrations (Penfield and Rasmussen 1950; Uematsu et al. 1992).

Assignment of activation to the probable position of areas

We used the sulcal and gyral pattern in individual subjects to demarcate the probable position of areal borders defined by cytoarchitecture and receptor binding studies (Brodmann 1994; Geyer et al. 1997; White et al. 1997; Zilles et al. 1995). We defined six anatomical regions of interest centered over the hand area in each subject. These regions corresponded to the cytoarchitectonic areas surrounding the central sulcus: areas 6, 4, 3a, 3b, 1, and 2 (Brodmann 1994; Geyer et al. 1997; White et al. 1997). Although there is between-subject variability in the correspondence between cytoarchitecture and gross human neuroanatomy, separate examinations of the pattern of cytoarchitecture within the human PreCG and PoCG support the following subdivisions across subjects at the level of the hand area (Brodmann 1994; Geyer et al. 1995; see Geyer et al. 1997 for a detailed assessment of radioligand binding in the PoCG; White et al. 1997, for a detailed assessment of the cytoarchitectonic extent of areas 4, 3a, and 3b in humans; and Jones and Porter 1980, for a review of the variability in the localization of area 3a in humans and primates). Area 6 was defined as the anterior wall and crown of the PreCG, area 4 as the anterior wall of the central sulcus, area 3a as the cortex in the fundus of the central sulcus, area 3b as the posterior bank of the central sulcus, area 1 as the crown of the PoCG, and area 2 as the posterior wall of the PoCG. Because the extent of these areas is less consistent across subjects, activation in the transition regions (e.g., on the anterior edge of a gyral crown) was designated as activation in a "border region" (thin wedges between areas in Fig. 3), reducing the likelihood of misattribution. For the tactile condition, the segregation of activation into these areas was completed independently by two observers (CIM and ACG), with agreement on 97% of assignments (29/30).

The displayed images in Figs. 1 and 4 were spatially filtered by averaging the statistical value at a surface vertex and its nearest neighbors on the reconstructed surface, for 15 iterations. This process is mathematically equivalent to spatially filtering with a Gaussian kernel with a SD on the order of 3 mm. This strategy is advantageous, as spatially filtering on the surface preempts the blurring of signal across cortical representations lining a sulcus, reducing the probability of mislocalization of activation. Anatomical analyses were conducted in tactile maps in three subjects with and without spatial filtering, with 100% agreement in segregation of activation into areas (18/18), and subsequent localization was conducted with spatially filtered data.

Group averages

Data were averaged as in Fischl et al. (1998, 2000). The goal of this intersubject averaging approach was to align individual cortical folding patterns. To achieve this goal, the reconstructed surface of each individual subject was mapped onto the unit sphere, using a maximally isometric transformation. These surfaces were then morphed into register with an average, canonical cortical surface, guided by a combination of folding-alignment (sulcus/gyrus) and isometry preserving forces. The canonical cortical surface was generated by computing the summary statistics describing the folding patterns of 40 previously aligned surfaces. The folding alignment force encourages the registration of folding patterns that are prominent and consistent across individuals, while the isometry term prevents excessive compression/expansion of the surfaces, as well as ensuring the invertibility of the mapping. Functional data were averaged across subjects by

taking the mean \pm SD of the fMRI signal at each time point, and calculating summary statistics from these measures.

To localize signals in the average activation patterns, the tactile average and the kinesthetic/motor average were projected onto the 3-D gray matter–white matter reconstructions of each subject, and the position of activation relative to the probable areas was assessed. The patterns of activation were identical with respect to the location of areas across all subjects, with variability limited to the extent of the border regions between areas.

RESULTS

Tactile and kinesthetic/motor stimulation each activated discrete areas within the central sulcus region. Here we describe the results for the five subjects analyzed individually, and then for the group average.

Individual subject analyses

Within the hand area, tactile stimulation of the palm activated foci within the PreCG and PoCG, with a "gap" region of nonactivation across the central sulcus in all subjects ($n = 5/5$ subjects). This pattern of activation can be seen in the palm and finger activation patterns (Fig. 1, *left* and *middle*). In contrast, kinesthetic/motor stimulation activated the PreCG, the gap region, and part of the PoCG as a single continuous region of activation in all subjects (Fig. 1, *right*). In the two subjects who received finger stimulation, the lateral border of kinesthetic/motor activation was approximately coextensive with the lateral boundary of activation during tactile finger stimulation, and the medial border of kinesthetic/motor activation was approximately coextensive with the medial border of activation during tactile palm stimulation ($n = 2$ subjects; Fig. 1).

Using the activation regions functionally defined by tactile stimulation of the palm, time series were generated for both stimulation conditions in each subject for the PreCG, gap, and PoCG regions. The Talairach coordinates for these three regions are shown in Table 1. The gap region in each individual was defined as the entire region between the PoCG and PreCG activated foci, bounded medially and laterally by the extent of these two activation patterns. As indicated by the statistical patterns, the PreCG and PoCG tactile regions showed sustained increases in percentage signal change during the tactile stimulation, whereas the gap region showed only a transient increase (0.3% signal change) followed by a return to baseline (Fig. 2, *top left*). During kinesthetic/motor activation, all three regions demonstrated increased percentage signal change (Fig. 2, *top right*). The signal increase in the gap region was significantly greater during the kinesthetic/motor stimulation than during the tactile stimulation (Gap: tactile 0.17 ± 0.29 vs. kinesthetic/motor 1.7 ± 0.71 ; mean \pm SD, $P < 0.01$, paired 2-tailed t -test), but there was no significant difference in the amplitude of signal increase in the PoCG and PreCG regions for the two stimulation paradigms (PreCG: tactile, $0.97 \pm 0.30\%$ vs. kinesthetic/motor, 1.13 ± 0.53 ; PoCG: 0.93 ± 0.17 vs. 1.44 ± 0.58 ; $P > 0.05$; Fig. 2, bar graphs).

As a companion analysis to the functional segregation of somatosensory representations, we used the sulcal and gyral pattern in individual subjects to demarcate anatomical borders that correspond to area borders (Brodmann 1994; Geyer et al. 1997; White et al. 1997; Zilles et al. 1995). We found that the cortex in the fundus of the central sulcus, corresponding to area

TABLE 1. Talairach coordinates for the mean location of the center of the PreCG, gap, and PoCG activated regions

	PreCG			Gap			PoCG		
	x	y	z	x	y	z	x	y	z
Talairach position	-35.5	-14.6	65.3	-36.6	-23.4	56.8	-43.3	-30.6	60.5
Standard deviation	6.0	4.5	5.6	7.6	4.1	9.4	7.4	2.3	7.5

Number of subjects is 5.

3a, was active in only one of five subjects during tactile stimulation: the single individual that demonstrated activation in 3a also demonstrated a gap region (see Fig. 4 for overlaid activation patterns from all subjects). In contrast, the same region was activated in all subjects during kinesthetic/motor stimulation (Fig. 3). Tactile stimulation activated the position of areas 6, 3b, and 1 in all subjects, area 2 in four of five subjects, and area 4 in two of five subjects. In two subjects, a pair of distinct regions of activation were present in the PoCG, a larger anterior activation (included in the above PoCG analysis), and a second smaller region located more posteriorly. In one subject, two regions of activation were observed within area 6. Kinesthetic/motor stimulation activated areas 6, 4, 3a, 3b, and 1 in all subjects, and area 2 in three of five subjects.

