Structural and functional changes in visual pathways and visual cortex associated with visual field improvement after therapy in a case of hemianopia

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INTRODUCTION: Despite the apparent success of Visual Restoration Therapy (VRT) [1], which seems to reduce the visual scotomata of patients with post-chiasmal lesions through repetitive training [1,2], no clear anatomical or physiological basis has yet been given for the apparent visual field enlargement in patients. Based on DTI and fMRI retinotopic mapping, we assessed a patient before and after VRT. The retinotopic mapping results have previously been reported [3]. In short, before therapy, there was residual neurovascular function and limited retinotopic organization around the lesion despite the patient's dense hemianopia. After therapy, the lower left visual field was improved and there appeared to be some functional recovery of primary visual cortex. Here, we report the novel DTI results, showing how the visual pathways were affected with therapy and discuss the results as a whole.

METHODS: The patient had a complete homonymous hemianopia (Figs 1, 2a) due to a right posterior cerebral artery ischemic stroke 1 year prior to therapy. Foveal vision and colour perception was preserved. He was assessed before and after VRT (lasted 9 months) with Humphrey automated visual fields analysis and MRI, which was done on a Philips 3.0T scanner. *DTI parameters*: TR/TE = 6238.5/70 ms, α=90°, diffusion gradient directions = 16, b-value = 1000 s/mm^2; FOV = 224x224 mm, matrix = 112x112, slices = 60, slice thickness = 2 mm, gap = 0 mm. *fMRI* parameters, analysis and angular retinotopic mapping parameters as in [3]. *Controls.* Five healthy volunteers (3 M, 2 F; 27 – 57 years) were scanned with the same protocol twice each about 2 weeks apart to assess reproducibility. *Data Analysis:* DTI data were analysed with FSL (www.fmrib.ox.ac.uk/fsl/), probabilistic tractography, 2-tensor model. Optic tract and optic radiation were identified in each hemisphere using ROIs positioned posteriorly to the chiasm, lateral to the calcarine and in the area of the lateral geniculate body (LGN). ROIs were identified on baseline acquisition and then co-registered to the second time point acquisition. Tracts were normalized to the number of streamlines reaching the target. b=0 s/mm^2 images, fractional anisotropy maps and normalized tracts were then co-registered to the MNI template. Finally the tracts were thresholded to 0.5% and overlapping between tracts acquired at different time points in the same subject were assessed with the Dice reproducibility score (volume of the overlapping tracts divided by the average volumes of the two compared tracts).

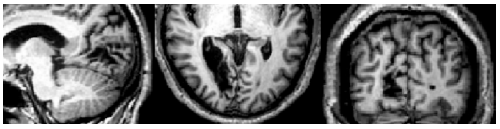

Fig. 1: The patient's right occipital lobe infarct.

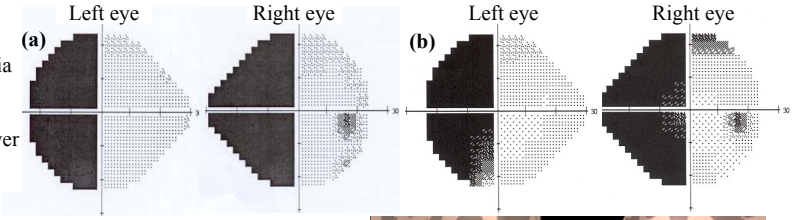

Fig. 2: Humphrey visual field analysis (a) dense hemianopia before therapy, and (b) after therapy, improvement in lower left field.

