Retinotopic Organization of Human Visual Cortex: Departures from the Classical Model

Retinotopic mapping strategies similar to those used for invasive electrophysiological studies to identify multiple visual areas in monkeys have been adapted for noninvasive studies in humans, using magnetic recordings of brain activity in conjunction with anatomical magnetic resonance imaging. The retinotopic organization of the primary visual area (V1) in the left hemisphere of human subjects was examined by presenting small patterned stimuli near the vertical and horizontal meridians in the lower right visual field. In contrast with the classical model of V1 retinotopy, our results suggest that the representation of the horizontal meridian does not necessarily correspond in a one-to-one manner with the base of the calcarine fissure and that some lower field stimuli can activate regions in the lower bank of the fissure. The results also indicate significant individual variability in the details of how V1 maps around the calcarine fissure.

A major goal of noninvasive studies of human vision is to identify and characterize the functions and arrangement of the neural systems involved in visual perception. One criterion for identifying different visual areas in nonhuman primates is a demonstration of retinotopic organization in each area (i.e., a point-to-point projection of the visual field onto striate and extrastriate cortex). The boundaries of different visual areas within a single hemisphere may be outlined by focusing on the representations of the vertical and horizontal meridians in the visual field since these locations typically correspond to the edges of cortical visual areas (Cragg, 1969; Zeki, 1969, 1978; Van Essen et al., 1982; Van Essen, 1985). Callosal fibers, for example, terminate preferentially in regions representing the vertical midline of the visual field, and an examination of their distribution has led to the identification of different visual areas in nonhuman primates (Cragg, 1969; Zeki, 1969, 1978; Van Essen et al., 1982; Van Essen, 1985) and in human autopsy specimens (Clarke and Miklossy, 1990).

Current understanding of the retinotopic organization of primary visual cortex (V1) in humans is based on an examination of the location and extent of lesions in the visual system correlated with visual field defects (Holmes, 1945; Spalding, 1952; McAuley and Russell, 1979; Spector et al., 1981; Horton and Hoyt, 1991). The classical retinotopic model, based on the human lesion data, depicts the representation of the horizontal meridian at the base of the fissure; consequently, lower field stimuli are expected to activate regions in the upper bank of the calcarine fissure and vice versa. Furthermore, there is a systematic relationship between depths of sources in the calcarine fissure and the eccentricity of stimuli in the visual field (i.e., peripheral placements activate regions deeper within the fissure). The retinotopic organization of human V1 has been investigated using a number of noninvasive brain mapping techniques such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), event-related potentials (ERPs), and event-related magnetic fields (ERFs). PET studies demonstrated a systematic shift in response location from posterior to anterior regions in occipital cortex consistent with the classical model (Fox et al., 1987). However, the spatiotemporal resolution of the PET results was inadequate to distinguish activity of V1 from the closely adjacent V2 (Fox et al., 1987; Zeki et al., 1991; Watson et al., 1993). fMRI studies identified locations of changes in regional blood volume and blood oxygenation in primary visual cortex in response to visual stimulation (Beliveau et al., 1991; Kwong et al., 1992; Ogawa et al., 1992; Schneider et al., 1993), but specific maps of retinotopic organization based on fMRI have not been published to date. Both PET and fMRI are limited by the time course of the hemodynamic response; consequently, neither method has the temporal resolution to separate adjacent but temporally asynchronous regions such as V1 and V2. Electromagnetic measures (ERFs and ERPs) have also been used, along with source localization strategies such as nonlinear least squares single dipole fitting and/or minimum norm reconstructions, to address the issue of V1 retinotopy (e.g., Maclin et al., 1983; Ossenblok and Spekreijse, 1991; Ahlfors et al., 1992). However, as in many of the PET and fMRI studies, stimulus sizes were typically too large (e.g., hemifields, quadrants, octants, etc.) to permit derivation of detailed retinotopic maps, and in many studies multisource, spatiotemporal models were not employed to isolate activity of V1 from other regions.

We examined human V1 retinotopy using neuromagnetic measures combined with multisource, spatiotemporal modeling and information about the anatomy of the calcarine region derived from MRI. By focusing on stimulus placements near the vertical and horizontal meridians, we have identified several different visual areas during the initial 80-165 msec response latency.