Averaged data analyses

In addition to the analysis in individual subjects, we also averaged the tactile or kinesthetic/motor functional data across subjects. As in the individual tactile activation patterns, PreCG and anterior PoCG activation areas were segregated by a gap of nonactivation in the cortex in the fundus of the central sulcus (Fig. 4). In the tactile average, activation was present in the hand area in the PreCG in the position of area 6 and in the border region between areas 6 and 4. In the PoCG, activation was present in an anterior and a posterior focus. The position of the two activations in the PoCG corresponded to area 3b

(anterior activation) and overlapping areas 1 and 2 (posterior activation). The kinesthetic/motor average revealed activation spanning the PreCG, gap, and part of the PoCG. The anterior border of the kinesthetic/motor activation was aligned with the anterior border of PreCG activation in the tactile activation, and the posterior edge extended into the anterior border of area 2.

DISCUSSION

Using high-resolution fMRI and whole-brain visualization techniques, we have described a region in the cortex in the fundus of the central sulcus, in the position of area 3a, that is inactive during punctate tactile stimulation, but is robustly activated during kinesthetic/motor stimulation. Further, we localized activation to specific positions within the PreCG and PoCG during both stimulation paradigms. These patterns were consistent among subjects in our sample (all subjects showed the gap pattern of activation in the central sulcus) and were confirmed in the across-subject averages. These findings replicated a preliminary study that observed the same activated regions using a 1.5-Tesla scanner and a 5-in. surface coil (Moore et al. 1998).

Our goal in relating the position of functional activation in individual subjects to the expected anatomical location of human areas was to record a probabilistic activation map. With this map, human activation patterns can then be related to

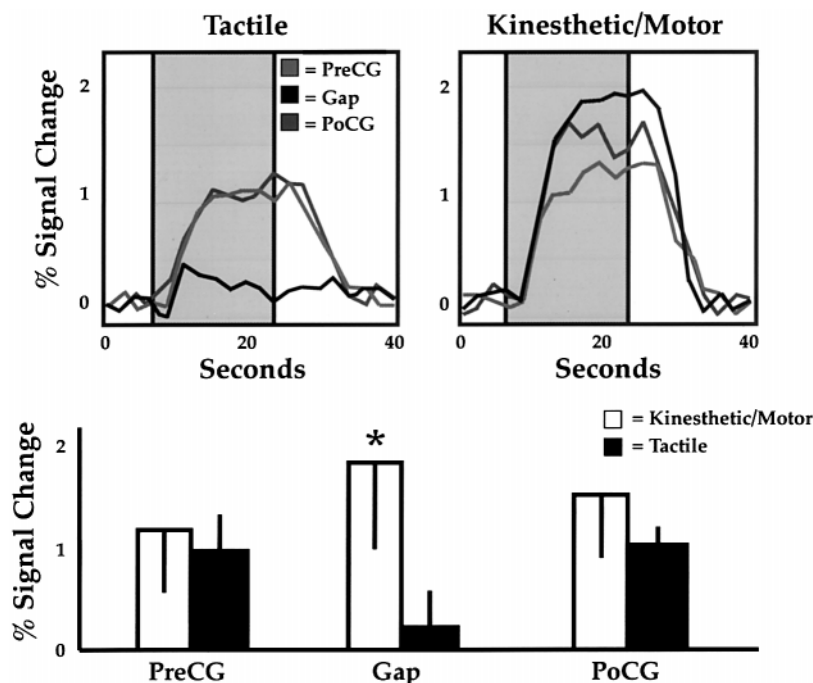


FIG. 2. Time course of activation in the PreCG, gap and PoCG regions for tactile and kinesthetic/motor stimulation conditions. *Top*: as predicted by the statistical maps, increased percentage signal change during tactile stimulation was observed in the PreCG (light gray) and PoCG (dark gray) regions, but not in the gap region (black). During kinesthetic/motor stimulation, activation was observed in all 3 regions. Light gray background indicates the duration of the stimulation (16 s). Each trace is the filtered ([1 1 1] moving average) mean of 8 stimulation epochs within a given subject, in turn averaged across 5 subjects. *Bottom*: the mean percentage signal change for the period 4–20 s following the onset of stimulation is shown. □, signal change during the kinesthetic/motor protocol; ■, signal change during the tactile protocol. The asterisk indicates significantly greater signal increase in the gap region during kinesthetic/motor compared with tactile stimulation ($P < 0.01$, paired Student's t -test). Each bar is the mean \pm SD of functional magnetic resonance imaging (fMRI) signal averaged 1st within subjects and then across the 5 subjects.

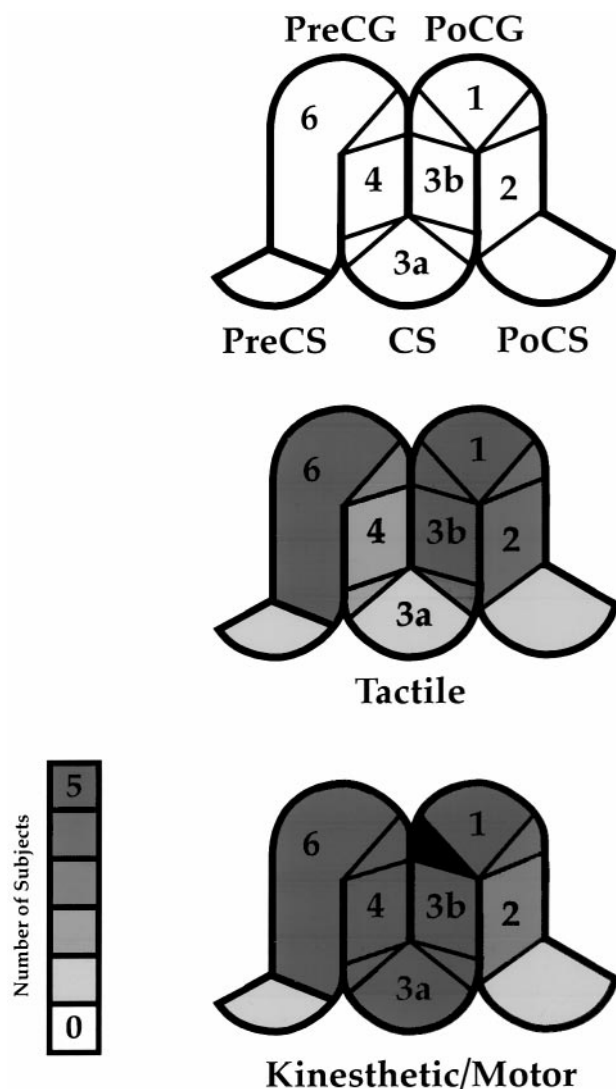


FIG. 3. Activation in discrete gross anatomical foci during tactile and kinesthetic/motor stimulation. *Top*: the presence of activation was quantified in 6 distinct regions within the central sulcus hand area. The corresponding cortical areas are displayed within each anatomically defined region on an idealized sagittal cross-section. Between areas, border regions (nonnumbered wedges) were defined to reduce the probability of misattribution of activation. PoCS, postcentral sulcus; PreCS, precentral sulcus; CS, central sulcus. *Middle and bottom*: gray scale coding corresponds to the number of subjects demonstrating activation in each region. Activation during tactile stimulation was localized to the PoCG (areas 3b, 1, and 2) and the PreCG (area 6) in all subjects, but was present in only 1 subject in the cortex on the fundus of the central sulcus (area 3a). Activation during kinesthetic/motor stimulation was present in areas 2 in 3 subjects, and in the remaining areas in all subjects.

reports on the monkey central sulcus region that employ these anatomical borders to demarcate sensory cortical areas (e.g., Kaas et al. 1979; Merzenich et al. 1978). We emphasize, however, that the assignment of functional activation to the probable position of areas is not tantamount to a description of human sensory cortical areas; without detailed cytoarchitecture, binding studies, myeloarchitecture, and patterns of efferent and afferent connectivity to account for the variability in each subject's anatomical organization, the attribution of areal borders is necessarily incomplete (Jones and Porter 1980; Kaas 1983; Roland and Zilles 1998; Zilles et al. 1995).

