COVER ILLUSTRATION
Checkerboard wedges illustrate proposed bifield stimulation retinotopic mapping technique. This method can be used to obtain retinotopic maps of equal quality to conventional means in approximately half the acquisition time. Roman numerals illustrate number of bifield stimulation cycles used to generate each inset retinotopic map. These maps were used to estimate map quality as a function of acquisition time. See Slotnick and Yantis, p. 22.
Efficient Acquisition of Human Retinotopic Maps

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Abstract: A bifield stimulation method for rapidly obtaining retinotopic maps in human occipital cortex using functional MRI was compared to conventional unifield stimulation. While maintaining central fixation, each participant viewed the conventional display, consisting of a single rotating checkerboard wedge and, in a separate run, the bifield display, consisting of two symmetrically placed rotating checkerboard wedges (a ‘propeller’ configuration). Both stimulus configurations used wedges with 30 degree polar angle width, 6.8 degrees visual angle extension from fixation, and 8.3 Hz contrast polarity reversal rate. Retinotopic maps in each condition were projected onto a distortion corrected computationally flattened cortical surface representation obtained from a high-resolution structural MRI. An automated procedure to localize borders between early visual areas revealed, as expected, that map precision increased with duration of data acquisition for both conditions. Bifield stimulation required 40% less time to yield maps with similar precision to those obtained using conventional unifield stimulation.


Key words: fMRI; retinotopy; mapping; vision; visual areas; striate cortex; extrastriate cortex

INTRODUCTION

Nearly a century ago, Inouye [1909] constructed a retinotopic map of human striate cortex by correlating visual field deficits with occipital lesions incurred in the 1904–1905 Russo–Japanese War [Glickstein and Fahle, 2000; see also Holmes and Lister, 1916; Holmes, 1917, 1945; Horton and Hoyt, 1991a, b]. Since then, the retinotopic organization of the primate visual system has been intensely investigated using a combination of invasive techniques (e.g., single-cell recording and cytoarchitectonics). However, such methods cannot be used to map human cortex if one is interested in studying the normal operation of the intact human brain.

With the advent of functional magnetic resonance imaging (fMRI), noninvasive retinotopic maps of human striate and extrastriate cortex can now be obtained [DeYoe et al., 1996; Engel et al., 1994, 1997; Sereno et al., 1995; Tootell et al., 1997]. Numerous studies have used retinotopic maps of early visual areas to study the locus of modulatory effects of perceptual and cognitive manipulations [e.g., Hadjikhani et al., 1998; Hadjikhani and Tootell, 2000; Lerner et al., 2001; Linden et al., 1999; Martinez et al., 2001; Mendola et al., 1999; Sasaki et al., 2001; Smith et al., 1999; Tootell and Hadjikhani, 2001; Tootell et al., 1998a, b; Wandell, 1999; Wandell et al., 1999]. Abnormal retinotopy due to stroke or congenital dysgenesis has been used to study cortical plasticity [Baseler et al., 1999, 2002; Goebel et al., 2001; Morland et al., 2001; Slotnick et al., 2002].
In most cases, retinotopic maps are acquired in the service of another scientific goal (e.g., “Does attention modulate cortical activity as early as area V1?”). Therefore, techniques to reduce their acquisition time are advantageous in that they allow additional time to acquire data for the primary question under investigation. Although there has been some use of multiple stimuli in retinotopic mapping [Engel et al., 1997; Tootell et al., 1995; Van Oostende et al., 1997], there has been no formal comparison with single stimulus mapping (i.e., conventional mapping). We describe a novel procedure for evaluating the precision of a given retinotopic map that was used to directly compare a multiple-stimulus method with the conventional method.

