fMRI Measurements of Human Visual Cortex

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Sir — The primate visual system contains many distinct visual areas, each containing its own rich structure[1]. Few detailed measurements of these areas have been made in humans, however, because of the poor spatial resolution of functional neuroimaging methods. For example, the spatial resolution in positron emission tomography studies[2] is typically 7 to 10 mm. Using functional magnetic resonance imaging (fMRI), we made detailed measurements of the topography of human primary visual cortex. Our experiments were performed using a conventional clinical scanner, and lasted only a few minutes. We measured reliable differences in activity between cortical locations separated by less than 1.4 mm along continuous strips of visual cortex. The method should have broad clinical and scientific applicability.

The receptive fields of neurons in human primary visual cortex follow a precisely organized retinotopic map: As a stimulus moves from the fovea to the periphery the locus of responding neurons varies from posterior to anterior portions of the calcarine sulcus, the site of human primary visual cortex[3]. Hence, we can use the periodic stimulus illustrated in Figure 1A to generate waves of neural activity along the length of the calcarine sulcus.

As the stimulus slowly expands, each visual field location alternates between the uniform field and checkerboard. Importantly, the timecourse of the alternation depends upon visual field location; peripheral locations are delayed relative to foveal locations. When subjects view this stimulus, neural activity in the anterior portions of the calcarine should be delayed relative to activity in the posterior calcarine.

Subjects viewed four cycles of this stimulus while fMRI measurements of neural activation were continuously acquired. The fMRI signal that we measured depends upon veinous blood oxygenation[4,5]. Further details of our methods will be published elsewhere. Figure 1C plots the time-varying fMRI signal measured at points along the calcarine sulcus. The measured activation oscillated with the stimulus period of 48 sec, and the signal was delayed systematically along the sulcus, as expected.

To evaluate the quality of our measurements, we estimated the distance in cortex over which we could obtain reliable differences in the timecourse of the fMRI signal. To do this, we found the best-fitting (least-squares) sinusoid at the stimulus frequency for each of the four stimulus cycles at each measured cortical location. The mean of the

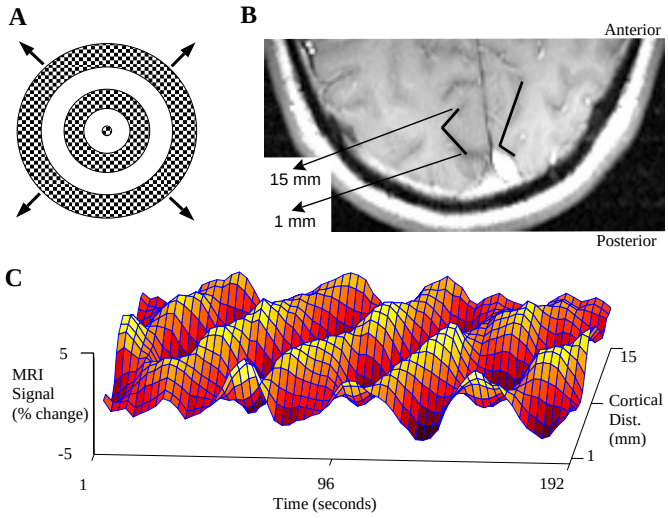

Figure 1: Mapping receptive field locations along the calcarine sulcus. The observer viewed two concentric expanding annuli presented on a gray background. Each annulus contained a high contrast flickering (8.3 hz) radial checkerboard pattern. The outer diameter of an annulus was bounded at 10 deg; as the larger annulus disappeared, a new annulus grew in the center of the display. The image sequence had a period of 48 seconds and was repeated four times in a single experiment. We acquired activation images every 1.5 sec in the plane of the calcarine while subjects viewed four cycles of the stimulus over a 192 second interval. We used a clinical scanner (GE Signa, Rev. 5.2, 1.5T), with a T^*_2 sensitive gradient recalled echo pulse sequence with spiral readout (TR = 75ms , TE = 40ms, flip angle = 23 degrees)[6]. The data had an in-plane voxel size of 1.03 mm square, a through-plane resolution of 5 mm, and were interpolated to a pixel size of 0.78 mm square to fit a 256 by 256 grid. **A**. The stimulus pattern at a single moment of time. **B**. A T_1 weighted anatomical image of cortex in the plane of the calcarine sulcus. We also acquired sixty 1.5 mm thick T_1 weighted anatomy images spanning the entire occipital lobe. We visualized these images using a three-dimensional imaging tool, and we identified points in the functional measurement plane that fell within the calcarine sulcus. We analyzed the fMRI signal at these points, indicated in black. **C** The in-plane anatomy showing the region V1 we analyzed. **D**. The timecourse of activation as a function of distance along the calcarine sulcus. For display purposes only, the activation data was first smoothed with a Gaussian ($\sigma_{spatial} = 3mm, \sigma_{temporal} = 7sec$), and then every other point was plotted.

