Retinotopic Mapping of the Visual Cortex Using Functional Magnetic Resonance Imaging in a Patient with Central Scotomas from Atrophic Macular Degeneration

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Purpose: To describe retinotopic mapping of the visual cortex when a central scotoma is present.
Design: Single observational case report.
Methods: Scanning laser ophthalmoscope perimetry was used to define the site and stability of fixation and the area of dense scotoma. Functional magnetic resonance imaging of the visual cortex was performed while the patient viewed an expanding annular stimulus.
Results: Retinotopic mapping of the visual cortex for a patient with a horseshoe scotoma from geographic atrophy involving the macular region showed a loss of stimulation to the cortical areas representing the site of the atrophic lesion.
Conclusions: Cortical retinotopic mapping can be performed successfully in patients with central scotomas from macular disease. This study can serve as a basis for the future investigation of cortical plasticity in visual cortex. *Ophthalmology 2004;111:1595–1598 © 2004 by the American Academy of Ophthalmology.*

Age-related macular degeneration (AMD) is the leading cause of severe vision loss among people over the age of 60 in the United States. Even with the limited treatments that are available, most of the 10.5% of the population 75 and over with advanced AMD[1,2] will have final visual acuity (VA) of 20/200 or worse, with a central scotoma in one or both eyes. Low vision intervention for these patients depends upon the optimal use of the remaining seeing retina and, in particular, upon the development of a stable eccentric preferred retinal locus.[3] There is significant variability among patients in terms of their ability to use an eccentric retina. Patients may actually have an improvement in vision in the worse eye with a central scotoma when the VA in the better eye decreases.[4] Scanning laser ophthalmoscope macular perimetry suggests that the improvement in vision is related to being able to move the object of interest out of the scotoma and onto the seeing retina. The processes responsible for this adaptation are not well understood.

An important open question concerns how the loss of neural input from the damaged retina to the cortex affects cortical function and, in particular, whether and how cortical remapping occurs. If remapping does occur, then regions of cortex that normally are innervated by the damaged retina are recruited to respond to stimuli falling on undamaged retinal areas. Such remapping, if present, may be important in determining how patients adopt a preferred eccentric retinal locus and are able to compensate for the scotoma. Cortical remapping has been observed in the somatosensory system after digit or limb amputation.[5–7] This remapping of cortical function is thought to reflect the unmasking of latent lateral connections in the cortex that are nonfunctional as long as normal afferent signals are present. Research in animal models of central scotomas caused by laser injury to the retina and artificial scotomas induced by visual stimulation has yielded evidence of cortical remapping.[8,9] It remains to be shown whether AMD would lead to similar remapping in the human visual cortex.

With the advent of the specialized techniques of scanning laser ophthalmoscope macular perimetry, we are now able to map carefully the scotoma size and location on the retina, and the location and stability of an eccentric preferred retinal locus.[10–12] Functional magnetic resonance imaging (fMRI) can be used to perform retinotopic mapping–that is, to determine which areas in the visual cortex are stimulated by specific retinal sites. Together, these 2