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**Stimuli in Lower Right Visual Field**

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*Figure 1. Circular sinusoids (as shown at lower right) were presented one at a time, in a random fashion, to seven different locations in the lower right visual field.*
Materials and Methods
Experiments were conducted in a magnetically shielded chamber and magnetic fields were recorded with a BTI 7-sensor, SQUID-coupled gradiometer system while subjects viewed computer-generated visual displays projected on a rear-projection screen via a system of mirrors. During a given experiment, the sensor array was moved to several locations over the surface of the head (e.g., 10-15) and the experimental conditions were repeated for each position of the array. Sensor positions were digitized using an automated Probe Position Indicator (Polhemus Navigation Systems).

Five subjects viewed the stimuli while lying prone on a table. Small circular sinuosids were presented one at a time, in random order, to seven different positions near the horizontal (3°, 4°, 6.5°, and 9°) and vertical (4°, 6.5°, and 9°) meridians in the lower right visual field (Fig. 1). All seven stimuli were centered either 3° to the right of the vertical meridian or 3° below the horizontal meridian in an attempt to avoid simultaneous activation of the left/right hemispheres or upper/lower banks of calcarine cortex. The stimuli ranged in size from 0.4-1° in diameter, the number of cycles was kept constant (four cycles) but the size of the stimuli was scaled by the cortical magnification factor to ensure strong signals for peripheral stimuli (Daniel and Whitteridge, 1961; Rovamo and Virsu, 1979; Perry and Cowey, 1985). Stimulus duration was 266 msec with an average presentation rate of 1 Hz. Stimulus and background intensity parameters were chosen to produce equal average luminance in stimulus and background screens. Spatial contrast of the gratings was 75%. All subjects were informed about the nature of the studies and were asked to give written consent by signing a form approved by the institutional Human Subjects Committee.

Certain findings were replicated within a subset of subjects to help evaluate the reliability of V1 identification and the reliability of the key observations. A partial replication of the basic experimental design was conducted for one subject in a different laboratory using a different neuromagnetometer (BTI 37-channel system). In this study, the circular sinuosids were larger in size (1.7-4.1° in diameter) and were presented to five different locations (1.7°, 6°, and 12°) with the edges of the stimuli remaining 0.5° from the vertical and horizontal meridians. Two of the subjects participated in a third study where 2-D difference of gaussians (DOG) stimuli were presented at parafoveal (3°) and peripheral (12°) locations along the 45° and 135° diagonals in the upper and lower right visual field. DOG stimuli appear as a small diffuse bright spot with a dark circular surround. The diameters of the bright centers of the stimuli were 0.9° and 2° for the 3° and poststimulus (Aine et al., 1995). Our results support the general features of the classical model for V1, but there can be significant departures from the classical model near the representation of the horizontal meridian in the depths of the calcarine fissure. In some cases, lower field stimuli are shown to activate regions in the lower bank of the fissure, contrary to the prediction of the classical model.
12° eccentricities. In all cases, within-subject analyses were performed. Five subjects participated in the basic experimental design to examine the range of individual variability but data from two subjects, considered representative of the results in general, are highlighted in this article. These data exhibited good signal-to-noise ratios permitting reliable identification of V1 source locations for all seven stimulus conditions and extensive evaluations performed on one of the subjects have provided an indication of the reliability of the results.

Field amplitudes were measured from the prestimulus baseline at 5 msec intervals and isoamplitude maps were constructed at these intervals by interpolation across all sensor locations. Multidipole, spatiotemporal models, using a Nelder-Mead simplex search and spherical head model were fit to various intervals of time (e.g., 80-120 msec, 80-150 msec, 80-165 msec, etc.). These models restrict the location of the dipoles to be constant throughout the measurement interval, but allow the dipole moments and orientations to vary. The center of the sphere, used for the head model, was determined from the intersection between lines connecting three anatomical reference points (i.e., periauricula and nasion). A homogeneous spherical conductive medium has generally been found to be adequate for neuromagnetic measurements acquired at the posterior region of the head (where the head tends to be more spherical in shape) and for superficial sources (Hamalainen and Sarvas, 1987; Cuffin, 1990).