Comparison of the stimulus conditions

The cortical representations surrounding the central sulcus have been implicated previously in two broadly defined domains: motor activity and somatosensory perception. The two tasks employed in this initial study of representations in the human hand area using 3-T fMRI were chosen from the two extremes of this sensorimotor continuum. The kinesthetic/motor condition is an active motor task that engages a variety of peripheral receptors, including joint receptors, muscle receptors and slowly adapting (SA) and fast-adapting (FA) skin mechanoreceptors (Burgess et al. 1982; Edin and Abbs 1991; Hulliger et al. 1979; Matthews 1982). Perceptually, this condition evokes primarily kinesthetic sensations and lacks a punctate tactile component. In contrast, the punctate tactile condition is a passive sensory stimulation that robustly drives skin mechanoreceptors (Johansson and Valbo 1980; Johansson et al. 1980) and may also evoke muscle spindle activity (Burke et al. 1976; Roll and Vedel 1982). Perceptually, this condition evokes the sensation of discrete contact varying in location on the glabrous surface of the palm at 3 Hz, without a kinesthetic or motor component. The principal dissociation observed in the activation generated by the two tasks was in the fundus of the central sulcus, the position of area 3a in the human. The failure of the punctate tactile condition to activate this region suggests that its activation during the kinesthetic/motor condition does not result primarily from the activation of low-threshold mechanoreceptors, which are engaged in both conditions. Rather, activation in this region apparently derives from the ensemble of peripheral receptors and central neural activity driven by changes in finger position and/or active motor behavior.

Area 3a in humans and monkeys

Lesion, electrophysiological, and neuroanatomical studies of the human central sulcus region have provided inconclusive evidence for the existence of a distinct cortical area 3a, and/or of a distinct region encoding proprioceptive information. Head (1920) concluded from the psychophysical evaluation of patients with cerebral lesion that a cortical proprioceptive area existed in the central sulcus region, independent of the representation of tactile perception. Penfield and Rasmussen (1950) and Corkin et al. (1970) also reported deficits in position sense following excisions of the PoCG hand area. Penfield and Rasmussen (1950) further observed that kinesthetic sensations were frequently reported following electrical stimulation of the PoCG. These authors, however, did not observe the segregation of distinct somatosensory representations in the central sulcus region for proprioceptive or for tactile processing. The cytoarchitectonic definition of area 3a in the human (and monkey) has varied across researchers (see Jones and Porter 1980, for a review), and the extent of this region shows greater variability between subjects and has less rigid cytoarchitectonic borders, than other regions within the central sulcus (Jones and Porter 1980; White et al. 1997; but see Geyer et al. 1997). Passive movement of the arm has been reported to activate the Rolandic cortex in the human (Weiller et al. 1996), but a recent positron-emission tomography (PET) study of the vibration-induced motion illusion of the arm failed to activate area 3a (Naito et al. 1999).

Electrophysiological and lesion studies in the monkey cortex

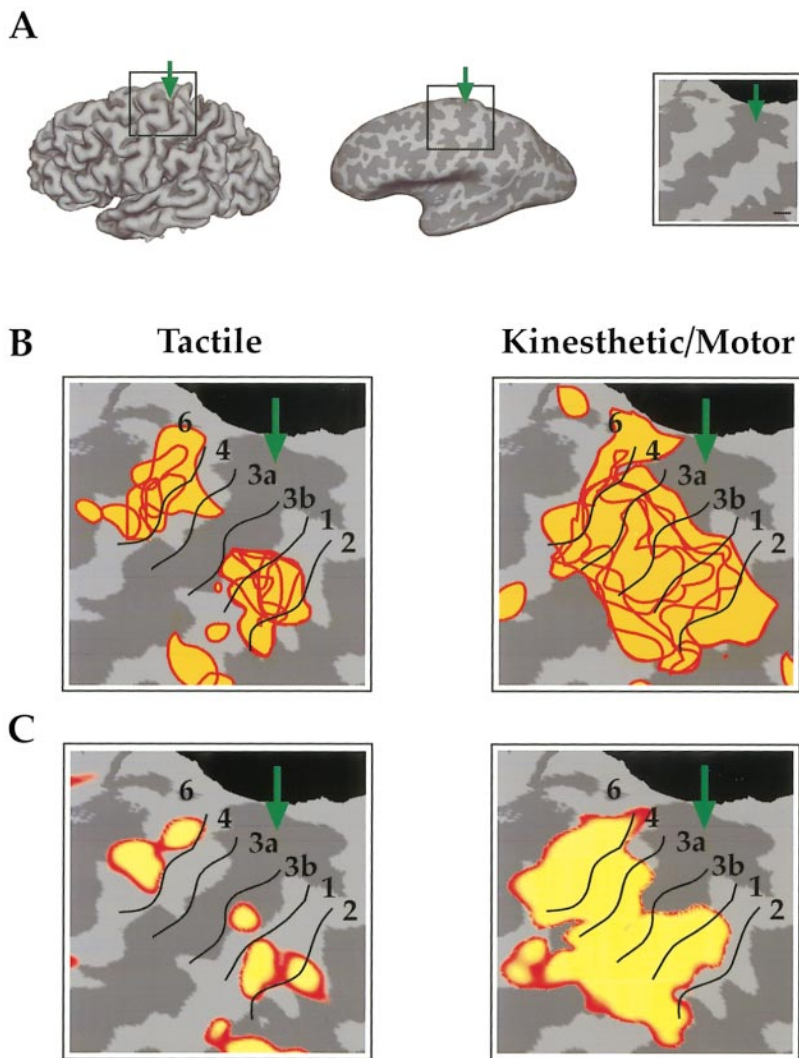


FIG. 4. Average tactile and kinesthetic/motor maps. *A, left:* a gray matter–white matter border reconstruction. *Middle:* an inflated reconstruction; dark gray regions are sulci, light gray are gyri. *Right:* a flattened reconstruction, centered over the hand area of the central sulcus. The black box demarcates the region expanded in the flattened reconstruction; green arrows mark the central sulcus. Scale bar is 1 cm. *B:* activation from all 5 subjects (red lines with yellow fill, *t*-test analysis) were projected onto the flattened reconstruction of a single subject after being transformed into the canonical representation space. Tactile activation is on the *left*, and kinesthetic/motor activation on the *right*. Solid black lines demarcate the areal borders derived from the sulcal/gyral anatomy, extending the mediolateral length of the anatomically defined hand area. *C:* the average tactile (*left*) and kinesthetic/motor (*right*) activation patterns are projected onto the same brain as in *B*.

have provided consistent evidence for a distinct representation in area 3a (Iwamura et al. 1993; Kaas et al. 1979; Pons et al. 1992; Recanzone et al. 1992). Area 3a in the monkey receives input from the ventral posterior superior nucleus of the thalamus, which encodes deep and proprioceptive inputs exclusively (Cusick et al. 1985; Jones 1983). Correspondingly, neurons in area 3a are driven effectively by deep and proprioceptive receptor inputs (Iwamura et al. 1993; Recanzone et al. 1992; Strick and Preston 1982; Taoka et al. 1998). Lesions of area 3a in the monkey lead to a decreased representation of proprioceptive information in SII, whereas lesions of areas 3b and 1 have little effect on the representation of deep and proprioceptive input in SII (Pons et al. 1992). In psychophysical experiments in monkeys, lesions of areas 3b and 1 produce specific deficits in tactile discrimination (the perception of roughness, grating orientation, and texture), and lesions of area 2 induce selective deficits in tasks requiring tactile and proprioceptive integration (the perception of the shape or angle of an object) (Carlson 1980; Semmes and Porter 1972; Semmes et al. 1974). Neither set of lesions induced a deficit in the perception of position sense (Semmes et al. 1974).

