Retinotopic mapping reveals extrastriate cortical basis of homonymous quadrantanopia

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It has been conventionally assumed that cortically based quadrantic visual field deficits (homonymous quadrantanopias) are caused by lesions in striate cortex (V1), extending precisely to the horizontal meridian representation. A more recent model, supported by anatomic MRI evidence, consists of an exclusively extrastriate cortical basis (e.g. V2, V3, VP, V4v). Employing fMRI, we sought to distinguish between these models through retinotopic mapping of a patient with an upper right homonymous quadrantanopia. As expected, maps of the lower right quadrant and left hemifield were normal. The map corresponding to the impaired upper right quadrant was normal in V1 and V2, with little or no activity in VP and V4v. These results provide functional evidence that extrastriate cortical lesions can elicit homonymous quadrantanopias. *NeuroReport* 14:1209–1213 © 2003 Lippincott Williams & Wilkins.

Key words: Extrastriate cortex; fMRI; Human; Patient; Quadrantanopia; Quadrantanopsia; Retinotopic map; Retinotopy; Striate cortex; V1

INTRODUCTION

One useful by product of the wars in the early 20th century was that scientists were able to correlate occipital cortical lesion locations with the spatial distribution of the ensuing visual field deficits, thereby detailing how the visual field maps onto the brain (i.e. a retinotopic map). It was found that the right visual field mapped onto the left occipital cortex, and vice versa, the upper and lower visual field mapped onto the ventral and dorsal occipital cortex, respectively, and the central to peripheral visual field was mapped anteriorly from the occipital pole [1,2]. In 1945, Holmes refined this retinotopic map showing that the striate cortex (V1) was organized such that the upper and lower visual fields of one hemifield are mapped onto the lower and upper lip of the calcarine sulcus, respectively, in the contralateral hemisphere, such that the horizontal meridian in the visual field is located at the base of the calcarine sulcus [3,4]. Considering Holmes' proposed retinotopic organization, a V1-based visual field deficit restricted to one quadrant of the visual field (i.e. a homonymous quadrantanopia), with a perfectly clean border along the horizontal meridian (see Fig. 1a), would necessarily be the result of a lesion that included either the upper or lower lip of the calcarine sulcus extending precisely to, but not beyond, the horizontal meridian (Fig. 2a). Since its inception, Holmes' model of a cortically based homonymous quadrantanopia (i.e. a V1 lesion extending to the base of the calcarine sulcus) has been widely accepted [5–7].

Recently, based upon evidence from structural MRI, Horton and Hoyt proposed an alternative model of cortically based homonymous quadrantanopia, where the lesion occurs in extrastriate cortex, rather than striate cortex [8]. Horton and Hoyt's model capitalizes upon the fact that early extrastriate visual areas (e.g. V2, VP, V3, and V4v) within a hemisphere each have a representation of a single quadrant in the visual field. Because of this, they argued that any lesion that includes at least one extrastriate visual area, even an irregularly shaped lesion, would yield a homonymous quadrantanopia (Fig. 2b). Horton and Hoyt's extrastriate lesion model is particularly compelling because, unlike Holmes' model, it does not require that the boundaries of the lesion precisely follow a cortical representation of the horizontal meridian. However, the experimental evidence supporting this model has been somewhat limited, given that abnormalities in cortical function may well extend beyond the lesion boundaries as defined by structural MRI alone. It could be argued, for example, that although the extent of a given occipital lesion appears to be restricted to extrastriate cortex, a functional lesion not defined with structural MRI could extend precisely to the horizontal meridian representation in V1, as predicted by Holmes.

The purpose of the present investigation was to perform retinotopic mapping, using fMRI of a patient with a right homonymous quadrantanopia (Fig. 1a), to gain additional evidence toward differentiating between the two cortical lesion models discussed above. In reference to the patient's