MATERIALS AND METHODS

The most widely used method for estimating the location of borders between adjacent retinotopically organized areas in early visual cortex involves the presentation of a single wedge-shaped checkerboard pattern that reverses contrast polarity at 8 Hz and rotates about fixation at a rate of approximately 1 cycle per minute (we shall refer to this as unifield stimulation). Such stimulation produces ‘waves’ of activity in each of the early visual areas (ventrally V1, V2, VP, V4v, and dorsally V1, V2, V3, V3A, and sometimes beyond), with a reversal in the phase of the moving wave demarcating the border between adjacent areas. Either cross-correlation or Fourier analysis can be used to estimate border locations; we used the former. The proposed procedure involves simultaneous stimulation of diametrically opposing retinal loci with two checkerboard wedges in a ‘propeller’ configuration (referred to as bifield stimulation), which reduces acquisition time by nearly half when compared to unifield stimulation.

Materials

A custom program was used to present the stimuli, acquire responses, and time-lock the visual stimulus sequence to the fMRI data acquisition. The stimulus was back-projected onto a screen positioned at the superior end of scanner bore. Participants were supine and viewed the stimulus through a 45-degree angled mirror attached to the head coil such that effective viewing distance was 78 cm. Button press responses were transmitted through a fiber-optic cable.

Images were acquired using a 1.5-T Philips Gyroscan ACS-NT scanner at the F.M. Kirby Research Center for Functional Brain Imaging. A receive-only Philips end-capped quadrature birdcage head coil was used to acquire anatomic images; a circular Philips C3 surface coil centered on the inion was used to acquire functional images.

Data analysis was conducted using BrainVoyager (Brain Innovation, Maastricht, The Netherlands). A custom program written in MATLAB (MathWorks, Natick, MA) was used to localize visual area borders.

Research protocol

Visual stimulation

Figure 1a illustrates unifield stimulation [see DeYoe et al., 1996, Engel et al., 1997; Sereno et al., 1995;
To encourage vigilance and attention to the stimulus, participants were instructed to press a button with their dominant hand whenever a single randomly selected square in the stimulus flashed red for 120 msec; these target events occurred on average every 15 sec, with random temporal jitter.

**Behavioral task**

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**fmRI data acquisition and preprocessing**

After the two participants fully understood the experimental procedures and potential risks, informed consent was obtained. For each participant, a T1-weighted scout image was acquired (8-sec acquisition time) and subsequently used as a reference for positioning anatomic and functional images. A T1-weighted MPRAGE (multiplanar rapidly acquired gradient echo) sequence was used for high-resolution whole brain anatomic imaging (12-min 24-sec acquisition time) with 3.7 msec TE, 8-degree flip angle, 8.1 msec TR, single excitation, coronal 256 × 256 matrix, 256 × 256 mm FOV, and 256 × 1-mm slices with no gap (yielding 1-mm isotropic voxels). A T2*-weighted echo planar imaging (EPI) sequence was used to acquire functional images with 40 msec TE, 90-degree flip angle, anterior-to-posterior phase encoding, 3,000 msec TR, oblique 64 × 64 matrix, 192 × 192 mm FOV, and at least 22 × 3 mm slices with no gap (yielding 3-mm isotropic voxels). To ensure adequate sampling of functional activity associated with early visual areas, the first slice was positioned to include the occipital pole and all slices were oriented perpendicular to the calcarine sulcus.

Functional data were slice-time corrected, motion corrected, and spatially lowpass filtered below 16 cycles/image matrix. A 3 cycles/run length temporal highpass filter was applied to the time series and the temporal lowpass filter was set to allow for a biphasic hemodynamic response. For example, in an 8-cycle run, a 32 cycles/run length temporal lowpass filter was used (i.e., twice the Nyquist frequency).

**Retinotopic mapping**

For each hemifield, the 42 sec of stimulation was artificially segmented to begin at 14 distinct phases. For each phase, a hemodynamic response model with δ = 2.5 and τ = 1.25 [see Boynton et al., 1996] was cross-correlated with the time series of every voxel. Voxels yielding a correlation above 0.20 were “painted” the color associated with the stimulus phase that resulted in maximal correlation (P < 0.01, uncorrected for multiple comparisons; see Fig. 2a). Borders of early visual areas were assumed to coincide with phase color reversals [Sereno et al., 1994].