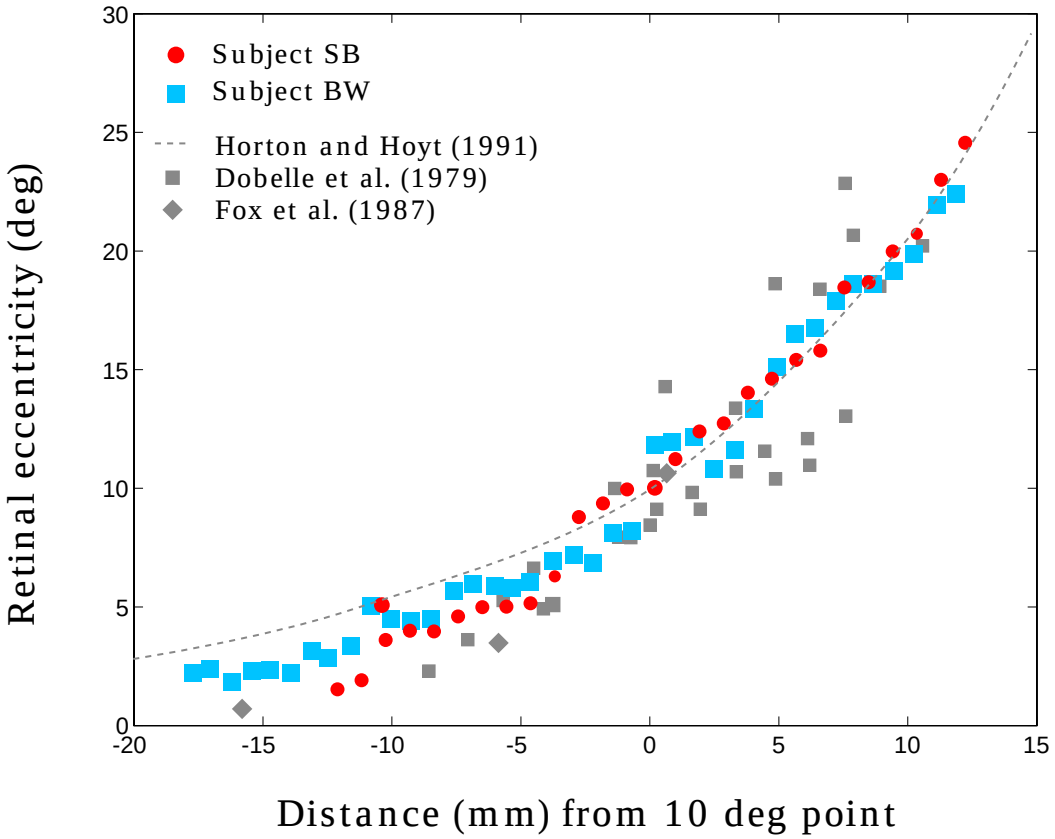

Figure 2: Measurements of human V1 retinotopic organization. Cortical distance is measured relative to the location responding best to a stimulus at 10 degrees of retinal eccentricity. The color symbols are measurements from two observers in the present study. The grey squares are from a microstimulation study on a single observer[4]. The diamonds are pooled data from 5 observers in a PET study[5]. The dashed line was estimated using the locations of scotoma in stroke patients and single-cell data from non-human primates[6].

phase-delays of these four sinusoids estimates the signal delay at that location, and the standard deviation of these phase-delays quantifies the precision of our measurements. If we define reliable separation as two standard errors, then the fMRI signal distinguishes activation at points in cortex separated by 1.35mm, on average.

We used this paradigm to measure the cortical representation of the central 24 degrees of the visual field. We tested two subjects with a 24 degree stimulus, and analyzed our data along regions of interest approximately 30 mm in length. We converted delay in activation to retinal eccentricity by assuming that the maximal observed delay equaled the maximal stimulus eccentricity. Figure 3 shows our results along with estimates of the retinotopic organization of human primary visual cortex based on direct electrical stimulation[7], positron emission tomography[2], and focal lesions in stroke patients[8].

Note the superior density and regularity of the fMRI results, which were obtained within a brief experimental session.

The method of measuring cortical properties by temporal correlation with a periodic stimulus has wide applicability[9]. It can be used without modification to map the retinotopic structure of other visual areas in human cortex. In addition, it should be possible to adapt our technique to measure response selectivity for properties such as color and motion, and to measure nonvisual cortical maps. Finally, the ability to quickly map brain areas using a conventional MRI scanner should be useful clinically for diagnosis, surgical planning, and studies of recovery of function.

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