In agreement with these monkey studies, our data provide strong evidence for a functionally distinct area 3a in humans. This region was activated during kinesthetic/motor but not

punctate tactile input, consistent with the existence of a discrete representation that participates in the perception of changes in body position. This finding was supported by anatomically derived definitions of area 3a, functionally defined activation borders, and by the pattern of percentage signal change. Future studies in humans will be required to further delineate the functional characteristics of area 3a, specifically the importance of motor activity and attentional context (Naito et al. 1999; Nelson 1984, 1996), and its role in processing nociceptive input (Tommerdahl et al. 1996, 1998).

A potential concern regarding the differential signal observed in area 3a is that greater signal increase in neighboring representations during the kinesthetic/motor protocol, particularly in the PreCG, might have extended nonspecifically into the cortex on the depth of the central sulcus. If this type of nonspecific “revealed iceberg” effect was underlying the statistical changes we observed, the level of activity in the PreCG or PoCG during the kinesthetic/motor condition would be greater than the signal increase in area 3a, and the overall pattern of increased signal change would parallel that recorded during tactile stimulation. In contrast, the opposite pattern was observed: there was greater signal change in the gap than in the PreCG or PoCG during the kinesthetic/motor condition, a reversal of the pattern seen in the tactile condition, supporting

a functional dissociation between the two conditions (Fig. 2). Further, we have employed a conservative statistical threshold, a Bonferroni correction for the number of pixels analyzed, which mitigates against the probability of false positives (Locasio et al. 1997), and have localized activation to the gray matter–white matter border, which minimizes the probability of anatomical misattribution.

Activation in the PreCG and PoCG during tactile input

The activation observed with punctate tactile stimuli is in general agreement with a variety of studies that have reported human PoCG activation during nonpainful somatosensory stimulation (e.g., Allison et al. 1991; Boecker et al. 1996; Burton et al. 1997; Coghill et al. 1994; Disbrow et al. 1998; Fox et al. 1987; Gelnar et al. 1998; Hammeke et al. 1994; Kurth et al. 1998; Lin et al. 1996; O'Sullivan et al. 1994; Puce et al. 1995; Roland and Larsen 1976; Servos et al. 1998). Many of these studies did not localize activation to discrete regions of the PoCG. Of those studies that reported more specific anatomic localization during stimulation of the hand, three basic patterns have emerged. First, fingertip stimulation with moving gratings and haptic length discrimination tasks elicited dual activation peaks in the anterior and posterior PoCG (PET) (Burton et al. 1997; O'Sullivan et al. 1994; see also Lin et al. 1996, for activation of the central sulcus and postcentral sulcus using fMRI). Second, electrical stimulation evoked dual peaks in the anterior PoCG [somatosensory evoked potentials (SEP), Allison et al. 1991; fMRI, Kurth et al. 1998; but see Puce et al. 1995]. Third, discrete vibrotactile stimulation of the fingertip, vibrating movement of the finger, and the haptic discrimination of roughness activated the posterior PoCG (PET, Burton et al. 1997; O'Sullivan et al. 1994; fMRI, Gelnar et al. 1998, although these authors also observed activity in more anterior PoCG regions in a minority of subjects). Our findings are most similar to the activation evoked by passive moving gratings contacting the fingertip (Burton et al. 1997). Both studies employed a tactile stimulus that changed position on the glabrous skin surface of the hand and would be anticipated to activate tactile receptive fields in areas 3b, 1, and 2.

Activation during tactile stimulation in the PreCG, corresponding to area 6, is predicted by patients' reports of tactile sensation during cortical stimulation of the crown of the PreCG (Nii et al. 1996; Penfield and Rasmussen 1950; Uematsu et al. 1996), the presence of tactile receptive fields in the macaque monkey (Gentilucci et al. 1988; Rizzolatti et al. 1981), and the effect of lesions to this area, which induce somatosensory neglect of the contralateral side (Rizzolatti et al. 1983). Area 4 also has been shown to have distinct tactile and deep/proprioceptive representations in the squirrel monkey (Strick and Preston 1982), and the macaque monkey (Tanji and Wise 1981), a dissociation that is supported by receptor binding and PET studies in humans (Geyer et al. 1995; Naito et al. 1999). In these studies, the tactile representation (area 4p) was located in the lower half of the anterior bank of the central sulcus, adjacent to area 3a, and >90% of neurons contained cutaneous receptive fields responsive to light moving contact, tapping, or hair movement (Strick and Preston 1982; Tanji and Wise 1981).

We did not observe consistent activation in the anterior bank of the central sulcus during tactile input. Only two of five

subjects in the individual subject analysis showed activation in this region (only 1 of these subjects showed activation in the lower half of the anterior bank of the central sulcus), and the tactile average did not reveal activation in this region. This absence of significant activation may be the product of the punctate tactile stimuli we employed. We did not examine a moving tactile stimulus or vibratory stimulation of ≥ 10 Hz, stimulus conditions that previously activated area 4p in humans (Geyer et al. 1995; Naito et al. 1999), nor did we administer the variety of tactile stimuli used to activate individual receptive fields in this representation in previous monkey studies (Strick and Preston 1982; Tanji and Wise 1981). Nevertheless, the data reported here do not support the position that a high concentration of cutaneous receptive fields exists in posterior area 4 in the human.

Although this signal did not achieve statistical significance, a small stimulus transient was present in the gap during punctate tactile stimulation (0.3% peak signal change, 0.17% mean signal change, Fig. 2). Activation of muscle spindles by the punctate tactile stimuli may have contributed to this response (Burke et al. 1976; Roll and Vedel 1982). In three of five subjects, the gap included area 4, and cutaneous receptive fields in this region or in area 3a also might have contributed to this nonsignificant signal increase (Iwamura et al. 1993; Strick and Preston 1982; Tanji and Wise 1981; Taoka et al. 1998). Studies in the unanesthetized monkey place the concentration of cutaneous receptive fields in area 3a at $\leq 15\%$ (Iwamura et al. 1993; Tanji and Wise 1981; Taoka et al. 1998). Similarly, the percentage signal change in the gap region during tactile input is between 10 and 15% of the signal change observed during kinesthetic/motor stimulation (2.0% peak signal change, 1.7% mean signal change). The temporal characteristics of the stimulus transient evoked by tactile stimulation suggest that the neurons in this region show rapid and sustained adaptation in response to punctate tactile stimulation.

Tactile activation in areas 3b and 1 in the human corresponds with the suprathreshold receptive fields that have been recorded in the monkey PoCG (Chapman and Ageranioti-Belanger 1991; DiCarlo et al. 1998; Iwamura et al. 1993; Johnson and Hsiao 1992; Kaas et al. 1979; Manger et al. 1996; Merzenich et al. 1978; Mountcastle and Powell 1959; Nelson et al. 1980; Paul et al. 1972; Pons et al. 1985; Sur et al. 1980). These neurons are effectively activated by the punctate von Frey stimulus employed in our study (Jain et al. 1997), and the rate of stimulation we employed (3 Hz) is beneath the adaptation rate of the majority of neurons in these regions (Sur et al. 1981, 1984). In individual subjects (4 of 5), and average maps, activation in area 2 was localized to the anterior half of this region. In the nonhuman primate, the anterior and posterior borders of area 2 have been the subject of ongoing discussion (Jones et al. 1978; Lewis et al. 1999; Pons and Kaas 1986). The position of area 2 in the current study (based on receptor binding and cytoarchitecture in the human) (Geyer et al. 1997) is relatively more posterior. With a more anterior placement of area 2, this region would have been activated uniformly by the tactile and kinesthetic/motor conditions in individual subjects and average maps (Fig. 4).

