Indications of residual neurovascular function in a case of hemianopia prior to visual field rehabilitation.

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INTRODUCTION: Visual field defects due to lesions in or near the occipital cortex recently have been shown to undergo recovery [1-2]. A relatively new therapy – Visual Restitution Treatment (VRT) [3] appears to reduce the visual scotomata of patients with post-chiasmal lesions but preserved foveal vision [2-3]. It involves daily computerized training for six months with incremental difficulty that is tailored to the individual patients' visual field deficits and response to treatment. However, no clear anatomical-physiological basis has been given for the apparent visual field enlargement in such patients, especially in the functional borderzone (edge of scotoma and the good field) where the improvements tend to be seen. In this study, we aim at tracking physiological changes in a patient undergoing VRT with fMRI and high-resolution DTI. The goals were (1) to assess the changes in retinotopic maps plus white matter FA before, during and after the treatment; (2) to assess within each scan session whether visual and attentional BOLD activity is affected when the stimulus moves from the 'good' field to the borderzone, compared to onset from the 'poor' field; and (3) to assess if BOLD activity with borderzone stimulation (as a ratio of the unaffected side) is influenced by the treatment across time. Here, we report the preliminary results of the initial baseline scans before VRT was started.

METHODS: A 59 year old, right-handed male who had a left complete homonymous hemianopia with preserved foveal vision, due to a right occipital lobe ischemic infarct, was recruited with informed consent. Prior to starting the VRT programme (a year after the infarct), he was scanned on a Philips Achieva 3.0T imager using the following sequences: GRE-EPI: TR/TE = 2000/30 ms, α=90°, FOV = 224x224 mm, matrix = 112x112, slices = 30, slice thickness = 4 mm, gap = 0 mm; DTI: TR/TE = 6238.5/70 ms, α=90°, diffusion gradients = 16; FOV = 224x224 mm, matrix = 112x112, slices = 60, slice thickness = 2 mm, gap = 0 mm; MPRAGE: FOV = 230x230 mm, matrix = 512x512. Stimuli were presented with the Eloquence system (InVivo) with horizontal visual angle ~ 30°. 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 flashed at 8Hz and lasted 10 time volumes at each of 8 positions. There were 4 cycles that lasted 320 time volumes in total. The data was analyzed with Brain Voyager v.10 using cross correlation ($r>0.4$, $p<0.0001$), convolved with HRF. The 'borderzone' paradigm consisted of 3 adjacent, vertical strips of checkerboard patterns that appeared to move in and out of the 'poor' visual field. Each strip consisted of 3x6 (horizontal x vertical) checkerboard squares, with strip width ~ 5° visual angle. The 3 strips corresponded to the subject's 'good' visual field, the borderzone, and the 'poor' visual field respectively. The sequence would either be 'good'->'borderzone'->'poor' (Condition "G-B-P") or vice versa (Condition "P-B-G"), with presentation either in the upper or lower half of the screen. Duration of this paradigm was 288 time volumes. The data, convolved with HRF, was analyzed with t-tests ($t>4$, $p<0.0001$). ΔBOLD (%) was measured in the occipito-temporal cortex, the middle temporal, the medial frontal and the dorsolateral prefrontal cortex (DLPFC). In both visual tasks, the subject had to fixate on a small, central circle that would randomly alternate between green and yellow. The subject had to press a button that corresponded to the colour of the circle each time it changed, so as to maintain alertness and fixation on the centre. DTI data was analyzed using DTI Studio. FA was calculated for the region of the optic radiation, i.e. between the thalamus (LGN) and the visual cortex in both hemispheres.

RESULTS & DISCUSSION: Figure 1 shows the high resolution perimetry (HRP) illustrating the left-sided hemianopia, while Figure 2 shows the retinotopic map in the visual cortex. Despite the hemianopia, there was still BOLD activation in the right visual cortex around the lesion (orange and yellow voxels) that was associated with the lower left visual field stimuli. Furthermore, stimuli in the lowest left visual field appear to activate the medial left visual cortex too (yellow voxels), suggesting some functional reorganization. A consistent FOV is important for retinotopic mapping, which was likely to be the case here, given the patient's high accuracy in the fixation task, though the lack of eye-tracking equipment limits definitive confirmation. It is interesting that the apparent 'activation' response to the lower left visual field does not result in conscious perception as shown in the HRP in Fig. 1. This BOLD activity suggests some surviving neurovascular function, which may predict future therapeutic gains. Such 'blindsight' activation has been observed with PET and fMRI [4,5]. Higher order attentional processes appear to be involved in assisting visual field recovery, particularly at the borderzone [6]. With stimulation in both the borderzone and the good field, we detected significant ΔBOLD (%) in the occipito-temporal junction and the visual processing/attentional areas – the middle temporal, the medial frontal and the DLPFC, similar to Marshall et al [7], who found that with VRT training, the BOLD response amplitudes increased relatively more compared with stimulation in the good field and attributed it to an attentional shift from the good field to the borderzone. We did not find differences in ΔBOLD (%) between the "G-B-P" (Good->Borderzone->Poor) and "P-B-G" conditions for the same cortical areas, though this too might change with training. FA was 0.64±0.19 (s.d.) for the optic radiation region in the left hemisphere, compared to 0.41±0.13 for the corresponding region in the infarcted, right hemisphere. Though ambiguous, the lower FA could possibly reflect decreased axonal integrity around the infarcted region [8]. To our knowledge, these baseline results represent the first report of retinotopic mapping and DTI in a patient set to undergo VRT therapy, in whom there are preliminary indications of residual neurovascular activity around the infarcted zone and suggest the possibility for plasticity.

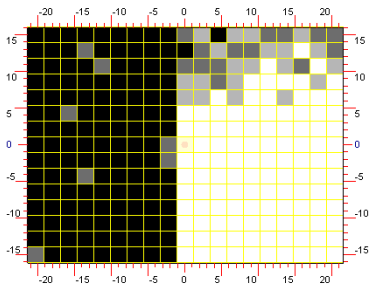

Fig. 1: High resolution perimetry map showing the patient's left-sided hemianopia in visual angles. (Black means 0% detection of target, while white means 100% detection of target.)

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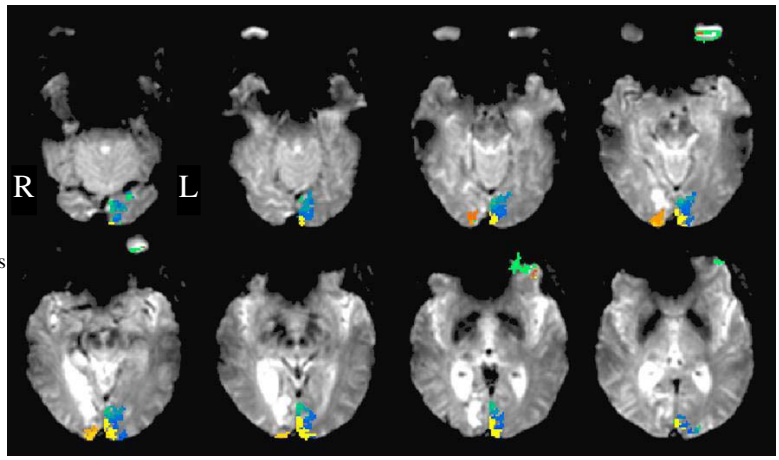

Fig. 2: Significant BOLD cross-correlations ($r>0.4$) with angular retinotopic mapping overlaid on T2*-weighted images in radiological convention. Colours correspond to the wedge positions above.