To aid in visualization, retinotopic maps were projected onto computationally flattened representations of the cortical surface [see Dale and Sereno, 1993; Dale et al., 1999; Drury et al., 1996; Fischl et al., 1999; Hadjikhani et al., 1998; Sereno et al., 1995; Tootell et al., 1997; Van Essen and Drury, 1997]. High-resolution anatomic volumes were transformed into Talairach space [Talairach and Tournoux, 1988], segmented, surface reconstructed, inflated, flattened, and linear distortion corrected to less than 15% [for details, see...
For each participant, unifield and bifield stimulation maps were then projected onto the flattened surface of the left hemisphere.

**Precision metrics**

A semi-automated procedure was developed to estimate the borders between adjacent visual areas. First, a rectangular region was defined by eye that surrounded the approximate location of each border (see Fig. 2a). Phase color can equivalently be represented as phase amplitude in units of degrees (range $-90$ degrees to $+90$ degrees; corresponding to the lower and upper vertical meridian, respectively). Similar to phase color-reversal border identification, phase amplitude valleys and peaks also represent early visual area borders.

Within the defined rectangular region, the maximum phase amplitude value in the $x$-direction was selected at each 3-mm increment in the $y$-direction (where 3 mm is the distance between the center of adjacent voxels). These selected values were further refined by only including those above half the maximum value. A similar procedure was used to obtain minimum values.

To model each border, a line was fit to the selected values using the Marquardt nonlinear least-squares algorithm [see Press et al., 1992] assuming independence in the $x$-direction, such that the intercept was the point at which the line intersected the $x$-axis (Fig. 2b, bottom edge). Admittedly, a linear model of visual area borders is an oversimplification; still, the model appears to be reasonable (see Fig. 3a,d) and, more importantly, model parameters can be objectively compared. Parameter values (i.e., intercepts and slopes) for all six borders per hemisphere specified a particular retinotopic map and parameters produced using unifield and bifield stimulation were directly compared.

**RESULTS**

We first compared the retinotopic maps produced using the two procedures. Note that 8 cycles of unifield stimulation required $\approx 10$ min while the same 8 cycles of bifield stimulation required $\approx 6$ min. Figure 3 shows, with 8 cycles of stimulation, that border locations resulting from unifield and bifield stimulation were similar.

Although unifield and bifield stimulation produced maps of similar precision using 8 cycles, there was a substantial difference in acquisition duration for these two procedures. To compare map precision for several different acquisition durations, each participant’s original 8 cycle datasets were truncated at the beginning and/or end to produce datasets consisting of 7, 6, 5, 4, 3, 2, and 1 cycle(s). The selection of the first cycle in a series was random with the constraint that all cycles were contiguous in time (e.g., the 6 cycle series could only begin at cycle 1, 2, or 3). For each participant, the same starting cycle for each series was used for both unifield and bifield stimulation methods to eliminate possible order effects. All 8 cycle intercepts and slopes (see Fig. 3) were assumed to estimate the “true” border locations (i.e., intercepts and slopes from V1/V2 ventral border, V2/VP border, VP/V4v border, V1/V2 dorsal border, V2/V3 border, and V3/V3A border). For each cycle length, the absolute difference between the six estimated intercepts, again using all six borders, and those of the 8-cycle standard was measured. The mean of these intercept differences provided a global measure of deviation from the 8-cycle standard. A similar computation was used to estimate slope deviation.

Figure 4 illustrates the results of this analysis. The mean absolute difference between the estimated border location and the standard location is plotted as a function of acquisition time. There are eight points per func-
Run durations for corresponding cycle numbers increase disproportionately. By definition, border deviation was zero in the 8-cycle run of each condition.