RESULTS & DISCUSSION: Before therapy, there were surviving optic radiation (OR) fascicles in the lesioned, right hemisphere (Fig. 4a), which were smaller in volume compared to the healthy, left side (Fig. 5a). This helps to explain the residual retinopy (Fig. 3a) despite the extensive infarct. However after therapy, contrary to the improved perimetry and retinotopic mapping results (Figs 2b, 3c), the volume of the right OR actually decreased (1 standard deviation (sd) < result < 2 sd, based on control subject range). The same was found in the left OR (result < 1 sd). There were no significant differences in fractional anisotropy, mean diffusivity or index of connectivity between sessions. On the other hand, the optic tract (OT) on the affected side showed a volume *increase* after therapy (1 sd < result < 2 sd), matching both the healthy side and controls (Fig. 5b). It is intriguing that before therapy, the patient's right OT was significantly smaller (1 sd < result < 2 sd) than in controls, possibly due to Wallerian degeneration retrograde from the OR. Fig. 6 shows the consistent Dice scores among the controls, indicating reproducibility of the analyses across sessions and volunteers. Except for the left OT, the patient's Dice scores indicated differences between sessions that were outside 2 sd of the control range. Any spontaneous recovery is expected to take place within the first 6 months of the stroke [4]. Taken together with the perimetry and retinotopic mapping results, this case study suggests that the reduced scotomata associated with VRT could be due to potential recovery of the optic tract and visual cortex. In addition to harnessing "top-down" attentional processes [5], the directed and repetitive stimulation in the blind field may also trigger a "bottom-up" process, whereby neurons in the visual cortex adjacent to the lesion may become more responsive to previously subthreshold inputs [6]. If the optic radiation is assumed to be dysfunctional, another possible processing and recovery route could be via extrastriate pathways [7], such as projections from the pulvinar nucleus in the posterior thalamus to the extrastriate visual areas. The strengthening of these alternate pathways could be at the expense of the optic radiation, which could explain the decreased volume, while at the same time, the optic tract to the thalamus is enlarged with usage.

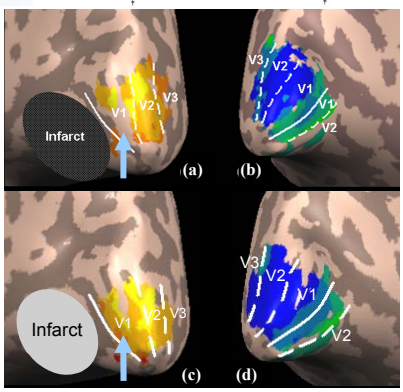

Fig. 3: Retinotopic organization before therapy: (a) Lesioned right hemisphere. Solid white line on inflated cortex shows the calcarine sulcus. Broken lines represent the visual area boundaries. Arrow shows 'hole' in activation. Colors according to retinotopic paradigm [3]. (b) Left hemisphere showing normal retinotopic organisation. After therapy: (c) Arrow shows activation of V1 superior to infarct, closing up part of the previous hole. (d) Left hemisphere has no significant change in retinotopic organisation.

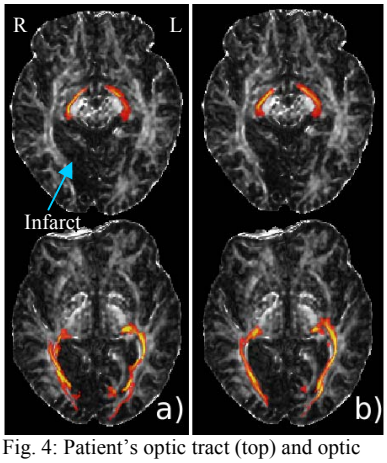

Fig. 4: Patient's optic tract (top) and optic radiation (bottom) before (a) and after (b) therapy.

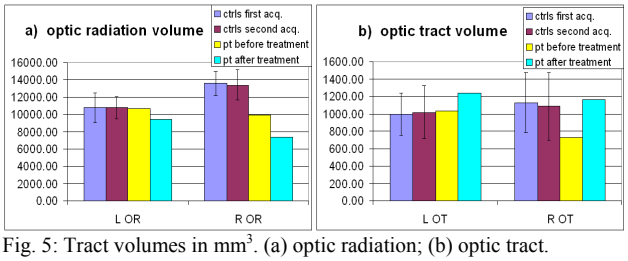

Fig. 5: Tract volumes in mm^3. (a) optic radiation; (b) optic tract.

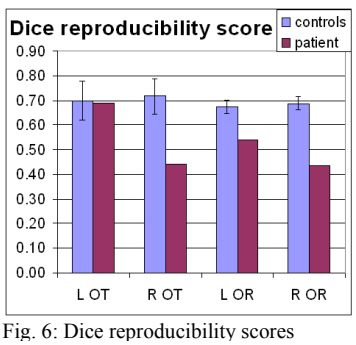

Fig. 6: Dice reproducibility scores

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