Model adequacy was assessed by examining the resulting reduced $\chi^2$ values ($\chi^2$: normalized by the number of degrees of freedom) at each latency as well as the overall ($\chi^2$: for spatiotemporal fits (Bevington, 1969; Supek and Pine, 1993). Percentage of variance is often used as a measure of goodness of fit by MEG and EEG researchers (e.g., brain electromagnetic source analysis, BESA). Our simulation studies, however, demonstrate that because percentage of variance measures neglect the contribution of noise, such measures cannot differentiate between a poor fit to the model due to noise and a poor fit due to using an incorrect model (Supek and Aine, 1993). Standard deviations of the noise in the data were estimated by calculating the average standard deviation (per stimulus condition) from the single trial data during the time interval of interest. Different model orders (i.e., number of dipoles) and multiple choices of starting parameters (i.e., location, orientation, and moment for each dipole) were applied to help assure a global minimum was achieved for each model. Errors in parameter estimation due to noise were assessed by Monte Carlo analyses (Press et al., 1986; Medvick et al., 1989). One hundred noisy field distributions were generated from the best-fitting model determined from the empirical data (assuming a normal distribution of noise with a standard deviation estimated from the poststimulus interval) and were fit with starting parameters corresponding to the underlying theoretical model. This analysis aids in resolving discrete brain regions active across an interval of time, to determine the number and locations of separable clusters. Sources labeled as V1 satisfied the following criteria: (1) they were identified in early time intervals (e.g., 80-100 msec and 80-120 msec), and (2) they were localized to the vicinity of the calcarine fissure on the MRIs.

3-D volumetric magnetic resonance images were acquired on a 1.5 T Siemens imager at the New Mexico Regional Federal Medical Center in Albuquerque. An imaging software program, MRTVIEW, developed by Ranken and George (1993), was utilized for integrating functional and anatomical information. The MRI coordinate system was reconciled with the head-centered coordinate system employed for neuromagnetic measurements by identifying the anatomical reference features used to define the MEG coordinate system on the 3-D surface renderings of the head based on MRIs.

**Results**

During the initial 80-165 msec interval of data (poststimulus), three to five sources were identified for each subject. Figure 2 displays sample empirical and theoretical field distributions for one subject when the stimulus was presented to the most foveal position in the lower right visual field. The theoretical fields were obtained from the best-fitting spatiotemporal model of the interval 80-165 msec (poststimulus). Five sources with fixed locations, unconstrained orientations, and differing time courses were demonstrated to be necessary and adequate to account for the data, according to the reduced $\chi^2$ criterion. Sample neuromagnetic waveforms are shown at the upper right.

Figure 3 shows volume histograms of source location estimates from 100 Monte Carlo trials (displayed as blue contour plots) on reconstructed 3-D images of this subject's brain (subject CA). Four of the five regions active in response to the stimulus are evident in the 3-D image in the top panel. The V1 source is shown in the midsagittal view in the bottom panel. The five active regions localized in this study for this subject include sources corresponding to V1, V2, and other areas in occipital-temporal, occipital-parietal and ipsilateral oc-
Figure 4. The calcarine fissure (white) can be seen projecting into the depths of the left occipital lobe (~1.5 cm) from this midsagittal view. This 3-D image of the calcarine was obtained by outlining the fissure (in white) in a series of contiguous MRI slices. The V1 source locations, evoked by the seven stimuli and modeled from 80 to 120 msec, are displayed relative to the fissure. Dot sizes shown around the fissure are arbitrary; they do not reflect measurement error as in the Monte Carlo data shown in Figure 3. The stimulus locations in the lower right visual field are shown in the inset (upper left corner). The left outermost region of the 3-D image (i.e., the detached section) represents the scalp at the posterior region of the head. A portion of the cerebellum is also displayed at the bottom.

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In the occipital cortex. These regions are also consistent with our results from other studies (e.g., Aine et al., 1995).