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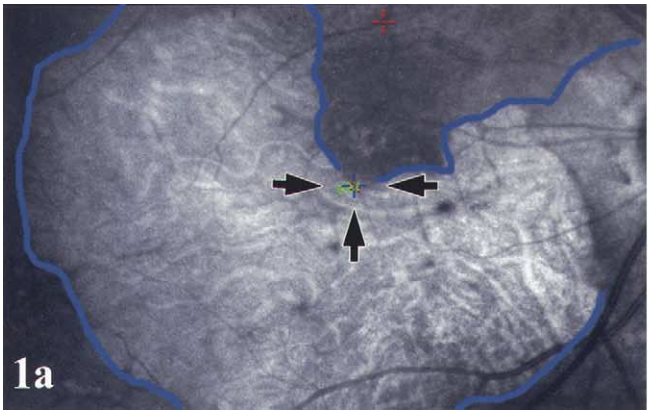
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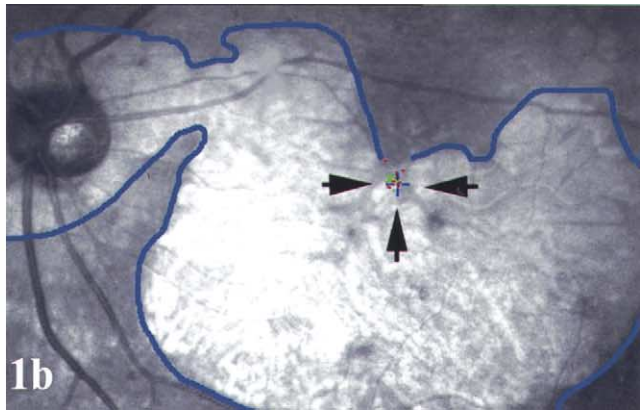
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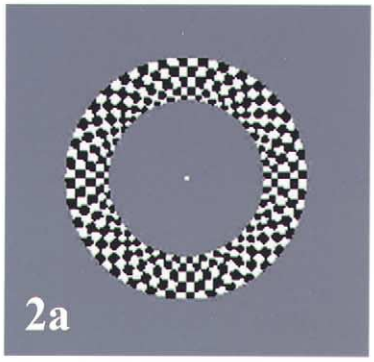
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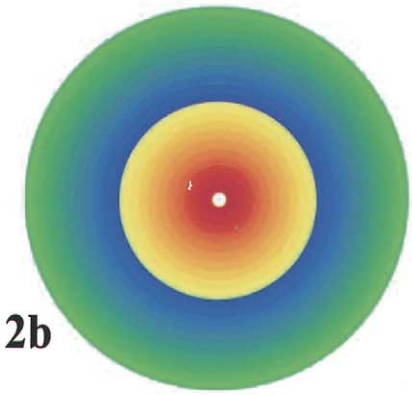
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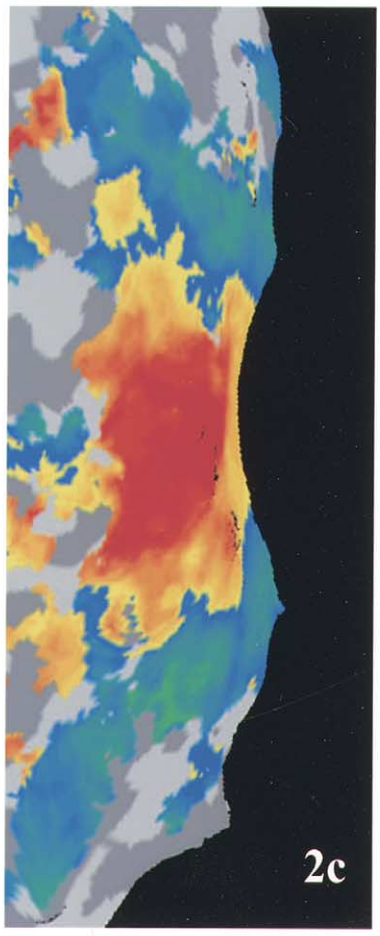
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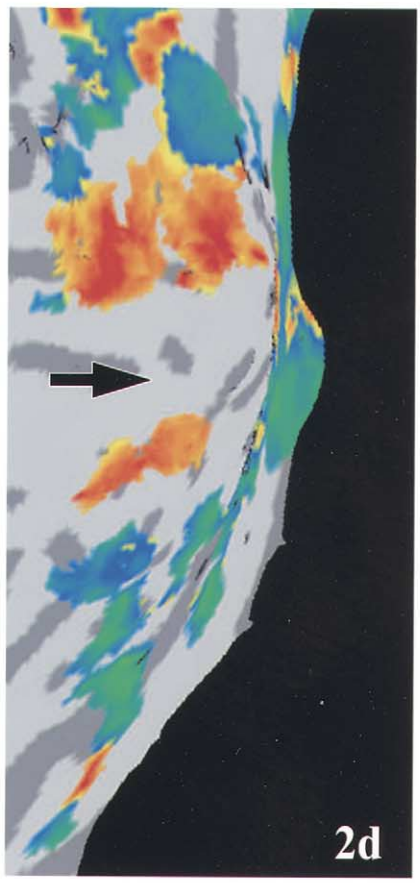
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Figure 1. a, b, Scanning laser ophthalmoscope fundus image and fixation map of right (a) and left (b) eyes. The cross just above the atrophy shows the fixation site (arrows). The area of geographic atrophy had an associated dense scotoma, with borders indicated by the thick blue line. Fixation is just at the foveal margin of the atrophy. The small dots show the variation in fixation position during the testing. The close clustering of points indicates stable fixation.

Figure 2. Retinotopic mapping using fMRI. **a**, Expanding annular stimulus. **b**, Pseudocolor representation of the timing of stimulation of the visual field used to visualize the cortical eccentricity map. **c**, Results of a single retinotopic mapping run in a healthy adult control subject, showing the large representation of the most central region (orange) and the smaller representations of the more peripheral areas (blue). **d**, Retinotopic map for patient with geographic atrophy (see Fig 1), showing intact dorsal cortical activity (orange) and the silent ventral cortex (arrow).

methods can provide insights about the presence and extent of cortical remapping after the onset of AMD.

