

Residual Neurovascular Function and Retinotopy in a Case of Hemianopia

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Abstract

Introduction: For occipital cortex strokes resulting in vision disorders, questions about the viability of residual visual cortex remain. **Clinical Picture:** In a patient with a one-year-old, left, complete, homonymous hemianopia due to a right, posterior cerebral artery, ischaemic infarct, we assessed the visual cortex with fMRI retinotopic mapping prior to starting vision restoration therapy. **Outcome:** The patient was found to have residual neurovascular function and retinotopic representation in the surviving visual cortex around the infarcted area. **Conclusion:** The ability to respond to stimuli in part of the blind field, though not consciously perceived, suggests the potential for recovery.

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Introduction

Homonymous hemianopia is one of the most common forms of acquired visual field defects.¹ It is typically produced by head injury, tumours or stroke that damage the occipital cortex, postgeniculate pathways or both.¹ This leads to the impairment in basic functions, such as reading, visual search and navigation. Thus, it is important to assess residual function and work towards rehabilitation. Indeed visual field defects may not be permanent and indeed have been shown to undergo recovery spontaneously² or with rehabilitation.³

Questions regarding the affected visual cortex with and without intervention remain. In the lesioned occipital lobe, does the surviving cortex maintain function or lose it due to network inactivity or lack of visual input? Is the surviving cortex or contralesional hemisphere re-organised to take on the functions of the adjacent lesioned cortex? We sought to probe these aspects in a case of complete left homonymous hemianopia prior to intervention.

The 59-year-old, right-handed male patient had a history of right posterior cerebral artery (PCA) ischaemic stroke one year prior, with resultant complete left homonymous hemianopia. The infarct was in the medial right occipital lobe, including part of the calcarine sulcus (Fig. 1). His



Fig. 1. Clinical images of the patient's infarct in radiological convention.

foveal vision and colour perception was preserved. He had not received any therapy to rehabilitate his vision, but was about to embark on a rehabilitation programme called Vision Restoration Therapy (VRT).⁴ This treatment programme by NovaVision Inc. (FL, USA) appears to reduce the visual scotomata of patients who have post-chiasmal lesions and preserved foveal vision. It involves daily computerised training for 6 months with incremental difficulty that is tailored to the individual patients' visual field deficits and response to treatment. This study was done to establish his baseline state before tracking any progress over time. The aim was to perform angular retinotopic mapping using the blood oxygen level dependent (BOLD) contrast in functional magnetic resonance imaging (fMRI) to chart the patient's working visual cortex via haemodynamic responses.

Based on the patient's left-sided, complete hemianopia

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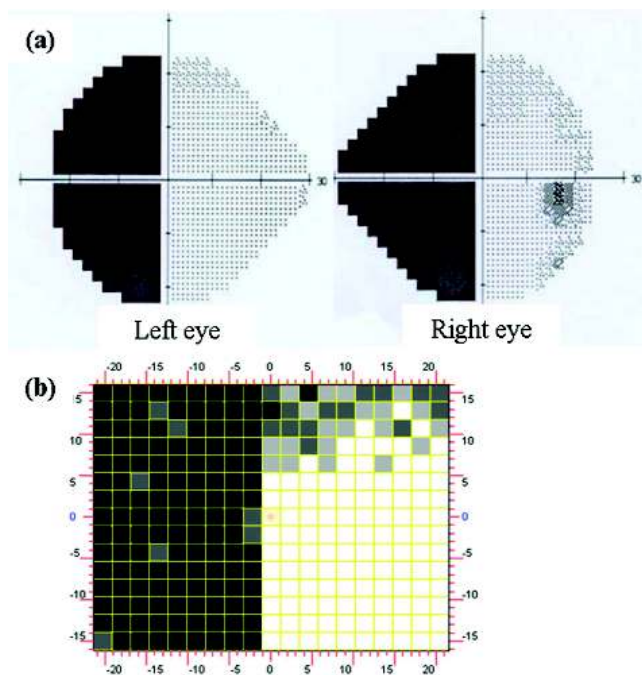


Fig. 2. (a) Perimetry measured by Humphrey's automated visual fields analyser. The blindspot for the right eye can be seen in the lower right quadrant. (b) High resolution perimetry using the VRT setup. Black areas in (a-b) illustrate the patient's left-sided hemianopia in visual angles.

