Extensive brain activation following recovery from optic neuritis: a pilot study using functional magnetic resonance imaging (fMRI)

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Introduction Optic neuritis is a common manifestation of multiple sclerosis, and is usually followed by a good clinical recovery. It provides a valuable model with which to increase our understanding of recovery mechanisms in demyelinating disease since it represents a single anatomically well-defined lesion that is readily evaluated using clinical and electrophysiological measures. Recovery has classically been attributed to resolution of optic nerve oedema and inflammation(1), but may occur despite significant and persistent conduction abnormalities(2) and axonal loss(3). This raises the possibility that cortical adaptation to a persistently abnormal visual input may play a role in the recovery process(4). We used fMRI study the cerebral response to a simple monocular visual stimulus in patients who had recovered from a single episode of unilateral optic neuritis without evidence of disseminated brain lesions.

Methods Subjects 7 patients (mean age 37.8yrs; 3 male, 4 female) and 7 normal volunteers (mean age 31.0yrs; 3 male, 4 female) were studied. The mean post-diagnosis interval was 7.9 years (range 0.5 to 14 years). On the day of study visual acuity and colour vision were measured, and formal perimeter and visual field testing performed. Visual evoked potentials (VEPs) were recorded using pattern reversal; four patients also had VEPs recorded at presentation. Imaging All imaging used a 1.5T Sigma Echospeed MRI system (General Electric, Milwaukee) equipped with a standard quadrature head coil. Echoplanar T2-weighted near-axial images of the whole brain were obtained (TR=6000ms, TE=40ms, matrix 256x256, FOV 24x24cm) together with fat-suppressed spin echo images of the optic nerve (FSE 3250/68, matrix 512x512, FOV 20cm). For fMRI 120 T2*-weighted images depicting blood oxygenation dependent (BOLD) contrast were acquired in each 8 minute experiment at each of 11 near-axial non-contiguous 5mm thick slices through the visual cortex oriented to match the structural brain images (TR=4000ms, TE=40ms, matrix 96x96, FOV 24x24cm, interslice gap 0.5mm). Experimental design Subjects passively viewed a display which alternated periodically between 20 second epochs of two contrasting conditions: (A) red 8Hz photic stimulus to the whole visual field of one eye using lightproof goggles (Grass instruments model SV10SB); (B) darkness to both eyes.

Analysis Images were corrected for head motion prior to time series analysis. Standardised power of experimentally determined signal change at the frequency of alternation between the A and B conditions was estimated by sinusoidal regression analysis of each fMRI time series in native space (5). Generic brain activation maps in the space of Talairach and Tournoux were generated by nonparametric hypothesis testing (6).

Results There were no significant differences between control and patient groups in stimulus-correlated head motion. Patients showed no evidence of abnormal eye movements and fixated normally during formal field perimetry; all had normal visual acuity and colour vision. MRI of the affected nerve was abnormal in five of seven cases, 3 of 4 patients had abnormally delayed VEPs at presentation, and 2 of the 7 had delay at follow-up. In normal controls activation in response to stimulation of either eye was demonstrated exclusively in visual cortex. However, in patients stimulating either eye activated additional areas outside the visual cortex; these additional areas were much more extensive on stimulating the clinically affected eye; preliminary group analysis in Talairach space indicates that the extra-occipital areas include the insula-claustrum, temporal and parietal cortices, corpus striatum and thalamus (fig. 1). Time series analysis revealed peak BOLD signal change in these areas to occur in the (B) phase (darkness) (fig. 2).

Conclusion In patients following optic neuritis we have demonstrated activation of multiple areas of the brain beyond the the occipital visual cortex. The location of these additional areas corresponds with sites known to have extensive visual connections, and they may represent an adaptive response to a persistently abnormal pattern of visual input. Further investigation of this unique group of patients is warranted to fully elucidate the anatomical location and temporal dynamics of the response in these novel brain areas, and their potential role in visual recovery after optic nerve demyelination.

References
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