Once multidipole models were derived for each stimulus condition, V1 retinotopy was examined by comparing anatomical locations for the best-fitting V1 sources across stimulus locations. Figure 4 displays V1 sources evoked by the seven stimuli. Note the systematic relationship between the stimulus placements in the visual field (upper left inset) and the source locations around the fissure. Two separate paths of V1 sources, representing placements near the vertical and horizontal meridians, can be seen in this figure (see connected dots). As predicted from the classical model, V1 sources for stimuli positioned in parallel with the vertical meridian were more anterior for the peripheral stimulus placements (e.g., the source evoked by the stimulus depicted in red was posterior to the sources evoked by the stimuli depicted in blue and green). However, source locations for stimuli positioned in parallel with the horizontal meridian (i.e., red-orange-yellow-green) were not located along the lateral extent or “base” of the calcarine fissure, as predicted by the classical model. These sources were more medial than the classical model predicts and a systematic shift in source location in an anterior direction, as a function of eccentricity, was not evident in this subject's data. These data suggest that for this subject, the representation of the horizontal meridian is cantled downward relative to the fissure in a posterior-anterior direction.

To assess the effect of measurement error for each of the stimulus conditions, Monte Carlo simulations were performed. One hundred noisy estimates were generated (80-120 msec) and were fit with the best-fitting two- or three-dipole model. The average standard deviations (SDs) calculated from the data during the 80-120 msec poststimulus interval ranged from 20.9 to 27.1 mm. The SDs for the x-values (positive z points through the top of the head) ranged from 0.17 to 0.32 cm for stimuli positioned near the horizontal meridian. In contrast, the x-values (reflecting depth from the occipital pole) for these same stimuli ranged from 0.21 to 0.69 cm. SDs for the y-values (ear-to-ear axis) ranged from 0.10 to 0.49 cm for stimuli located near the horizontal meridian. Based on this information, it is unlikely that the source localized to the lower bank of the fissure, evoked by the peripheral stimulus near the horizontal meridian, can be attributed to error alone (SD for z = 0.32 cm). When the mean source location for the 9.0°
Figure 5. Mean V1 source locations derived from the Monte Carlo analyses are shown on MRIs for two stimulus conditions (3.0° and 9.0° in parallel with the horizontal meridian). The cross hairs represent V1 source locations. In this figure the left hemisphere is shown on the right side, according to radiological convention (i.e., MRI sections are viewed from in front of or underneath the head). The white arrows represent the posterior portion of the calcarine fissure.

Figure 6. V1 source locations for 2-D, difference of gaussians (DOGs) presented along the 45° and 135° diagonals in the upper and lower right visual field. The dot array (upper left corner) shows the relative locations of the four stimuli. The projection of the calcarine fissure in this figure differs slightly from Figure 4; it has been rotated away from the viewer to provide a better view of the four V1 source locations.
stimulus near the horizontal meridian, derived from the Monte Carlos \((x = -6.16, y = 0.66, z = 4.52)\), was located on the appropriate MRI slice, the source was still localized to the lower bank of the fissure. An error of 0.32 cm in the z-axis would not have placed it above the fissure. Mean V1 source locations for two stimulus locations (3.0° and 9.0° horizontal) are shown in Figure 5.

The reliability of these results were assessed by examining data from a partial replication of the study (i.e., five circular sinusoids were presented near the meridians and data were acquired using a BTi 37-channel system). Results from both studies showed the same general pattern for this individual (CA): (1) stimulus placements near the vertical meridian (e.g., red-blue) activated regions that were superior and lateral to stimulus placements near the horizontal meridian (e.g., red-green), and (2) stimuli near the horizontal meridian (red-green) activated medial regions that crossed into the lower bank of the calcarine fissure for more peripheral stimulus placements.

This pattern of results was supported by a third study for this subject (CA) where DOG stimuli were presented at parafoveal and peripheral locations in both the upper and lower right visual field (unpublished results; see Fig. 6). In this study, upper field stimuli activated V1 regions below the fissure (yellow and orange dots) and lower field stimuli activated V1 regions above the fissure (red and pink dots), as predicted by the classical model. Furthermore, V1 sources for the parafoveal stimulus locations (yellow and red dots) were posterior to V1 sources for peripheral stimulus locations (orange and pink dots), consistent with the classical model. 