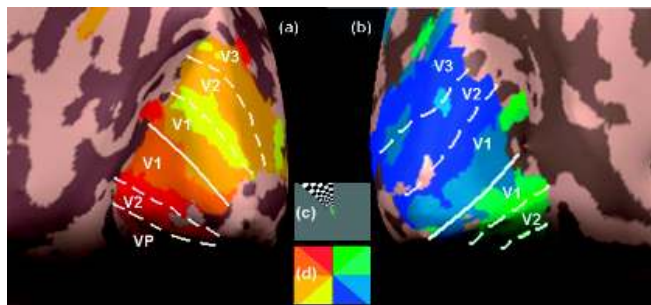


Fig. 3. Retinotopic maps of an age-matched, healthy volunteer overlaid onto images of inflated cerebral cortex to visualise the gyri (light pink) and sulci (grey-pink) for the (a) right and (b) left medial occipital lobes. Coloured activations represent significant BOLD cross-correlations ($r \geq 0.03$) according to the retinotopic mapping paradigm – (c) a wedge with checkerboard pattern reversing at 8 Hz and rotated around eight positions, represented by the colour logo in (d). Solid white lines represent the calcarine sulcus and broken white lines represent the boundaries of the visual areas.

(Figs. 2a-b), we expected typical BOLD changes in the intact left visual cortex due to the retinotopic mapping stimuli, together with little or no significant response in the lesioned right hemisphere. In this case report, we describe the interesting findings of significant haemodynamic response and retinotopic organisation in the visual cortex of the lesioned hemisphere that indicate residual visual function, but which does not seem to be consciously perceived by the patient. We discuss the implications of such residual function.

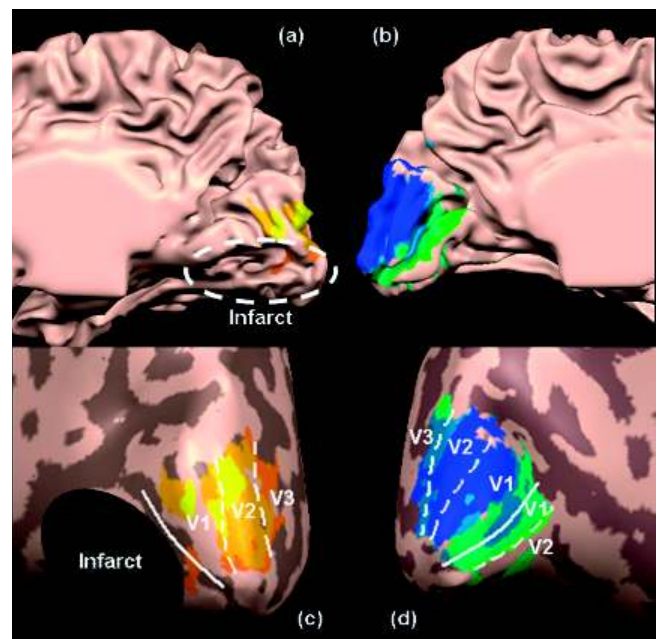


Fig. 4. Retinotopic maps of the patient overlaid onto anatomical brain images for the medial right and left occipital lobes respectively (a-b), and their corresponding inflated images (c-d). The activations are according to polar angle as described in Figure 3, with the solid white lines denoting the calcarine sulcus and the V1-3 border estimations as broken white lines. The infarct in the right occipital lobe is circled.

Case Report

The patient gave informed, written consent prior to participation in the study, which took place approximately 1 year after his ischaemic infarct. The protocol was approved by the Institutional Review Boards of the hospitals involved.

Perimetry

As part of standard ophthalmology assessment, the patient's working visual fields were assessed using a Humphrey automated visual fields analyser. High resolution perimetry using the VRT setup was also performed.

Magnetic Resonance Imaging and Retinotopic Mapping

Prior to starting the VRT programme, the patient was scanned on a Philips Achieva 3.0T clinical scanner (Philips Healthcare, Best, The Netherlands) to determine his baseline state. Angular retinotopic mapping was done during a full brain GRE-EPI scan: TR/TE = 2000/30 ms, $\alpha = 90^\circ$, FOV = 224x224 mm, matrix = 112x112, slices = 30, slice thickness = 4 mm, gap = 0 mm, scan time = 10 min 40 s. The retinotopic mapping paradigm was presented to the patient during the scan using the Eloquence system (InVivo Corp, FL, USA), which consisted of a hooded LCD screen (horizontal visual angle $\sim 30^\circ$, vertical visual angle $\sim 25^\circ$) that was mounted onto the head coil. The retinotopic mapping paradigm consisted of an anti-clockwise rotating wedge of 45° , starting at and aligning the right edge to the

12 o'clock position. The wedge had a checkerboard pattern that reversed contrast polarity at 8Hz. The wedge rotated through 8 positions with 20 s at each position (Fig. 3c). There were 4 cycles. Throughout the retinotopic mapping paradigm, the patient had to fixate on a small, central circle ($\sim 1^\circ$) that would randomly alternate between green and yellow (3 to 5 s range). He had to press one of two buttons that corresponded to the colour of the circle each time it changed. This was done in order to maintain the patient's alertness and fixation on the centre.

