Macular volume determined by optical coherence tomography as a measure of neuronal loss in multiple sclerosis.

Background: Inner (area adjacent to the fovea) and outer regions of the macula differ with respect to relative thicknesses of the ganglion cell layer (neurons) vs retinal nerve fiber layer (RNFL; axons).

Objective: To determine how inner vs outer macular volumes relate to peripapillary RNFL thickness and visual function in multiple sclerosis (MS) and to examine how these patterns differ among eyes with vs without a history of acute optic neuritis (ON).

Design: Study using cross-sectional optical coherence tomography.

Setting: Three academic tertiary care MS centers.

Participants: Patients with MS, diagnosed by standard criteria, and disease-free control participants.

Main outcome measures: Optical coherence tomography was used to measure macular volumes and RNFL thickness. Visual function was assessed using low-contrast letter acuity and high-contrast visual acuity (Early Treatment Diabetic Retinopathy Study charts).

Results: Among eyes of patients with MS (n = 1058 eyes of 530 patients), reduced macular volumes were associated with peripapillary RNFL...
Thinning; 10-microm differences in RNFL thickness (9.6% of thickness in control participants without disease) corresponded to 0.20-mm³ reductions in total macular volume (2.9% of volume in control participants without disease, P < .001). This relation was similar for eyes of MS patients with and without a history of ON. Although peripapillary RNFL thinning was more strongly associated with decrements in outer compared with inner macular volumes, correlations with inner macular volume were significant (r = 0.58, P < .001) and of slightly greater magnitude for eyes of MS patients with a history of ON vs eyes of MS patients without a history of ON (r = 0.61 vs r = 0.50). Lower (worse) visual function scores were associated with reduced total, inner, and outer macular volumes. However, accounting for peripapillary RNFL thickness, the relation between vision and inner macular volume remained significant and unchanged in magnitude, suggesting that this region contains retinal structures separate from RNFL axons that are important to vision.

**CONCLUSIONS:** Analogous to studies of gray matter in MS, these data provide evidence that reductions of volume in the macula (approximately 34% neuronal cells by average thickness) accompany RNFL axonal loss. Peripapillary RNFL thinning and inner macular volume loss are less strongly linked in eyes of MS patients without a history of ON than in eyes of MS patients with a history of ON, suggesting alternative mechanisms for neuronal cell loss. Longitudinal studies with segmentation of retinal layers will further explore the relation and timing of ganglion cell degeneration and RNFL thinning in MS.