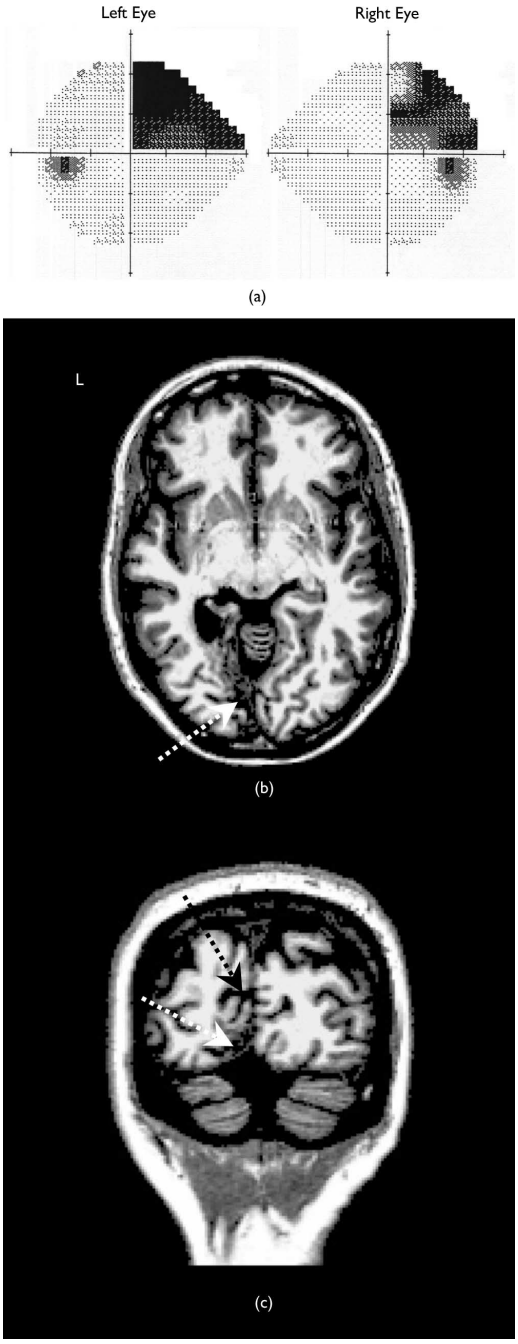

Fig. 1. (**a**) A visual field perimetry map of the patient's homonymous quadrantanopia, restricted to the upper right quadrant of the visual field in both eyes. Dark regions indicate poor or absent ability to detect visual stimuli at those visual field locations. The axes intersection represents the fixation point, and tick marks on the horizontal and vertical meridia are separated by 10° of visual angle. The small dark circular regions in each eye, just below the horizontal meridia, represent the blind spot in each eye; these are normal under monocular viewing conditions. (**b**) An axial slice through the patient's MRI at the level of the ventral extrastriate cortex (the left hemisphere is on the left, L, and anterior is toward the top). The white dotted arrow indicates the ventral extrastriate lesion caused by a stroke. (**c**) Coronal view in which the white dotted arrow indicates the same ventral extrastriate lesion (superior is toward the top). The black dotted arrow points out the calcarine sulcus in the left hemisphere.

upper right quadrantanopia, that maps onto the left ventral visual areas, Holmes' model would predict no activity in V1 or extrastriate cortex, while and Horton and Hoyt's model would predict activity in V1, but no activity in one or more extrastriate visual areas. It should be apparent that these models differ, particularly, in their predictions regarding the presence or absence of functional activity in V1. Also note, due to the hierarchical nature of the visual processing stream (e.g. ventral visual processing goes from V1 to V2 to VP, and so on) [9], the earliest level in the visual processing stream at which a lesion occurs is expected to eliminate activity associated with that region in addition to activity in downstream visual areas.

MATERIALS AND METHODS

The patient, a caucasian female 51 years of age, initially presented with a right homonymous hemianopia following a cerebral infarct to the left inferior occipital lobe. Two years later, at the time of testing, only an upper right quadrantanopia remained (Fig. 1). A neurologically normal control participant underwent identical imaging procedures. The experimental protocol was approved by the internal review board of the Johns Hopkins Hospital, and informed consent was obtained. Visual field mapping was conducted using automated full-field perimetry testing (Humphrey Systems, Dublin, CA).

