Pushing the Spatial Resolution of BOLD Imaging, the fMRI Cortical Representation of Rat Digits at 9.4T.

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Abstract: Spatial resolution necessary to resolve individual cortical columns will be important to the future of functional imaging. (1,2,3) In this study the individual digits of the rat were stimulated and the BOLD fMRI signal studied with cubic 0.3 mm voxels at 9.4 T. Discrimination between digits is possible at this resolution with the activation very columnar in nature. Each digit spans about three slices in the anterior to posterior direction. Input from three of the major nerves in the brachial plexus (Median, Ulnar, Radial) feed the forepaw. Individual digits can be innervated by multiple nerves and therefore may span multiple columns. The layer specific BOLD signal timecourses act like an integrator with the upper layers receiving the drainage from activation in the lower layers.

Materials and Methods: Six Sprague-Dawley rats were used in this study. The animals underwent an initial surgery under isoflurane anesthesia. A catheter was inserted into the left femoral artery and vein and Medetomidine (Domitor) anesthesia started. (Infusion 0.1mg/kg/hr) 150μm diameter stainless-steel bipolar electrodes were attached to the each of the 4 individual digits of the left and right forepaw (8 total). Arterial blood pressure, end-tidal/inspired CO2 and O2, pulse oximetry, and temperature were monitored and maintained within normal limits throughout the protocol. The data were acquired with a Bruker AVANCE 9.4 T MRI animal scanner equipped with a Bruker receiving surface coil and linear transmit coil. Acquisition parameters for gradient echo sequence were 3.84 cm FOV, 20 contiguous interleaved 0.3 mm thick slices, TE=18.76 ms, TR=2 seconds, matrix size=128x128, 110 repetitions, and 3 minutes 40 seconds total acquisition time. The digits were stimulated with a 20 seconds on / 40 seconds off (3 blocks) boxcar sequence with an initial 40 seconds off. A p-value of 0.005 was the activation threshold.

Results and Discussion: Figure 1 displays the area of BOLD activation map for each of the four digits of the rat forepaw for a single animal. The activation extends from cortical layer 1 at the top of the brain to layer 6 at the bottom next to the corpus callosum. The slice position is listed in the top left of each of the close-up inserts. The digit number is listed in-between the left and right side representations. Figure 2 is a graphical display of the number of activated voxels as a function of 0.3 mm slice position moving from anterior to posterior for a single rat. Both the left and right forepaw are displayed. The digits progress in an orderly somatotopic fashion from front to back. The 2nd and 3rd digit are the most separable in this direction. Generally the highest number of activated voxels is located in the center slice. Figure 3a is a display of the average percent BOLD signal change of activated voxels in the layers of the cortex for all six rats. Layers 1,2 and 3,4 have equally the largest percent signal change. In figure 3b the activation from 3,4 and 5,6 is subtracted from layer 1,2 (green). Also layer 5,6 is subtracted from 3,4 (blue). Layer 5,6 stays the same (red). Drainage occurs from bottom layers to top layers. The layer-specific BOLD signal acts like an integrater with the highest activation occurring in layers 3,4 as expected. This study demonstrates the possibilities of using small cubic voxel sizes in studies of layer specific BOLD fMRI studies.

References: 1.) MRM 50:1215-1222 2.) PNAS 99:23:15182-15187 3.) MRI 25:784-794

Figure 1: Cortical representation of the individual digits of the forepaw

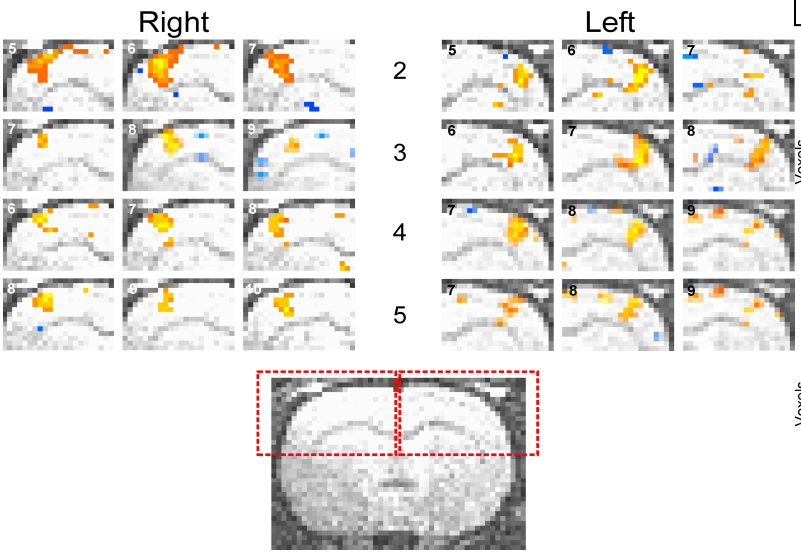

Figure 2: Spatial distribution of the BOLD activation of the digits in the anterior to posterior direction

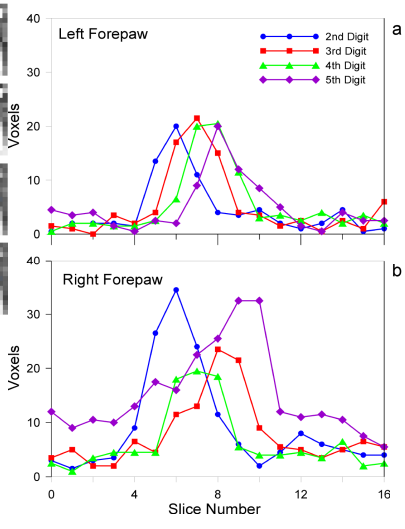

Figure 3: a.) Layer specific percent signal change b.) Originating blood oxygenation levels with the integration of the signal taken into effect.