Conclusive delineation of fine somatotopy will require higher resolution studies designed to answer this question. Nevertheless, the data reported here may provide insight into detailed somatotopic organization in the human PoCG. In the

average and in two individual subjects, dual activation regions were observed in the PoCG, localized anterior and posterior within the gyrus. This pattern is similar to the mirror representations observed in the monkey PoCG [Kaas et al. 1979; Merzenich et al. 1978; Nelson et al. 1980; see also Burton et al. (1997) for a similar observation in the human and Gelnar et al. (1998) for a diverging view]. Comparison of the finger and palm representation in individual subjects demonstrates that, while there is overlap in the two activation patterns, the center and extent of the palm representation in the PoCG was more medial than the third digit representation ($n = 2$ subjects, Fig. 1). This more medial position is similar to owl and macaque monkey maps, where the ulnar nerve representation (which was preferentially stimulated in our study, as the thenar eminence was not contacted) is positioned more medially than the third digit (Merzenich et al. 1978; Nelson et al. 1980; Pons et al. 1987).

Activation in the PreCG and PoCG during kinesthetic/motor input

Activation in the PreCG during the kinesthetic/motor protocol is consistent with the well-documented position of the primary motor and premotor cortices, as described by in vivo stimulation (e.g., Penfield and Rasmussen 1950; see Uematsu et al. 1992, for a review) and functional imaging studies in the human (e.g., Kim et al. 1993; Rao et al. 1993; Roland et al. 1980; Sanes et al. 1995). Activation in the PoCG during kinesthetic/motor stimulation has been observed in several PET and fMRI studies that reported activation spanning the PreCG, central sulcus, and PoCG during stimulation that combined kinesthetic/motor grasping type movements with tactile stimulation (Boecker et al. 1996; Grafton et al. 1996; O'Sullivan et al. 1994; Rizzolatti et al. 1996) and without tactile stimulation (Fink et al. 1997). Engagement of areas 3b and 1 during the kinesthetic/motor condition probably results from a variety of inputs. Recordings from unanesthetized monkey preparations reveal a significant minority of neurons in area 3b, and a lesser number in area 1, are deep or proprioceptive in character (Arezzo et al. 1981; Iwamura et al. 1993). As discussed above, SA and FA skin mechanoreceptors in the fingers are activated by the type of movement engaged in the kinesthetic/motor task (Burgess et al. 1982; Edin and Abbs 1991; Hulliger et al. 1979; Matthews 1982), and these receptors should contribute to the activation of representations within the PoCG. Also, this finding may in part result from the modulation of firing in neurons in areas 3b and 1 during and prior to movement of the hand (Jiang et al. 1990; Lebedev et al. 1994; Nelson et al. 1991; Prud'homme et al. 1994; see Nelson 1996 for a review).

Conclusion

Prior to the introduction of modern extracellular recording techniques, there was little appreciation of the submodality-specific representations of the body within the central sulcus region of humans or monkeys (e.g., Penfield and Rasmussen 1950). With their advent, the understanding of the organization of distinct cortical areas in this region in monkeys advanced markedly (Kaas et al. 1979; Merzenich et al. 1978). The current progress in the resolution of hemodynamic imaging and

reconstruction techniques applied to the human cortex mirrors this advance in monkeys. We are now able to address segregation in this region with relatively high resolution. The fMRI data reported here, while lower resolution than single unit techniques, present a strong correspondence with the physiology of the monkey central sulcus region, especially with studies of the unanesthetized monkey cortex (e.g., Iwamura et al. 1993). This agreement suggests a conservation of somatosensory cortical representations across species (Kaas 1983; Krubitzer 1995). Further, this correlation provides a point of cross-validation for the use of monkey physiology as a model for the function of the human somatosensory cortex, and, by the same token, suggests that the fMRI signal in the human somatosensory cortex provides an accurate reflection of underlying neural activity in this region.

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REFERENCES

- AGERANIOTI-BELANGER SA AND CHAPMAN CE. Discharge properties of neurons in the hand area of primary somatosensory cortex in monkeys in relation to the performance of an active tactile discrimination stimulation. *Exp Brain Res* 91: 207–228, 1992.
- ALLISON T, WOOD CC, MCCARTHY G, AND SPENCER DD. Cortical somatosensory evoked potentials. II. Effects of excision of somatosensory or motor cortex in humans and monkeys. *J Neurophysiol* 66: 64–82, 1991.
- AREZZO JC, VAUGHAN HG JR, AND LEGATT AD. Topography and intracranial sources of somatosensory evoked potential in the monkey. II. Cortical components. *Electroencephalogr Clin Neurophysiol* 51: 1–18, 1981.
- BOECKER H, KHORRAM-SEFAT D, KLEINSCHMIDT A, MERBOLDT K-D, HANICKE W, REQUARDT M, AND FRAH J. High-resolution functional magnetic resonance imaging of cortical activation during tactile exploration. *Hum Brain Mapp* 3: 236–244, 1996.
- BRODMANN K. *Localisation in the Cerebral Cortex* (L. J. Garey, translator). London: Smith-Gordon (original work published 1909), 1994.
- BURGESS PR, WEI JY, CLARK FJ, AND SIMON J. Signaling of kinesthetic information by peripheral sensory receptors. In: *Annual Review of Neuroscience*, edited by Cowan WM, Hall ZW, and Kandel ER. Palo Alto, CA: Annual Reviews, 1982, p. 171–188.
- BURKE D, HAGBARTH KE, LOFSTEDT L, AND WALLIN BG. The response of human muscle spindles endings to vibration of non contracting muscles. *J Physiol (Lond)* 261: 673–693, 1976.
- BURTON H, MACLEOD AM, VIDEEN TO, AND RAICHEL ME. Multiple foci in parietal and frontal cortex activated by rubbing embossed grating patterns across fingerpads: a positron emission tomography study in humans. *Cereb Cortex* 7: 3–17, 1997.
- CARLSON M. Characteristics of sensory deficits following lesions of Brodmann's areas 1 and 2 in the postcentral gyrus of *Macaca mulatta*. *Brain Res* 204: 424–430, 1980.
- CHAPMAN CE AND AGERANIOTI-BELANGER SA. Discharge properties of neurons in the hand area of primary somatosensory cortex in monkeys in relation to the performance of an active tactile discrimination stimulation. I. Areas 3b and 1. *Exp Brain Res* 87: 319–339, 1991.
- COGHILL RC, TALBOT JD, EVANS AC, MEYER E, GJEDDE A, BUSHNELL MC, AND DUNCAN GH. Distributed processing of pain and vibration by the human brain. *J Neurosci* 14: 4095–4108, 1994.
- CONSTANZO RM AND GARDENER EP. A quantitative analysis of responses of direction-sensitive neurons in somatosensory cortex of awake monkeys. *J Neurophysiol* 43: 1319–1341, 1980.
- CORKIN S, MILNER B, AND RASMUSSEN T. Somatosensory thresholds: Contrasting effects of postcentral-gyrus and posterior parietal-lobe excisions. *Arch Neurol* 23: 41–58, 1970.
- CROSS MJ AND MCCLOSKEY DI. Position sense following surgical removal of joints in man. *Brain Res* 55: 443–445, 1973.
- CUSICK CG, STEINDLER DA, AND KAAS JH. Corticocortical and collateral thalamocortical connections of postcentral somatosensory cortical areas in