Anatomical and functional imaging were conducted using a 1.5 T Phillips Gyroscan ACS-NT scanner. The patient lay supine and viewed the stimulus display through a mirror, which was located at the superior end of the magnet bore. T1-weighted anatomic data were acquired with a multiplanar rapidly acquired gradient echo sequence (MPRAGE, 12.4 min acquisition time, birdcage head coil, 8.1 ms repetition, 3.7 ms echo time, 8° flip angle, 256×256 mm field of view, 256×256 acquisition matrix, 256 slices, 1 mm slice thickness, no gap, i.e. 1 mm isotropic resolution). T2*-weighted functional data were acquired with an echo planar imaging sequence, using a circular surface coil centered on the inion to maximize signal in the occipital region (3 s time of repetition, 40 ms echo time, 90° flip angle, foot to head phase encoding, 192×192 mm field of view, 64×64 acquisition matrix, 33 slices, 3 mm slice thickness, no gap, i.e. 3 mm isotropic resolution). The most posterior functional slice was positioned to include the occipital pole, and all functional slices were oriented perpendicular to the calcarine sulcus. fMRI preprocessing included slice-time correction, motion correction, spatial lowpass filtering at 16 cycles/image matrix, and temporal bandpass filtering between 3 and 32 cycles/run length.

Retinotopic maps were obtained using a flickering checkerboard wedge that stimulated unique angular positions in the visual field, the cortical representations of which were localized through statistical correlation with fMRI activity [10–14]. The stimulus wedge was 30° in polar angle width, extended 6.8° of visual angle from fixation, was comprised of squares scaled by the human cortical magnification factor [15], reversed in contrast 8.3 times/s, and rotated continuously about the fixation point in the counterclockwise direction, taking 72 s to complete a single cycle (Fig. 3). The retinotopic mapping run consisted of eight cycles, with an additional 6 s to complete stimulation of the right visual field, and a 15 s fixation period at the

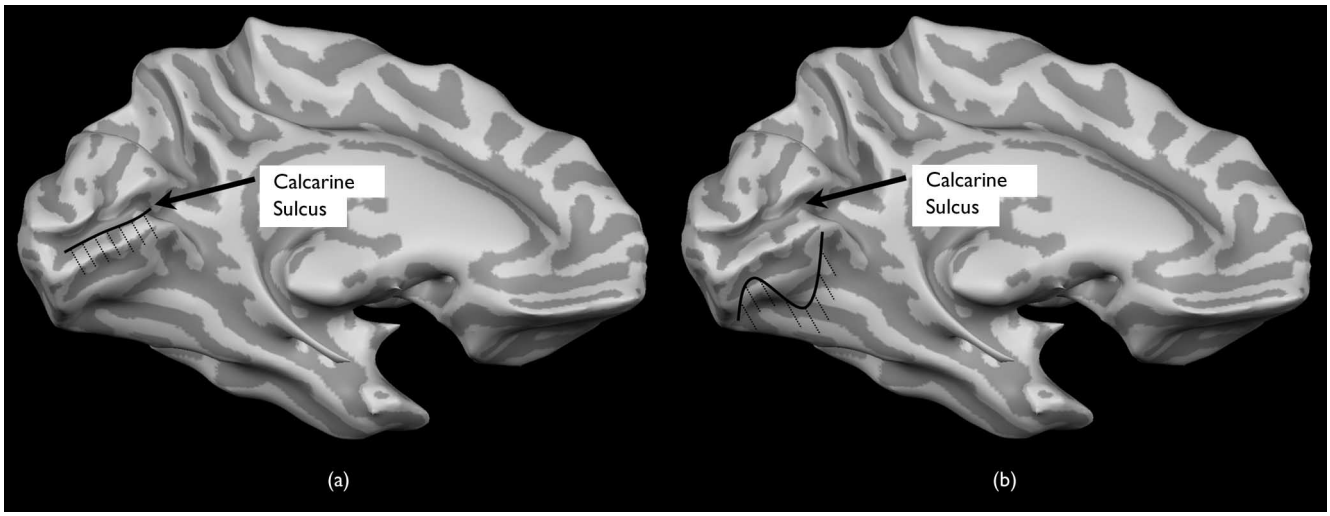

Fig. 2. (**a**) Surface reconstruction of the control participant's left hemisphere, slightly inflated to allow for viewing into the calcarine sulcus. Gyri and sulci are shown in light and dark gray, respectively. Holmes' model of cortically based homonymous quadrantanopia mandates that the lesion, represented by dotted lines, extend precisely to the V1 representation of the horizontal meridian, shown as a solid curve near the base of the calcarine sulcus. (**b**) Horton and Hoyt's model proposes a lesion in extrastriate visual areas, that allows for an irregular border, as shown by the solid black curve. Either of the illustrative lesions shown would, in theory, give rise to an upper right homonymous quadrantanopia as shown in Fig. 1a.

end to allow the hemodynamic response to return to baseline, taking a total of 8 min 42 s.