A 3D anatomical scan (MPRAGE: FOV = 230x230 mm, matrix = 512x512) was also performed for structural overlay.

Data Analysis

Post-processing and analyses were done using Brain Voyager v.10 (Brain Innovation, Maastrich, The Netherlands). The BOLD-fMRI data were corrected for motion and slice timing. Low frequency drifts were removed. No spatial smoothing was done. Cross correlations ($r \geq 0.3$, $P < 0.002$, corr.) of each time point at each voxel were performed to create the retinotopic maps. Anatomical images of the brain were segmented from the non-cortical structures, such as the skull and brain stem, and computationally "inflated" using the Brain Voyager software. The retinotopic maps were then co-registered to these segmented and inflated anatomical images. Given that the cerebral cortex grey matter is a folded but continuous sheet, the "inflation" of the folded sheet of grey matter allows the visualisation of cortex deep within the brain sulci. It was important here to visualise the calcarine sulcus and its BOLD activations, given that the primary visual cortex (V1) is centred on the calcarine sulcus.

Comparison with Healthy Volunteers

Five healthy volunteers with normal vision (3 males, 2 females; age range, 27 to 57 years) were scanned with the same MRI parameters and retinotopic mapping paradigm to provide standard references for the patient case.

Results

Figures 2a-b show the results from the Humphrey automated visual field analysis and the high resolution perimetry (HRP), respectively. Both techniques clearly show the complete left hemianopia as represented by the black areas in the charted visual field.

Figures 3a-b show representative retinotopic maps from an age-matched, healthy subject overlaid onto images of cerebral cortex inflated to visualise the gyri and sulci for the occipital lobes in both hemispheres from the posterior, medial aspects. The colours of the activations represent visual areas that respond to the various positions of the rotating wedge, as illustrated in the colour legend. The V1

areas extend from the calcarine sulcus (solid white line) and the extrastriate visual areas can be delineated with the rotating wedge paradigm.

Figures 4a-b show the patient's retinotopic map overlaid onto anatomical brain images for the right and left hemispheres respectively, and Figures 4c-d show the cortical images computationally inflated to visualise the cortex within the sulci more clearly for the corresponding hemispheres. The left visual cortex, which is intact, displays the expected activations corresponding to the stimulation in the contralateral visual field (i.e. the right field, which is represented by the green and blue colours). In the right visual cortex, surprisingly there were responses to the stimulation in the 6:00 to 10:30 o'clock areas of the visual field (represented by the colours yellow, mustard and orange), together with some retinotopic organisation. V1 appeared to be limited. No response was detected for stimulation in the 10:30 to 12:00 o'clock area in the visual field (represented by red).

Discussion

Retinotopic Maps and BOLD fMRI

Within the occipital lobe, the primary visual cortex (V1) surrounds the calcarine sulcus and contains a retinotopic representation of the entire visual field. It is organised in a rough polar coordinate system.⁵ Moving from the lower to the upper lip of the calcarine sulcus, the representation of the visual field shifts from above the horizontal meridian to that below. Also, from the posterior to anterior visual cortex, the representation of the visual field moves from the centre to the periphery. Finally, the visual cortex in each hemisphere represents input from the contralateral visual field.

The angular retinotopic mapping paradigm allowed us to delineate the borders of V1 and the extrastriate areas like V2-3 and VP, based on polar angle responses as mapped out in publications like Sereno et al.⁶ and Tootell et al.⁷ The checkerboard wedges did not straddle the vertical meridian, so responses to stimulation in the right and left visual fields could also be differentiated. An important consideration in retinotopic mapping is the maintenance of a consistent visual field, which necessitates the subject's constant focus on the centre of the screen. Although there was no eye-tracking equipment to certify this, the fixation task helped to monitor the visual focus of the patient and healthy subjects. The subtle colour change of the small, central target can only be perceived with central vision. The patient and healthy subjects performed well in this task (>99% detection accuracy), indicating consistency of the visual fields throughout the retinotopic mapping sessions.