- squirrel monkeys: a double-labeling study with radiolabeled wheat germ agglutinin conjugated to horseradish peroxidase. *Somatosens Res* 3: 1–31, 1985.
- DALE A AND SERENO MI. Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach. *J Cogn Neurosci* 5: 162–176, 1993.
- DALE AM, FISCHL B, AND SERENO MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage* 9: 179–194, 1998.
- DEYOE EA, CARMAN GJ, BANDETTINI P, GLICKMAN S, WIESER J, COX R, MILLER D, AND NEITZ J. Mapping striate and extrastriate visual areas in human cerebral cortex. *Proc Natl Acad Sci USA* 93: 2382–2386, 1996.
- DI CARLO JJ, JOHNSON KJ, AND HSIAO SS. Structure of receptive fields in area 3b of primary somatosensory cortex in the alert monkey. *J Neurosci* 18: 2626–2645, 1998.
- DISBROW E, BUONCORE M, ANOTGNINI J, CARSTENS E, AND ROWLEY HA. The somatosensory cortex: a comparison of the response to noxious, thermal, mechanical and electrical stimuli using functional magnetic resonance imaging. *Hum Brain Mapp* 6: 150–159, 1998.
- EDIN BB AND ABBS JH. Finger movement responses of cutaneous mechanoreceptors in the dorsal skin of the human hand. *J Neurophysiol* 65: 657–670, 1991.
- ENGEL SE. Looking into the black box: new directions in neuroimaging. *Neuron* 17: 375–378, 1996.
- FINK GR, FRACKOWIAK RSJ, PIETRZYK U, AND PASSINGHAM RE. Multiple nonprimary motor areas in human cortex. *J Neurophysiol* 77: 2164–2174, 1997.
- FISCHL B, SERENO MI, AND DALE AM. Cortical surface-based analysis. II. Inflation, flattening, and a surface-based coordinate system. *Neuroimage* 9: 195–207, 1998.
- FISCHL B, SERENO MI, TOOTELL RBH, AND DALE AM. High-resolution intersubject averaging and a coordinate system for the cortical surface. *Human Brain Map* 8: 272–284, 1999.
- FOX PT, BURTON H, AND RAICHLE ME. Mapping human somatosensory cortex with positron emission tomography. *J Neurosurg* 67: 34–43, 1987.
- GELNAR PA, KRAUSS BR, SZEVERENYI NM, AND APKARIAN AV. Fingertip representation in the human somatosensory cortex: an fMRI study. *Neuroimage* 7: 261–283, 1998.
- GENTILUCCI M, FOGASSI L, LUPPINO G, MATELLI M, CABARDA R, AND RIZZOLATI G. Functional organization of inferior area 6 in the macaque monkey. I. Somatotopy and the control of proximal movements. *Exp Brain Res* 71: 475–490, 1988.
- GEYER S, LEDBERG A, SCHLEICHER A, KINOMURA S, SCHORMAN T, BURGEL U, KLINBERG T, LARSSON J, ZILLES K, AND ROLAND PE. Two different areas within the primary motor cortex of man. *Nature* 382: 805–807, 1995.
- GEYER S, SCHLEICHER A, AND ZILLES K. The somatosensory cortex of human: Cytoarchitecture and regional distribution of receptor-binding sites. *Neuroimage* 6: 27–45, 1997.
- GRAFTON ST, FAGG AH, WOODS RP, AND ARBIB MA. Functional anatomy of pointing and grasping in humans. *Cereb Cortex* 6: 226–237, 1996.
- HAMMEKE TA, YETKIN FZ, MUELLER WM, MORRIS GL, HAUGHTON VM, RAO SM, AND BINDER JR. Functional magnetic resonance imaging of somatosensory stimulation. *Neurosurgery* 35: 677–681, 1994.
- HEAD H. *Studies in Neurology*. London: Henry Frowde and Hodder and Stoughton, 1920, vol. II.
- HULLIGER M, NORDH E, THELIN A-E, AND VALLBO AB. The responses of afferent fibers from the glabrous skin of the hand during voluntary finger movements in man. *J Physiol (Lond)* 291: 233–249, 1979.
- HYVARINEN J AND PORANEN A. Movement-sensitive and direction and orientation-selective cutaneous receptive fields in the hand area of the postcentral gyrus in monkeys. *J Physiol (Lond)* 283: 523–527, 1978.
- IWAMURA Y, TANAKA M, SAKAMOTO M, AND HIKOSAKA O. Vertical neuronal arrays in the postcentral gyrus signaling active touch: a receptive field study in the conscious monkey. *Exp Brain Res* 58: 412–420, 1985.
- IWAMURA Y, TANAKA M, SAKAMOTO M, AND HIKOSAKA O. Rostrocaudal gradients in the neuronal receptive field complexity in the finger region of the alert monkey's postcentral gyrus. *Exp Brain Res* 92: 360–368, 1993.
- IWAMURA Y AND TANAKA M. Representation of reaching and grasping in the monkey postcentral gyrus. *Neurosci Lett* 214: 147–150, 1996.
- JAIN N, CATANIA KC, AND KAAS JH. Deactivation and reactivation of somatosensory cortex after dorsal spinal cord injury. *Nature* 386: 495–498, 1997.
- JIANG W, CHAPMAN CE, AND LAMARRE Y. Modulation of somatosensory evoked responses in the primary somatosensory cortex produced by intracortical microstimulation of the motor cortex in the monkey. *Exp Brain Res* 80: 333–344, 1990.
- JOHANSSON RS AND VALLBO AB. Spatial properties of the population of mechanoreceptive units in the glabrous skin of the human hand. *Brain Res* 24: 184: 353–366, 1980.
- JOHANSSON RS, VALLBO AB, AND WESTLING G. Thresholds of mechanosensitive afferents in the human hand as measured with von Frey hairs. *Brain Res* 184: 343–351, 1980.
- JOHNSON KO AND HSIAO SS. Neural mechanisms of tactual form and texture perception. In: *Annual Review of Neuroscience*, edited by Cowan WM, Shooter EM, Stevens CF, and Thompson RF. Palo Alto, CA: Annual Reviews, 1992, p. 227–250.
- JONES EG. Lack of collateral thalamocortical projections to fields of the first somatic sensory cortex in monkeys. *Exp Brain Res* 52: 375–384, 1983.
- JONES EG. Connectivity of the primate sensory-motor cortex. In: *Cerebral Cortex*, edited by Peters A and Jones EG. New York, NY: Plenum, 1985, p. 113–184.
- JONES EG, COULTER JD, AND HENDRY SHC. Intracortical connectivity of architectonic fields in the somatic sensory, motor and parietal cortex of monkeys. *J Comp Neurol* 181: 291–348, 1978.
- JONES EG AND PORTER R. What is area 3a? *Brain Res Rev* 2: 1–43, 1980.
- KAAS JH. What, if anything, is SI? Organization of first somatosensory area of cortex. *Physiol Rev* 63: 206–231, 1983.
- KAAS JH. Why does the brain have so many visual areas? *J Cogn Neurosci* 1: 121–135, 1989.
- KAAS JH, NELSON RJ, SUR M, LIN, C-S, AND MERZENICH MM. Multiple representations of the body within the primary somatosensory cortex of primates. *Science* 204: 521–523, 1979.
- KENNEDY DN, LANGE N, MAKRI N, BATES J, MEYER J, AND CAVINESS VS JR. Gyri of the human neocortex: an MRI-based analysis of volume and variance. *Cereb Cortex* 8: 372–384, 1998.
- KIDO DK, LEMAY M, LEVINSON AW, AND BENSON WE. Computed tomographic localization of the precentral gyrus. *Radiology* 135: 373–373, 1980.
- KIM S-G, ASHE J, GEORGIOPOULOS AP, MERKLE H, ELLERMAN JM, MENON RS, OGAWA S, AND UGURBIL K. Functional imaging of human motor cortex at high magnetic field. *J Neurophysiol* 69: 297–301, 1993.
- KRUBITZER L. The organization of neocortex in mammals: are species differences really so different? *Trends Neurosci* 18: 408–417, 1995.
- KURTH R, VILLRINGER K, MACKERT BM, SCHWIEHMANN J, BRAUN J, CURIO G, VILLRINGER A, AND WOLF KJ. fMRI assessment of somatotopy in human Brodmann area 3b by electrical finger stimulation. *Neuroreport* 9: 207–212, 1998.
- LEBEDEV MA, DENTON JM, AND NELSON RJ. Vibration-entrained and premovement activity in monkey primary somatosensory cortex. *J Neurophysiol* 72: 1654–1673, 1994.
- LEWIS JW, BURTON H, AND VAN ESSEN DC. Anatomical evidence for the posterior boundary of area 2 in the macaque monkey. *Somatosens Mot Res* 16: 382–390, 1999.
- LIN W, KUPPUSAMY K, HAACKE EM, AND BURTON H. Functional MRI in human somatosensory cortex activated by touching textured surfaces. *J Magn Reson Imaging* 6: 565–572, 1996.
- LOCASIO JJ, JENNINGS PJ, MOORE CI, AND CORKIN S. Time series analysis in the time domain and resampling methods for studies of functional magnetic resonance brain imaging. *Hum Brain Mapp* 5: 168–193, 1997.
- MANGER PR, WOODS TM, AND JONES EG. Representation of face and intra-oral structures in area 3b of macaque monkey somatosensory cortex. *J Comp Neurol* 371: 513–521, 1996.
- MATTHEWS PBC. Where does Sherrington's "muscle sense" originate? Muscles, joints, corollary discharges? In: *Annual Review of Neuroscience*, edited by Cowan WM, Hall ZW, and Kandel ER. Palo Alto, CA: Annual Reviews, 1982, p. 189–218.
- MERZENICH MM AND KAAS JH. Principles of organization of sensory-perceptual systems in mammals In: *Progress in Psychobiology and Physiological Psychology*, San Diego, CA: Academic, 1980, vol. 9, p. 1–42.
- MERZENICH MM, KAAS JH, SUR M, AND LIN C-S. Double representation of the body surface within cytoarchitectonic areas 3b and 1 in "SI" in the owl monkey (*Aotus trivirgatus*). *J Comp Neurol* 181: 41–74, 1978.
- MOORE CI, GEHI A, GUIMEREAS AR, CORKIN S, ROSEN BR, AND STERN CE. Somatotopic mapping of cortical areas SI and SII using FMRI (Abstract). *Neuroimage* 6: S333, 1996.
- MOORE CI, STERN C, CORKIN S, GRAY A, THELUSMA F, ROSEN BR, AND DALE A. Segregation of multiple somatosensory maps within the human postcentral gyrus using fMRI (Abstract). *Neuroimage* 8: S406, 1998.
- MOREL A, GARRAGHTY PE, AND KAAS JH. Tonotopic organization, architectonic fields, and connections of auditory cortex in macaque monkeys. *J Comp Neurol* 335: 437–459, 1993.