For a given position in the visual field, this resulted in 6 s of stimulation, 66 s of no stimulation, 6 s of stimulation, and so on (i.e. a square wave protocol with eight peaks). The associated hemodynamic response model was constructed by convolving this protocol with a canonical impulse response function of the form

$$((t - \delta)/\tau)^2 e^{-((t-\delta)/\tau)}$$

where independent variable t = time, and the constants $\delta = 2.5$ and $\tau = 1.25$ [16]. Hemodynamic response models were estimated at intervals of 3 s, translating into a polar angle resolution of 15°. Each hemodynamic response model was then correlated with the activity timecourse associated with each voxel in the functional image volume, and those voxels with correlations that reached a threshold value of 0.25 were painted the color associated with that stimulus position (see key to upper right, Fig. 4a). This relatively strict correlation threshold was selected ($p < 0.05$, Bonferroni corrected for multiple comparisons) to ensure that the retinotopic activity reported was not due to type I error, given that differentiation between the hypotheses under investigation hinged upon whether activity in striate cortex existed.

Anatomical volumes were segmented at the grey/white matter boundary, and the cortical surfaces were reconstructed [10,12,17–19]. The appropriate retinotopic map was then projected onto each hemisphere's surface reconstruction. Fig. 4a shows the control participant's right visual field retinotopic map projected onto a surface reconstruction of their left hemisphere. As expected, the lower and upper right quadrants of the visual field map to dorsal and ventral visual areas, respectively (e.g. red and yellow are mapped superior to the calcarine sulcus). It is more straightforward to identify the borders between visual areas, indicated by color reversals, on an inflated surface representation (Fig. 4b). Visual area V1 is bounded by the upper and lower vertical meridia, and the horizontal meridian falls near the base of the calcarine sulcus. This control data confirms the quadrantic representation of extrastriate visual areas (e.g. V2d, V3, V2v, and VP), as each is bound by a representation of the horizontal and vertical meridian, where the lower and upper vertical meridia representations map to dorsal and ventral visual areas, respectively. Note, that ventral extrastriate areas should be restricted to blue and green color; however, the yellow color in these visual areas suggests that the cortical representation of the horizontal meridian is, in fact, below the visual field representation of the horizontal meridian, a finding that has been reported previously [20,21]; this is routinely observed in our retinotopic maps [13,14]. The retinotopic map shown in Fig. 1c is highly consistent both within and across normal participants, and as such, served as a reasonable baseline for comparison with the patient's retinotopic map.

RESULTS

Figure 4c illustrates the patient's retinotopic map corresponding to the right visual field. The retinotopic organization of dorsal visual areas, corresponding to the intact lower quadrant of the right visual field, was normal (compare Fig. 1c to Fig. 1b). Of theoretical interest, the retinotopic map in ventral visual areas, corresponding to the impaired upper quadrant of the right visual field, was normal in V1 and V2v, and showed little or no retinotopic activity in more anterior extrastriate areas (VP and V4v). The retinotopic map corresponding to the left visual field (not shown) was also completely normal.

DISCUSSION

The present study was the first to use functional evidence to discriminate between two models of cortically based lesions resulting in homonymous quadrantanopia. It was