Retinotopic mapping can be performed with a variety

of methods ranging from single-cell recording to visual evoked potentials.⁸ Using fMRI with the natural BOLD effect⁹ retinotopic mapping can be performed non-invasively and with relatively high signal-noise ratio.^{6,7,10} Retinotopic mapping using BOLD-fMRI has been used to study the healthy visual system as well as in disease, such as stroke¹¹⁻¹³ or cortical dysgenesis.¹⁴

Hemianopia and Blindsight

In the healthy left hemisphere, the patient's retinotopy appeared normal, as compared to the controls. There was no response to stimulation in the ipsilateral blind field, which is typical since visual input to V1 is well known to be crossed.

Remarkably in the lesioned right hemisphere, there were significant BOLD changes (Figs. 4) when retinotopic mapping stimuli were presented in the 6:00 to 10:30 o'clock areas of the blind field, even though the perimetry (Figs. 2a-b) clearly shows the functional blindness of the patient's left visual field. The response in the V1 area is limited, but the extrastriate areas above the calcarine sulcus showed robust response. The representation for the 11:30 to 12:00 o'clock visual area in the left visual field may have been lost, which was not surprising, since the upper visual field representation lies in the infarcted area. These findings suggest some preserved postgeniculate input, neurovascular function and retinotopic organisation for the lower left visual field in the patient's remaining right occipital cortex. Whether this is due to spontaneous recovery or tissue that was not damaged in the first place is unclear. Nonetheless, in a very similar case, Baseler et al¹¹ found substantial retinotopic organisation with BOLD-fMRI in the lesioned visual cortex of a subject with hemianopia due to a PCA stroke. With PET and SPECT, Celesia et al¹⁵ found that there was retained metabolic activity in a subset of patients whose V1 was not totally destroyed in occipital lobe infarction.

Interestingly, in this patient's case and those described above, the neurovascular response to visual input in the blind field does not result in conscious perception. Nevertheless, this residual function could still be considered useful. In a phenomenon known as 'blindsight', some cortically blind people appear to have the ability to detect and discriminate visual stimuli at above chance level in forced choice tasks without any awareness of perception.¹⁶ Standard perimetry techniques do not show this because they rely on conscious awareness of target presentations.¹⁷ While blindsight is not common in patients with V1 lesions,¹⁸ it is worth noting that the parallel case of hemianopia studied by Baseler et al¹¹ as highlighted above was found to have blindsight.¹⁷ Although the patient in our study has not been psychologically tested for blindsight, it is known that blindsight abilities tend to correspond with 'islands' of surviving function or

tissue,¹⁷ which has been observed in this case. This could be promising for visual recovery in the light of a recent study¹⁹ on stroke patients with homonymous visual field deficits that demonstrated increased visual sensitivity by seemingly activating residual extrastriate pathways associated with blindsight.²⁰

Caution must, however, be made in interpreting the rest of the visual cortex without significant BOLD changes as having no surviving neurovascular function. Given that the BOLD signal change depends on the balance of the cerebral blood flow change with the change in the cerebral metabolic rate of oxygenation,⁹ in areas where this coupling is altered due to damaged tissue for example, there might still be neuronal activity but no detectable BOLD signal changes.²¹

Implications for Treatment and Recovery

The observed residual neurovascular function and response around the patient's lesion indicates viable tissue and allows potential for further recovery. This might entail bringing the primary visual response to the patient's conscious awareness and possible recruitment of other parts of surviving occipital cortex. The patient is currently undergoing the VRT programme with the aim of enlarging his functional visual field (as consciously perceived). It remains to be seen if the treatment will be effective, but his baseline retinotopic mapping results suggest the possibility of improvement, particularly in the lower quadrant of the impaired left visual field. The success of vision under degraded conditions and vision rehabilitation programmes have been thought to engage attentional processes and higher order visual areas.²²⁻²⁴ If tested to be predictive of the results of VRT or other therapies to restore vision, fMRI retinotopic mapping could be used as a simple, non-invasive tool to assess suitability for these relatively costly and time-intensive programmes as well as to highlight specific locations in the visual field on which to focus rehabilitation efforts.

To conclude, using fMRI retinotopic mapping, the patient was found to have residual neurovascular function and retinotopic representation for part of the blind field in the surviving cortex around the infarct in the occipital lobe, with the extrastriate areas strongly activated. The healthy hemisphere was not recruited. The ability to respond to stimuli in the lower quadrant of the blind field, though not brought to consciousness, suggests the potential for recovery.

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