- MOUNTCASTLE VB AND POWELL TPS. Neural mechanisms subserving cutaneous sensibility, with special reference to the role of afference inhibition in sensory perception and discrimination. *Bull Johns Hopkins Hosp* 105: 173–200, 1959.
- NAITO E, EHRSOON HH, GEYER S, ZILLES K, AND ROLLAND PE. Illusory arm movements activate cortical motor areas: A positron emission tomography study. *J Neurosci* 19: 6134–6144, 1999.
- NELSON RJ. Responsiveness of monkey primary somatosensory cortical neurons to peripheral stimulation depends on 'motor-set'. *Brain Res* 304: 143–148, 1984.
- NELSON RJ. Interactions between motor commands and somatic perception in sensorimotor cortex. *Curr Opin Neurobiol* 6: 801–810, 1996.
- NELSON RJ, LI B, AND DOUGLAS VD. Sensory response enhancement and suppression of monkey primary somatosensory cortical neurons. *Brain Res Bull* 27: 751–757, 1991.
- NELSON RJ, SUR M, FELLEMAN DJ, AND KAAS JH. Representation of the body surface in postcentral parietal cortex of *Macaca fascicularis*. *J Comp Neurol* 192: 611–643, 1980.
- NII Y, UEMATSU S, LESSER RP, AND GORDON B. Does the central sulcus divide motor and sensory functions? Cortical mapping of human hand areas as revealed by electrical stimulation through subdural grid electrodes. *Neurology* 46: 360–367, 1996.
- O'SULLIVAN BT, ROLAND PE, AND KAWASHIMA R. A PET study of somatosensory discrimination in man. Microgeometry versus macrogeometry. *Eur J Neurosci* 6: 137–148, 1994.
- PAUL RL, MERZENICH M, AND GOODMAN H. Representation of slowly adapting and rapidly adapting cutaneous mechanoreceptors of the hand in Brodmann's areas 3 and 1 of *Macaca mulatta*. *Brain Res* 36: 229–249, 1972.
- PENFIELD W AND RASMUSSEN T. *The Cerebral Cortex of Man: A Clinical Study of Localization of Function*. New York: Hafner, 1950.
- PONS TP, GARRAGHTY PE, CUSICK CG, AND KAAS JH. The somatotopic organization of area 2 in macaque monkeys. *J Comp Neurol* 241: 445–466, 1985.
- PONS TP, GARRAGHTY PE, AND MISHKIN M. Serial and parallel processing of tactual information in somatosensory cortex of rhesus monkeys. *J Neurophysiol* 68: 518–527, 1992.
- PONS TP AND KAAS JH. Corticocortical connections of area 2 of somatosensory cortex in macaque monkeys: a correlative anatomical and electrophysiological study. *J Comp Neurol* 248: 313–335, 1986.
- PONS TP, WALL JT, GARRAGHTY PE, CUSICK CG, AND KAAS JH. Consistent features of the representation of the hand in area 3b of macaque monkeys. *Somatosens Res* 4: 309–331, 1987.
- PRUD'HOMME MJL, COHEN DAD, AND KALASKA JF. Tactile activity in primate primary somatosensory cortex during active arm movements: cytoarchitectonic distribution. *J Neurophysiol* 71: 173–181, 1994.
- PUCE A, CONSTABLE RT, LUBY ML, MCCARTHY G, NOBRE AC, SPENCER DD, GORE JC, AND ALLISON T. Functional magnetic resonance imaging of sensory and motor cortex: comparison with electrophysiological localization. *J Neurosci* 83: 262–270, 1995.
- RAO SM, BANDETTINI PA, BINDER JR, BOBHOLZ JA, HAMMEKE TA, STEIN EA, AND HYDE JS. Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex. *J Cereb Blood Flow Metab* 16: 1250–1254, 1996.
- RAO SM, BINDER JR, BANDETTINI PA, HAMMEKE TA, YETKIN FZ, JESMANOWICZ A, LISK LM, MORRIS GL, MUELLER WM, ESTKOWSKI LD, WONG EC, HAUGHTON VM, AND HYDE JS. Functional magnetic resonance imaging of complex human movements. *Neurology* 43: 2311–2318, 1993.
- RAUSCHER JP, TIAN B, AND HAUSER M. Processing of complex sounds in the macaque nonprimary auditory cortex. *Science* 268: 111–114, 1995.
- RENCANZONE GH, MERZENICH MM, AND JENKINS WM. Frequency discrimination training engaging a restricted skin surface results in an emergence of a cutaneous response zone in cortical area 3a. *J Neurophysiol* 67: 1057–1070, 1992.
- RIZZOLATTI G, CAMARDA L, FOGASSI M, GENTILUCCI M, LUPPINO G, AND MATELLI M. Functional organization of inferior area 6 in the macaque monkey. II. Area F5 and the control of distal movements. *Exp Brain Res* 71: 491–507, 1988.
- RIZZOLATTI G, FADIGA L, MATELLI M, BETTINARDI V, PAULESU E, PERANI D, AND FAZIO F. Localization of grasp representations in humans by PET. I. Observation versus execution. *Exp Brain Res* 111: 246–252, 1996.
- RIZZOLATTI G, MATELLI M, AND PAVESI G. Deficits in attention and movement following the removal of postarcuate (area 6) and prearcuate (area 8) cortex in macaque monkeys. *Brain* 106: 655–673, 1983.
- RIZZOLATTI G, SCANDOLARA C, MATELLI M, AND GENTILUCCI M. Afferent properties of periarculate neurons in macaque monkeys. I. Somatosensory responses. *Behav Brain Res* 2: 125–146, 1981.
- ROLAND PE AND LARSEN B. Focal increase of cerebral blood flow during stereognostic testing in man. *Arch Neurol* 33: 551–558, 1976.
- ROLAND PE, LARSEN B, LASSEN NA, AND SKINJH E. Supplementary motor area and other cortical areas in organization of voluntary movements in man. *J Neurophysiol* 43: 118–136, 1980.
- ROLAND PE AND ZILLES K. Structural divisions and functional fields in the human cerebral cortex. *Brain Res Brain Res Rev* 26: 87–105, 1998.
- ROLL JP AND VEDEL JP. Kinesthetic role of muscle afferents in man, studied by tendon vibration and microneurography. *Exp Brain Res* 47: 177–190, 1982.
- SANES JN, DONAGHUE JP, THANGARAJ V, EDELMAN RR, AND WARACH S. Shared neural substrates controlling hand movements in human motor cortex. *Science* 268: 1775–1777, 1995.
- SASTRE-JANER FA, REGIS J, BELIN P, MANGIN J-F, DORMONT D, MASURE M-C, REMY P, FROULIN V, AND SAMSON Y. Three-dimensional reconstruction of the human central sulcus reveals a morphological correlate of the hand area. *Cereb Cortex* 8: 641–647, 1998.
- SCHLAUG G, SANES JN, THANGARAJ V, DARBY DG, JANCKE L, EDELMAN RR, AND WARACH S. Cerebral activation covaries with movement rate. *Neuroreport* 7: 879–883, 1996.
- SEMMES J AND PORTER L. A comparison of precentral and postcentral cortical lesion on somatosensory discrimination in the monkey. *Cortex* 8: 249–264, 1972.
- SEMMES J, PORTER L, AND RANDOLPH MC. Further studies of anterior postcentral lesions in monkeys. *Cortex* 10: 55–68, 1974.
- SERENO MI, DALE AM, REPPAS JB, KWONG KK, BELLIVEAU JW, BRADY TJ, ROSEN BR, AND TOOTELL RBH. Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science* 268: 889–893, 1995.
- SERVO P, ZACKS J, RUMELHART DE, AND GLOVER GH. Somatotopy of the human arm using fMRI. *Neuroreport* 9: 605–609, 1998.
- SOBEL DF, GALLAN CC, SCHWARTZ BJ, WALTZ TA, COPELAND B, YAMADA S, HIRSCHKOFF EC, AND BLOOM FE. Locating the central sulcus: comparison of MR anatomic and magnetoencephalographic methods. *Am J Neuroradiol* 14: 915–925, 1993.
- STRICK PL AND PRESTON JB. Two representations of the hand in area 4 of a primate. II. Somatosensory input organization. *J Neurophysiol* 48: 150–159, 1982.
- SUR M, MERZENICH MM, AND KAAS JH. Magnification, receptive field area, and "hypercolumn" size in areas 3b and 1 of adult somatosensory cortex in owl monkeys. *J Neurophysiol* 44: 295–311, 1980.
- SUR M, WALL JT, AND KAAS JH. Modular segregation of functional cell classes within the post-central somato-sensory cortex of monkeys. *Science* 212: 1059–1061, 1981.
- SUR M, WALL JT, AND KAAS JH. Modular distribution of neurons with slowly adapting and rapidly adapting responses in area 3b of somatosensory cortex in monkeys. *J Neurophysiol* 51: 724–744, 1984.
- TALAVAGE TM, LEDDEN PJ, SERENO MI, BENSON RR, AND ROSEN BR. Preliminary fMRI evidence for tonotopicity in human auditory cortex. *Neuroimage* 6: S355, 1996.
- TANJI J AND WISE SP. Submodality distribution in sensorimotor cortex of the unanesthetized monkey. *J Neurophysiol* 45: 467–481, 1981.
- TAOKA M, TODA T, TAKASHI T, AND IWAMURA Y. Representation of the midline trunk, bilateral arms, and shoulders in the monkey postcentral somatosensory cortex. *Exp Brain Res* 123: 315–322, 1998.
- TOMMERDAHL M, DELEMOES KA, FAVOROV OV, METZ CB, VIERCK CJ JR, AND WHITSEL BL. Response of anterior parietal cortex to different modes of same-site skin stimulation. *J Neurophysiol* 80: 3272–3283, 1998.
- TOMMERDAHL M, DELEMOES KA, VIERCK CJ JR, FAVOROV OV, AND WHITSEL BL. Anterior parietal cortical response to tactile and skin-heating stimuli applied to the same skin site. *J Neurophysiol* 75: 2662–2670, 1996.
- TOOTELL RB, REPPAS JB, KWONG KK, MALACH R, BORN RT, BRADY TJ, ROSEN BR, AND BELLIVEAU JW. Functional analysis of human MT and related visual cortical areas using magnetic resonance imaging. *J Neurosci* 15: 3215–3230, 1995.
- TOOTELL RBH, MENDOLA JD, HADJIKHANI NK, LEDDEN PJ, LIU AK, REPPAS JB, SERENO MI, AND DALE AM. Functional analysis of V3A and related areas in human visual cortex. *J Neurosci* 17: 7060–7078, 1997.
- UEMATSU S, LESSER RP, AND GORDON B. Localization of sensorimotor cortex: the influence of Sherrington and Cushing on the modern concept. *Neurosurgery* 30: 904–913, 1992.
- VAN ESSEN DC, ANDERSON CH, AND FELLEMAN DJ. Information processing in the primate visual system: an integrated systems perspective. *Science* 255: 419–423, 1992.