Figure 3.
Left hemisphere retinotopic maps of two participants using unifield or bifield stimulation; borders for each map obtained independently. a: Participant 1, unifield stimulation with borders shown in black. b: Participant 1, bifield stimulation with borders shown in black. For comparative purposes, borders from unifield stimulation are also shown in white. c: Participant 1, intercepts of unifield borders on x-axis are plotted against intercepts of bifield borders on y-axis. Also shown to upper left, slopes of unifield borders on x-axis are plotted against slopes of bifield borders on y-axis. For intercept plot and slope plot, respectively, x-axis and y-axis scaling equivalent. Circles, V1/V2 ventral borders; triangles, V2/VP borders; squares, VP/V4v border; diamonds, V1/V2 dorsal borders; stars, V2/V3 borders; six-point stars, V3/V3A borders. For all points, one standard error reported. Proximity to the diagonal illustrates similarity in unifield and bifield border location. d–f: Same plots for participant 2.
The first result illustrated in Figure 4 is that the deviation scores decrease as run-duration increases for both unifield and bifield stimulation. This is due to decreased dependence on noise with increasing number of stimulation cycles. Second, when results were dominated by signal (i.e., at acquisition times greater than 4 min), bifield stimulation always yielded smaller deviations than did unifield stimulation for the same data acquisition duration.

**DISCUSSION**

The results show that retinotopic maps obtained using the bifield stimulation approach can be acquired...
in approximately 40% less time than conventional mapping procedures while maintaining similar precision. Considered from the perspective of a single hemifield, the stimulus used in both methods is identical; thus, the results are not surprising. Overall, the similarity of quality to conventional retinotopic mapping methods and reduction in acquisition time indicates that the proposed method of bifield stimulation is more efficient than conventional unifield stimulation. It is important to note that the efficiency advantage reported here applies only to polar angle mapping; it does not apply to eccentricity mapping (which produces maps in the orthogonal direction).

As pointed out previously (see Visual Stimulation), the bifield stimulation method rests on the assumption that visual stimulation activates contralateral early visual areas only. For example, if visual stimulation activated both contralateral and ipsilateral early visual areas, phase uncertainty and map distortion would occur. However, the fact that retinotopic maps produced with bifield stimulation were similar to those produced with unifield stimulation, which does not rely on the contralateral activation assumption, suggests that there was no appreciable ipsilateral activation during bifield stimulation. One related caveat to consider when comparing bifield and unifield results is that the border similarity between these methods is likely restricted to the visual area boundaries discussed (i.e., the V1/V2 ventral border, V2/VP border, VP/V4v border, V1/V2 dorsal border, V2/V3 border, and V3/V3A border); Tootell et al. [1998c] have reported robust ipsilateral activation anterior to the VP/V4v border and V3/V3A border, which would be expected to distort more anterior border locations when using bifield stimulation (e.g., the V3A/V7 border). Thus, if the regions of interest include higher-tier visual areas (e.g., V7, V8, MT, and the lateral occipital region), we suggest using unifield stimulation, rather than bifield stimulation, to avoid map distortion caused by ipsilateral activation.

Given that bifield stimulation has proven to be more efficient than unifield stimulation, the next obvious step is simultaneous stimulation in each quadrant, octant, and so on. As appealing as ad infinitum increases in efficiency may appear, a physiological upper limit necessarily exists due to hemodynamic recovery time using fMRI (which is on the order of 20 sec). Additionally, multiple stimuli in each hemifield would necessarily result in phase uncertainty.

Finally, we note that across participants and methods, at least 6 cycles of stimulation were required to produce maps of similar quality to the full 8-cycle sequence (see Fig. 4). Six cycles of stimulation may, therefore, represent a lower bound for obtaining high-quality retinotopic maps, at least using the methods described. Thus, using a single run consisting of 6 cycles of bifield stimulation, a high-quality retinotopic map can be acquired in just over 4 min.

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