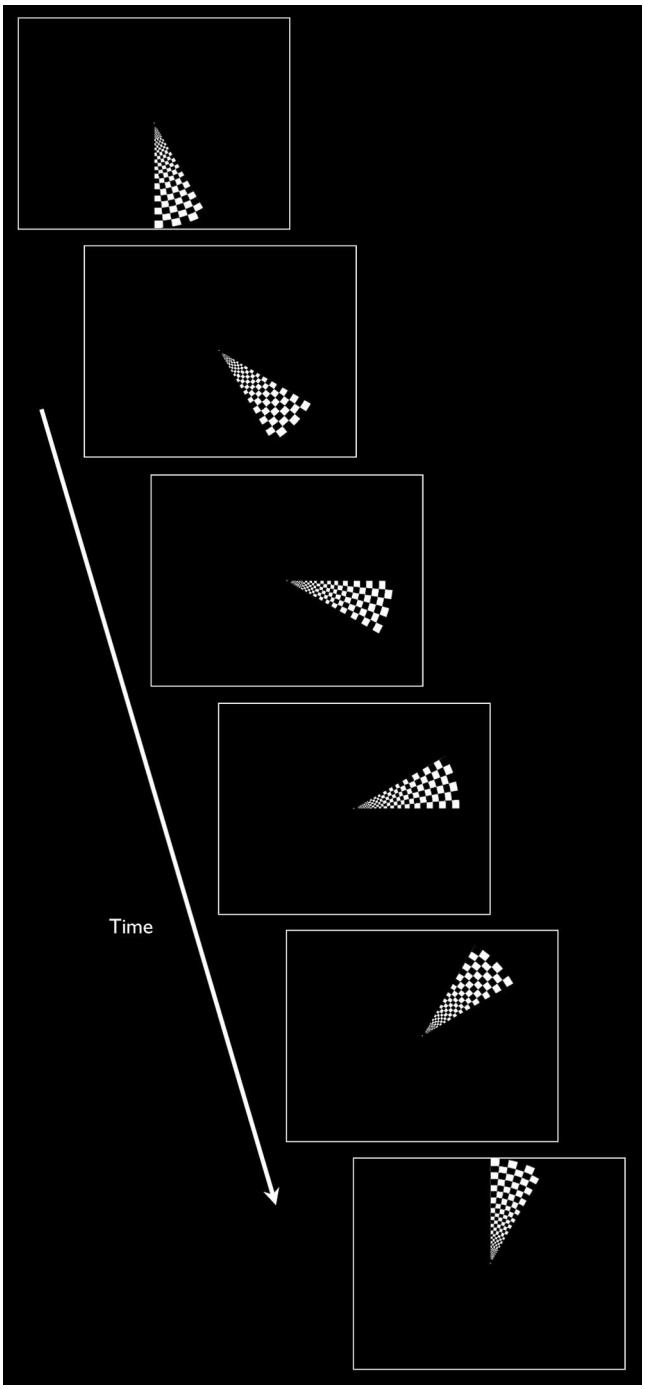

Fig. 3. Snapshots of rotating checkerboard stimulus used to map the right visual field.

found that retinotopic activity was spared in striate cortex, but impaired in extrastriate cortex. In particular, in association with the patient's upper right quadrantanopia, activity was normal in ventral visual areas V1v and V2v, but impaired in VP and those extrastriate visual areas downstream, in accordance with the known visual cortical hierarchical processing architecture [9]. These results are exactly those predicted by Horton and Hoyt's model of homonymous quadrantanopia. Although fMRI has been used previously to functionally investigate visual field deficits [22], the full-field stimulation method employed precluded the identification of activity uniquely associated with striate or extrastriate cortical activity.

Given that the patient's homonymous quadrantanopia followed an initial presentation of a homonymous hemianopia, one potential concern is whether cortical reorganization may have influenced the results. Specifically, the loss and then subsequent return of visual function in the lower right quadrant may have been caused by damage to cortex typically subserving that function (i.e. dorsal occipital cortex), followed by recruitment of other cortex capable of subserving normal visual function. Such cortical recruitment or reorganization is usually evidenced by activation in atypical regions, while a given task is performed [13,23]. However, the fact that the recovered retinotopic map in dorsal occipital cortex was entirely normal indicates that the loss of function in this region was due to a temporary cortical lesion, with no evidence for cortical reorganization. Of primary importance, the patient's visual function in the upper right quadrant was consistently impaired, thus providing no evidence that cortical reorganization in ventral occipital cortex occurred (had it done so, recovery of visual function should have followed).

The fMRI results of the present study in conjunction with the anatomic MRI evidence reviewed by Horton and Hoyt [8] provide evidence that isolated extrastriate cortical lesions can give rise to a homonymous quadrantanopia. Given the extremely low probability that a cortical lesion extends precisely to, but not beyond, the representation of the horizontal meridian near the base of the calcarine sulcus, these findings are perhaps not surprising. In fact, it may well be the case that the vast majority of cortically based homonymous quadrantanopias are due to such lesions. In further support of this point, it should also be noted that the shape of the functional lesion observed in the present study was irregular (Fig. 4c), as would be expected given the numerous factors that contribute to the extent of a cortical lesion due to stroke (e.g. occluded artery distribution, duration of occlusion, and patency of alternate vascular supplies). Holmes' model of cortically based quadrantanopia would mandate a perfectly regular cortical lesion (situated exactly at the V1 horizontal meridian representation); this is highly unlikely, as has been voiced by others [8,24,25].