Figure 7 shows the predicted source locations for the present study based on the classical model along with results from...
subject CA for comparison. The classical model suggests that all lower field stimuli will activate regions above the fissure (see patterned circles in B). The empirical results displayed on the schematic map of flattened V1 cortex (C) show the same general pattern as the predicted results (compare solid squares with circles, respectively). It is primarily the tilt of this pattern relative to the fissure that differs, suggesting that the representation of the horizontal meridian is tilted downward.

Comparable results to those shown in Figure 4 are shown for a second subject (KC) in Figure 8. VI source locations are displayed as cross hairs on appropriate MRI sections for this subject. This figure indicates that stimulus placements near the vertical meridian, produced V1 activity above the calcarine fissure. However, stimulus placements near the horizontal meridian resulted in V1 activity beneath the calcarine fissure (see cross hairs on the MRIs for horizontal stimulus placements at 6.5° and 9.0°). Also note that although the source coordinates appear similar for the 3.0° and 9.0° placements near the vertical meridian, the MRI slice for the 9.0° vertical placement indicates that the V1 source appears to follow along the upper bank of the calcarine fissure, which can be seen deviating upward in this slice (see differences in the cross hairs and z-values). The coordinates become more meaningful when they are related to anatomical structures. The results for subject KC suggest that the representation of the horizontal meridian does not follow the lateral extent of the calcarine fissure but instead is located primarily on the lower bank of the fissure. However, the cant of V1 relative to the fissure for this subject was not as marked as in the previous case.

Discussion

These results confirm the major features of the classical model: lower field stimuli generally activated regions in the upper bank of the calcarine fissure and V1 sources were more anterior for eccentric placements along the vertical meridian. However, there is an important discrepancy between our results and the classical model for that portion of the V1 retinotopic map corresponding to the horizontal meridian. These data suggest that lower field stimuli may activate regions in the lower bank of the fissure when peripheral stimuli are located near the horizontal meridian. The representation of the horizontal meridian for the second subject was not as canted relative to the calcarine, but rather, most of it mapped onto the lower bank of the calcarine. These data imply that the representation of the horizontal meridian does not lie precisely at the base (i.e., lateral extent) of the fissure, but rather, deviates downward from a posterior-anterior direction or lies primarily in the lower bank for these individuals.

This interpretation is also supported by analyses that take the orientation of the equivalent current dipoles into account. Substantial shifts in orientation of V1 sources evoked by lower field stimuli suggest that the sources were arrayed across the upper and lower banks of the calcarine fissure.

The evidence for variability in the shape and location of calcarine fissures and in the way V1 maps onto the fissure as reported here is consistent with human anatomical studies. Stensaas et al. (1974), for example, showed that in 52 human hemispheres only 55% of V1 or striate cortex was found in the calcarine fissure. Poljak (1957) reports that the anterior boundary of striate (V1) is ordinarily found only in the lower lip of the fissure. In some cases, striate cortex may be completely displaced onto the upper bank of the calcarine fissure or it may be located entirely on the lower bank of the fissure. These are extreme cases, but cases where striate lines both lower and upper banks of the fissure symmetrically (as suggested by the classical model) are also rare occurrences (Poljak, 1957). J. C. Horton, who has dissected V1 in 15 normal human autopsy specimens, suggests that in the majority of his cases, the representation of horizontal meridian tends to run along the lower bank of the calcarine fissure, rather than precisely at the base of the fissure (personal communication). While this result is inferred (by examining the representation of the upper and lower vertical meridians that form the outer- most boundary of V1), Dobelle and Mladjeovsky (1974) found extreme variability in the topographical distribution of V1, based on the position of phosphenes in the visual field due to direct electrical stimulation of human visual cortex.

These results indicate that a direct and comprehensive examination of retinotopic organization in human visual cortex can be obtained from neuromagnetic measures coupled with appropriate modeling procedures and anatomical MRI. These data represent the most detailed demonstration of human V1 retinotopy to date, obtained in vivo from noninvasive measurement techniques.

Notes

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References


