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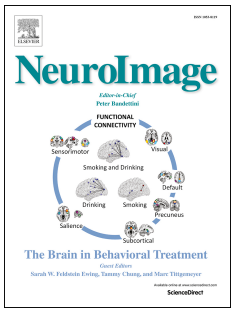

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Exploring experimental autoimmune optic neuritis using multimodal imaging

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Abstract

BACKGROUND: Neuro-axonal injury is a key contributor to non-reversible long-term disability in multiple sclerosis (MS). However, the underlying mechanisms are not yet fully understood. Visual impairment is common among MS patients, in which episodes of optic neuritis (ON) are often followed by structural retinal damage and sustained functional impairment. Alterations in the optic nerve and retina have also been described in rodent experimental autoimmune encephalomyelitis (EAE), a model of MS. Thus, investigating structural anterior visual pathway damage may constitute a unique model for assessing mechanisms and temporal sequence of neurodegeneration in MS. We used a multimodal imaging approach utilizing optical coherence tomography (OCT) and diffusion tensor imaging (DTI) to explore the mechanisms and temporal dynamics of visual pathway damage in the animal model of MS.

METHODS: 7 EAE-MOG_{35-55} and 5 healthy female C57BL/6J mice were used in this study. Ganglion cell complex (GCC) thickness was derived from an OCT volume scan centred over the optic nerve head, while the structure of the optic nerve and tracts was assessed from DTI and co-registered T2-weighted sequences performed on a 7T MRI scanner. Data was acquired at baseline, disease onset, peak of disease and recovery. Linear mixed effect models were used to account for intra-subject, inter-eye dependencies, group and time point. Correlation analyses assessed the relationship between GCC thickness and DTI parameters. Immunofluorescence staining of retina and optic nerve sections was used to assess distribution of marker proteins for microglia and neurodegeneration (nerve filaments).

RESULTS: In EAE mice, a significant increase in GCC thickness was observed at disease onset ($p < 0.001$) followed by a decrease at recovery ($p < 0.001$) compared to controls. The EAE group had significant GCC thinning at recovery compared to all other time points ($p < 0.001$ for each). Signal increase on T2-weighted images around the optic nerves indicative of inflammation was seen in most of the EAE mice but in none of the controls. A significant decrease in axial diffusivity (AD) and increase in radial diffusivity (RD) values in EAE optic nerves (AD: $p \leq 0.02$,