Even when taking the empirical evidence and theoretical arguments into consideration, it is important to acknowledge that the present results are that of a single patient, and therefore only prove that an extrastriate cortical lesion can give rise to a homonymous quadrantanopia, not that all such visual field deficits are referable to this type of cortical lesion. Even so, the present results, in conjunction with those of Horton and Hoyt [8] call into question the popular notion that a V1 lesion at the base of the calcarine sulcus gives rise to a homonymous quadrantanopia [5–7]. A study involving a series of patients, each with a homonymous quadrantanopia, will be required to definitively resolve this issue.

CONCLUSION

Perhaps because it was theoretically possible, cortically based homonymous quadrantanopia has long been consid-

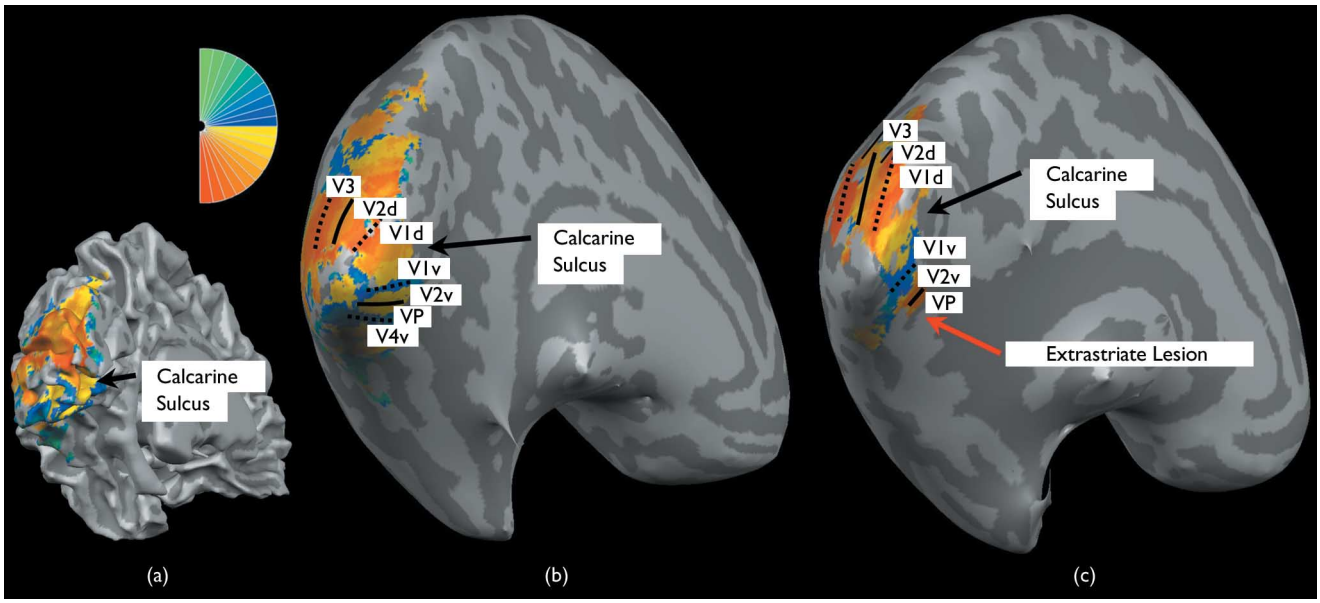

Fig. 4. (**a**) Control participant's left hemisphere surface reconstruction with retinotopic map corresponding to right visual field stimulation. Each stimulus position in the visual field (Fig. 3) is associated with a unique color (see key to upper right). The lower right quadrant of the visual field (shown in red and yellow) is mapped onto the dorsal visual areas superior to the calcarine sulcus, which contains the V1 representation of the horizontal meridian, and the upper right quadrant (shown in green and blue with some yellow), is mapped onto the ventral visual areas inferior to the calcarine sulcus. (**b**) The same retinotopic map projected onto an inflated surface reconstruction to assist in viewing borders between visual areas, as indicated by color reversals. Vertical meridia are demarcated by dotted lines, horizontal meridia by solid lines, and early visual areas are labeled in black. (**c**) The patient's left hemisphere retinotopic map projected onto an inflated surface reconstruction. Dorsal visual areas, corresponding to the intact lower right quadrant of the visual field (Fig. 1a), show a normal retinotopic organization. Although ventral visual areas V1v and V2v also show a normal pattern of activity, a functional lesion is apparent in ventral extrastriate cortex (indicated by the red arrow), illustrated by little or no activity in visual areas VP and V4v.

