Using fMRI to explore secondary somatosensory areas in the lateral sulcus of squirrel monkeys

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Introduction: While primary somatosensory cortex (SI) in non-human primates has been extensively mapped using electrophysiology (Kaas), optical imaging of intrinsic signal (OIS; Chen), and fMRI (Chen), less is known about the fine scale topographic organization of secondary somatosensory cortex (SII), due in large part to its inaccessibility for optical imaging. We previously demonstrated that somatotopic maps collected using high field BOLD fMRI are in close agreement with those obtained in the same animal using OIS and electrophysiology [1]. We further demonstrated the ability of high field BOLD fMRI to resolve submillimeter shifts in cortical activation that are the neural correlates of the sensory funneling illusion in SI. We have now used the same BOLD fMRI methods to examine the fine somatotopic organization of digits in SII of squirrel monkey, and to determine whether similar cortical correlates of sensory funneling are present in SII.

Methods: Under a protocol approved by the Vanderbilt IACUC, squirrel monkeys were anesthetized with ketamine hydrochloride, intubated and maintained under isoflurane anesthesia with mechanical ventilation. Physiological status (respiration rate, temperature, SpO2, heart rate, ET-CO2) of each animal was carefully monitored throughout each study. All scans were performed on 9.4T 21-cm bore Varian INOVA MI system using a 3cm surface transmit-receive coil secured over the sensory cortex. Gradient echo images (TR/TE= 200/14 ms; 512x512 matrix) and GE-EPI (TR/TE=1500/16 ms; 64x64 matrix) were used to acquire anatomical and functional images respectively. A custom-designed MR cradle with ear and eye bars was used to reduce motion. The monkey's fingers were secured, leaving the glabrous surfaces available for vibro-tactile stimulation by a rounded plastic probe (2mm diameter) connected to a piezoelectric device. Piezos were driven by Grass stimulators at a rate of 8Hz. Stimulation was synchronized to image acquisition. Stimuli were presented in a block-design (30s on/ 30s off, TR=1.5s). Reconstructed images were imported to custom Matlab software for drift correction, temporal smoothing, and statistical analysis as described previously (Chen et al., 2007).

Results: Consistent with our previous studies [1], composite activation maps collected from six monkeys during individual stimulation of multiple digits., the activations in SI (Fig. 1a-f) revealed fine topographically organized fingerpad maps (D1 to D4 ordered lateral to medial). Activations in SII spanned one or two of the deeper oblique slices and each digit activated distinct somatotopically organized anterior and posterior areas of SII in all six animals, separated by 4.32 ±1.96 mm (Fig. 1g-l). The distance between adjacent digits were 0.97±0.76 mm in the anterior, and 2.56±1.41 mm in the posterior area of SII, and on both areas digit topography was organized in a medial to lateral / rostral to caudal pattern for individual digits (e.g. Fig 2). This organization in SII was consistently reproducible within and across animals. Furthermore, collection of oblique axial (as in Fig 1) and coronal fMRI data sets from the same animal in the same imaging session demonstrated close agreement of the activation foci in SI and SII, and confirmed the sites of anterior and posterior SII activation in the upper bank of lateral sulcus (Fig. 3).

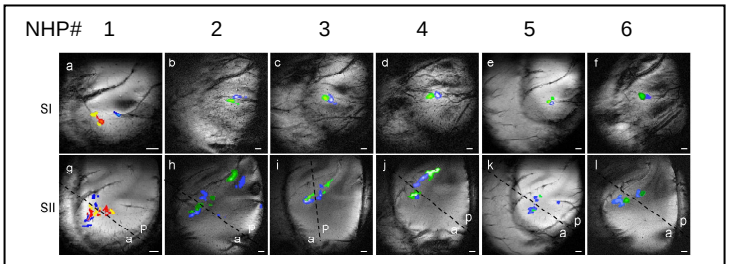

Fig. 1. Fine digit topography in SI and SII (g-i) in six monkeys. SII activations overlaid on a single deep slice for clarity.