- WEILLER C, JUPTNER M, FELLOWS S, RIJNTJES M, LEONHARDT G, KIEBEL S, MULLER S, DIENER HC, AND THILMANN AF. Brain representation of active and passive movements. *Neuroimage* 4: 105–110, 1996.
- WHITE LE, ANDREWS TJ, HULETTE C, RICHARDS A, GROELLE M, PAYDARFAR J, AND PURVES D. Structure of the human sensorimotor system. I. Morphology and cytoarchitecture of the central sulcus. *Cereb Cortex* 7: 18–30, 1997.
- WHITSEL BL, ROPPOLO JR, AND WERNER G. Cortical information processing of motion on primate skin. *J Neurophysiol* 35: 691–717, 1972.
- WOODS RP. Modeling for intergroup comparisons of imaging data. *Neuroimage* 4: S84–S94, 1996.
- WOOLSEY CN, MARSHALL WH, AND BARD P. Representation of cutaneous tactile sensibility in cerebral cortex of monkey as indicated by evoked potentials. *Bull Johns Hopkins Hosp* 70: 399–441, 1942.
- YOUSRY TA, SCHMID UD, ALKADHI H, SCHMIDT D, PERAUD A, BEUTTNER A, AND WINKLER P. Localization of the motor hand area to a knob on the precentral gyrus: a new landmark. *Brain* 120: 141–157, 1997.
- ZILLES K, SCHLAUG G, MATELLI M, LUPPINO G, SCHLEICHER A, QU M, DABRINGHAUS A, SIETZ R, AND ROLAND PE. Mapping of human and macaque sensorimotor areas by integrating architectonic, transmitter receptor, MRI and PET data. *J Anat* 187: 515–537, 1995.