ered reflective of a striate cortex lesion, restricted to either the upper or lower lip of the calcarine sulcus, and extending precisely to the horizontal meridian representation [3]. The present results are inconsistent with this model, and rather provide fMRI evidence favoring the model proposed by Horton and Hoyt, which was based upon detailed anatomical MRI evidence [8], where a lesion restricted to extrastriate cortex causes homonymous quadrantanopia. The empirical results, in addition to the theoretical arguments against the plausibility of a perfectly placed lesion in striate cortex, suggest that a homonymous quadrantanopia of cortical origin can be mediated by a lesion in extrastriate cortex.

REFERENCES

1. Inouye T. *Die Sehstorungen bei Schussverletzungen der kortikalen Sehsphare nach Beobachtungen an Verwundeten der letzten japanischen Kriege*. Leipzig: W Engelmann, 1909.
2. Holmes G and Lister WT. *Brain* **39**, 34–73 (1916).
3. Holmes G. *Proc R Soc Lond B Biol Sci* **132**, 348–361 (1945).
4. Horton JC and Hoyt WF. *Arch Ophthalmol* **109**, 816–824 (1991).
5. Zeki S. *A Vision of the Brain*. Oxford: Blackwell Scientific Publications, 1993.
6. Kitajima M, Korogi Y, Kido T *et al*. *Neuroradiology* **40**, 710–715 (1998).
7. Valenstein E and Nadeau SE. Visual field defects. University of Florida College of Medicine Web Site, http//www.medinfo.ufl.edu/year2/neuro/neuroexam/visfield.html, Retrieved February 2, 2003.
8. Horton JC and Hoyt WF. *Brain* **114**, 1703–1718 (1991).
9. Felleman DJ and Van Essen DC. *Cerebr Cortex* **1**, 1–47 (1991).
10. Sereno MI, Dale AM, Reppas JB *et al*. *Science* **268**, 889–893 (1995).
11. DeYoe EA, Carman GJ, Bandettini P *et al*. *Proc Natl Acad Sci USA* **93**, 2382–2386 (1996).
12. Tootell RBH, Mendola JD, Hadjikhani NK *et al*. *J Neurosci* **17**, 7060–7078 (1997).
13. Slotnick SD, Moo LR, Krauss G and Hart J. *Neuroreport* **13**, 41–46 (2002).
14. Slotnick SD and Yantis S. *Hum Brain Mapp* **18**, 220–29 (2003).
15. Slotnick SD, Klein SA, Carney T and Sutter EE. *Clin Neurophysiol* **112**, 1349–1356 (2001).
16. Cohen MS. *NeuroImage* **6**, 93–103 (1997).
17. Van Essen DC and Drury HA. *J Neurosci* **17**, 7079–7102 (1997).
18. Dale AM, Fischl B and Sereno MI. *NeuroImage* **9**, 179–194 (1999).
19. Joshi M, Cui J, Doolittle K *et al*. *NeuroImage* **9**, 461–476 (1999).
20. Aine CJ, Supek S, George JS *et al*. *Cerebr Cortex* **6**, 354–361 (1996).
21. Clark VP, Fan S and Hillyard SA. *Hum Brain Mapp* **2**, 170–187 (1995).
22. Sorensen AG, Wray SH, Weisskoff RM *et al*. *Am J Neuroradiol* **16**, 1753–1762 (1995).
23. Moo LR, Slotnick SD, Krauss G and Hart J. *Neuroreport* **13**, 665–669 (2002).
24. Monbrun A. *Arch Ophthalmol* **36**, 641–670 (1919).
25. Rönne H. *Klin Monatsbl Augenheilkd* **63**, 358–374 (1919).

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