Optic nerve mean area and magnetization transfer ratio at two years following acute optic neuritis

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Introduction

Optic neuritis is an ideal model for the study of relapse in multiple sclerosis as there are reliable clinical measures of optic nerve function, conduction in the optic pathways can be measured using Visual Evoked Potentials (VEP), and modern MRI techniques enable the lesion to be visualised. We are conducting a prospective study of acute unilateral optic neuritis with clinical assessment, VEP, and MRI of the optic nerves to quantify mean area and magnetisation transfer ratio (MTR). We now present two year data from 16 patients and 7 controls.

Methods

16 of the 21 patients and 7 of the 8 controls studied at one year were available for the two year examination but one patient was excluded from further analysis due to bilateral disease recurrence. Two patients developed optic neuritis in the contralateral eye and were therefore excluded from intra-patient affected vs unaffected analysis. The mean time from onset of optic neuritis was 2 years, 25 days. The mean time from baseline scan for controls was 2 years and 31 days. Clinical assessment consisted of pupillary and fundal examination, logMAR visual acuity, Humphrey 30-2 visual field assessment, contrast sensitivity using a Pelli-Robson chart, and colour vision using the square root of the error score of the Farnsworth Munsell 100 Hue test. Whole-field and central-field pattern-reversal VEP was measured with waveform analysis performed blind to subject identity. MRI was performed using a 1.5 T Signa machine (General Electric, Milwaukee, WI, USA) with a fat-saturated short echo fast fluid attenuated inversion recovery (sTE fFLAIR) sequence (coronal-oblique, TR=2740ms, TE=16ms, TI=1072ms, NEX 6, ETL 6, matrix size 512x384, 24x18cm field of view, 3mm contiguous slices, acquisition time 13.5 minutes)[1] and a 3D gradient echo sequence (TR 23.1ms, TE 5.6ms, NEX 2, flip angle 12º, 256x192 matrix, 19x14.25cm field of view, in-plane resolution 0.75x0.75mm, 60x1.5mm contiguous slices, acquisition time 18mins) both with and without a pre-pulse to saturate the broad resonance of immobile macromolecular protons (offset frequency 2kHz, equivalent on-resonance flip angle 500º). MTR was calculated on a voxel-by-voxel basis from the expression: 100x(Mo-Ms) / Mo percent units (pu) where Ms and Mo represent signal intensities with and without the saturation pulse respectively.[2] A quadrature birdcage head coil was used as both transmitter and receiver coil. Subjects were asked to close their eyes and avoid any deliberate eye movements during image acquisition. A single observer (SJH), experienced in interpreting optic nerve images and blinded to subject identity, carried out the image analysis on a workstation (Sun Microsystem, Mountain View, CA, USA) using the DispImage display tool.[3] The mean cross-sectional area of the intra-orbital portion of each optic nerve was derived from five consecutive 3mm slices anterior to the orbital apex by intensity-based contouring.[1] The optic nerves and optic chiasmata were segmented from the MTR maps using threshold-based contouring with the threshold fixed at 30pu to exclude partial volume voxels and the mean MTR was determined.[2] Statistical analysis was performed using the 'SPSS 10.0 for Windows' statistical package (SPSS Inc., Chicago, Ill., USA). Paired and independent samples t tests were used for the group analyses as appropriate. Analysis of correlations was by Spearman's rank correlation.

Results

Optic nerve mean area was significantly smaller in affected compared to unaffected nerves in patients (10.4 mm^2 vs 13.0 mm^2, n=13, p=0.0001) and smaller compared with control nerves, although not significantly (10.6 mm^2 vs 12.4 mm^2, n=15, p=0.072). Mean optic nerve MTR was significantly smaller in affected compared with unaffected nerves in patients (44.3 pu vs 48.2 pu, n=13, p=0.00001) and also compared with control nerves (44.6 pu vs 47.6 pu, n=15, p=0.004).

Correlation with clinical and VEP data is shown in the table (significant correlations in bold):

	logMAR visual acuity	Visual field mean deviation	Contrast sensitivity	Colour vision	Whole-field VEP amplitude	Whole-field VEP latency
Optic nerve mean area	**r = -0.58** **p = 0.025**	**r = 0.57** **p = 0.025**	**r = 0.56** **p = 0.030**	r = -0.34 p = 0.26	**r = 0.546** **p = 0.044**	**r = -0.93** **p < 0.001**
Optic nerve MTR	**r = -0.54** **p = 0.036**	**r = 0.55** **p = 0.035**	**r = 0.68** **p = 0.005**	r = -0.43 p = 0.14	r = 0.40 p = 0.16	r = -0.018 p = 0.95

Discussion

We have shown that optic nerve atrophy and reduced MTR persist at two years following an attack of optic neuritis and correlate with visual acuity, visual field mean deviation and contrast sensitivity. Interestingly, analysis of this cohort at one year did not demonstrate any correlation of these MR parameters with visual function or VEP data.[4,5] We have also shown that optic nerve area, but not MTR, correlates with VEP amplitude and latency. The remarkably tight correlation with latency could be explained biologically by a protective effect of remyelination (indicated by a shorter VEP latency) on axonal integrity thereby slowing axonal loss and atrophy. The lack of correlation of latency with MTR suggests that MTR may not be a marker for myelination alone, and could also reflect other aspects of tissue structure. Wallerian degeneration may explain an additional relationship found between reduced optic chiasm MTR and optic nerve area (r=0.52, p=0.046). Optic nerve MTR, however, did not correlate with area. We plan to continue the follow up of this cohort at three years when a longitudinal analysis will be performed.

References

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Acknowledgements

The NMR Research Unit is supported by the Multiple Sclerosis Society of Great Britain & Northern Ireland. SJH was supported by The Wellcome Trust and ATT by Action Research.