To assess the feasibility of performing retinotopic mapping in patients with central scotomas, and to develop a metric that can be used to assess the presence and degree of remapping, patients with geographic atrophy serve as an excellent model system, because their scotomas are well demarcated and grow slowly over time. In addition, there is no associated fluid or scarring that affects the surrounding retina. This report is, to our knowledge, the first published case of retinotopic mapping of the visual cortex in a patient with central scotoma from macular disease. The patient had geographic atrophy in a large horseshoe pattern surrounding the fovea in both eyes. The patient was able to maintain stable foveal vision for extended periods of time; this is a crucial precondition for retinotopic mapping, which requires that visual stimulation be presented to specific retinal locations over time.

Case Report

Cortical responses of a 60-year-old woman with bilateral geographic atrophy were evaluated. The study was approved by the Institutional Review Board at the Johns Hopkins Medical Institutions, and written informed consent was obtained.

The patient reported decreased vision for the past 3 years. When seen by her ophthalmologist 2.5 years before fMRI imaging, VA was 20/64 (right eye) and 20/40 (left eye). Visual acuity 1.5 years before imaging was recorded at 20/100 (right eye) and 20/70 (left eye). She was noted to have atrophy partly surrounding the center of the macula, but photographs from that time are not available.

At the time of fMRI imaging, the patient's best-corrected VA was 20/50−2 in the right eye and 20/50−2+2 in the better-seeing left eye. Scanning laser ophthalmoscope imaging and perimetry were performed to define the site and stability of fixation and the areas of dense scotoma. Figure 1 shows the presence of a large area of fairly symmetric geographic atrophy in each eye. The fixation cross is placed just at the superior edge of the atrophy nearest the fovea. Fixation stability was excellent during testing (indicated by the small spots near the fixation cross). There was a dense scotoma corresponding to the area of geographic atrophy (area outlined).

The patient and a healthy control subject underwent fMRI retinotopic eccentricity mapping using the scanning protocol described by Slotnick and Yantis.[13] To map the retinotopic organization of the visual cortex, we presented an expanding annulus (Fig 2a) containing black and white checks that reversed contrast at 8 Hz.[14] A small annulus (inner radius, 0.3° visual angle; outer radius, 1.3°) appeared in the fovea and expanded smoothly and continuously outward at a rate of 1 cycle per minute. The most peripheral sizes of the annulus were 8.3° (inner radius) and 9.3° (outer radius) horizontally. (Because the back projection screen extended to only ±7° vertically, the top and bottom of the annulus disappeared from the screen at its largest extent. However, this provided a larger mapping field in the horizontal direction than would have been possible with an annulus that only extended to 7° eccentricity.) A single run of the scan was 8 minutes in duration. The patient was instructed to maintain fixation on a crosshair that remained in the center of the display throughout the run. The patient viewed the stimulus monocularly, with one eye covered by an eye patch. Two runs were carried out for each eye.

The high-resolution anatomical volume was segmented at the gray–white boundary and then computationally inflated, cut, and flattened to allow visualization of the calcarine sulcus and adjacent regions.[15,16] The fMRI time series resulting from the annulus was used to create a retinotopic eccentricity map.[14,17,18] Figure 2b shows a pseudocolor representation of the timing of stimulation of the visual field. Figure 2c shows the results of a single retinotopic mapping run in the left hemisphere of a healthy adult control subject; the right edge of this image is the cut fundus of the calcarine sulcus. The image reveals a large representation of the most central regions of the visual field (orange and yellow) and smaller representations of the more peripheral areas (blue and green). This geometric distortion is due to cortical magnification.[19,20]

Figure 2d shows the eccentricity map for the AMD patient, obtained in one scan while she viewed the stimulus with her left eye, shown at the same statistical threshold as was used to create Figure 2c. There is a loss of activity in the ventral visual cortex, which corresponds to the inferior retina containing the scotoma, whereas the representation in the dorsal cortex, corresponding to the undamaged superior retina, is intact. (The right eye, which was tested first in the fMRI, gave unreliable results, perhaps because the task was not understood initially.)

Discussion

The data from this patient show that we are able to perform retinotopic mapping in patients with scotomas in the central visual field. Patients with geographic atrophy provide a good model system for assessing cortical remapping that may accompany retinal scotomas using fMRI. In this patient, fixation was at or very near the fovea and was very stable. Testing of similar patients will allow us to estimate the size and shape of the cortical area rendered silent by a central retinal scotoma. Likewise, performing fMRI mapping longitudinally during the course of macular disease may provide new information about the time course of cortical remapping. For patients with central scotomas including the fovea, techniques to stabilize fixation, including training in the scanning laser ophthalmoscope and eye tracking in the magnetic resonance scanner, will be employed. This may allow us to determine whether remapping

occurs in the adult human visual cortex, its spatial extent, and its impact on visual function.

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