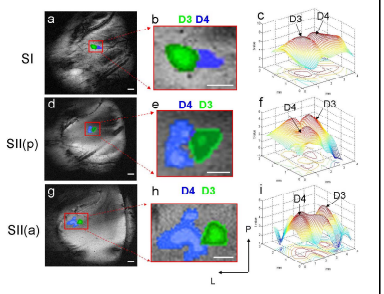

Fig. 2. Distinct activation for adjacent digits in SI, posterior (SIIa) and anterior SII (SIIa).

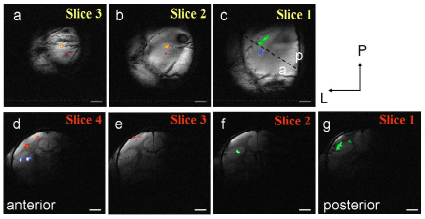

Fig. 3. D4 activation maps collected in both axial oblique (a-c) and coronal (d,g) planes, showing focal activation in SI (red), SIIa (blue) and SIIp (green).

We previously demonstrated that high field BOLD fMRI could resolve the sub-millimeter activation shifts in area 3b of SI that are neural correlates of sensory funneling [1]. Fig. 4 reproduces this, and extends the observation of funneling correlates to SIIp and SIIa. Individual stimulation of D3 and D4 generated distinct activations in SI (Fig. 4 a, b, m, n). Simultaneous stimulation of D3 and D4 produced a single, focal activation, midway between the activation centers generated by stimulation of D3 and D4 alone (Fig. 4h). For each condition, SII activations were revealed in both posterior and anterior regions. In both regions, individual stimulation of D3 and D4 generated distinct activations (separated by ~ 0.72mm and 0.50 mm for posterior and anterior SII respectively). Simultaneous stimulation of D3 and D4 produced activation with multiple additional peaks (green and blue arrows).

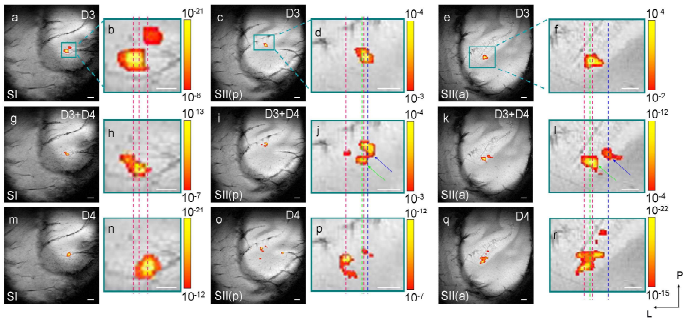

Fig. 4. Correlates of sensory funneling in SI (a, b, g, h, m, n) and SII (c-f, i-l, o-r). Stimulation of single digits D3 (a-f) and D4 (m-r) generate single focal somatotopically organized activations in area 3b of SI. Stimulation of paired adjacent digits (D3+D4) generated a single activation in area 3b of SI (g, h), located between the sites of individual D3 (a, b) and D4(m, n). (Corresponding activations linked by dashed lines). For each stimulus condition, SIIp (c, d, i, j, o, p) and SIIa (e, f, k, l, q, r) activations are also present. Neural correlates of sensory funneling evident as appearance of additional activations in SIIp, SIIa midway between single digits loci during simultaneous stimulation of adjacent digits (D3+D4). Color scale bars indicate p values. Inset scale bars = 1mm. P: posterior. L: lateral.

Conclusion: These studies demonstrate the ability of high field BOLD fMRI to map the functional organization of the non-human primate brain at submillimeter resolution in areas that are inaccessible to optical imaging techniques, and require the sacrifice of the animal for electrophysiological mapping studies. Furthermore, they represent some of the first data suggesting that sensory funneling may have neural correlates beyond SI.

References: [1] Chen LM, Turner GH, Friedman RM, Zhang N, Gore JC, Roe AW, Avison MJ. J Neurosci 2007; 27(34): 9181-9191