The Early MS Pathology in the Corpus Callosum by Atrophy, Magnetization Transfer and Diffusion Tensor Measures at 3T in Patients With a Clinically Isolated Syndrome and a Positive MRI

J. H. Simon[1], M. Brown[2], D. E. Miller[2], J. Bennett[3], J. Corboy[4], D. Singel[5]

[1]Radiology, University of Colorado Health Sciences Center, Denver, Colorado, United States, [2]Radiology, University of Colorado HSC, Denver, Colorado, United States, [3]Neurology and Opthalmology, University of Colorado HSC, Denver, Colorado, United States, [4]Neurology, University of Colorado HSC, Denver, Colorado, United States, [5]Psychiatry, University of Colorado HSC, Denver, Colorado, United States

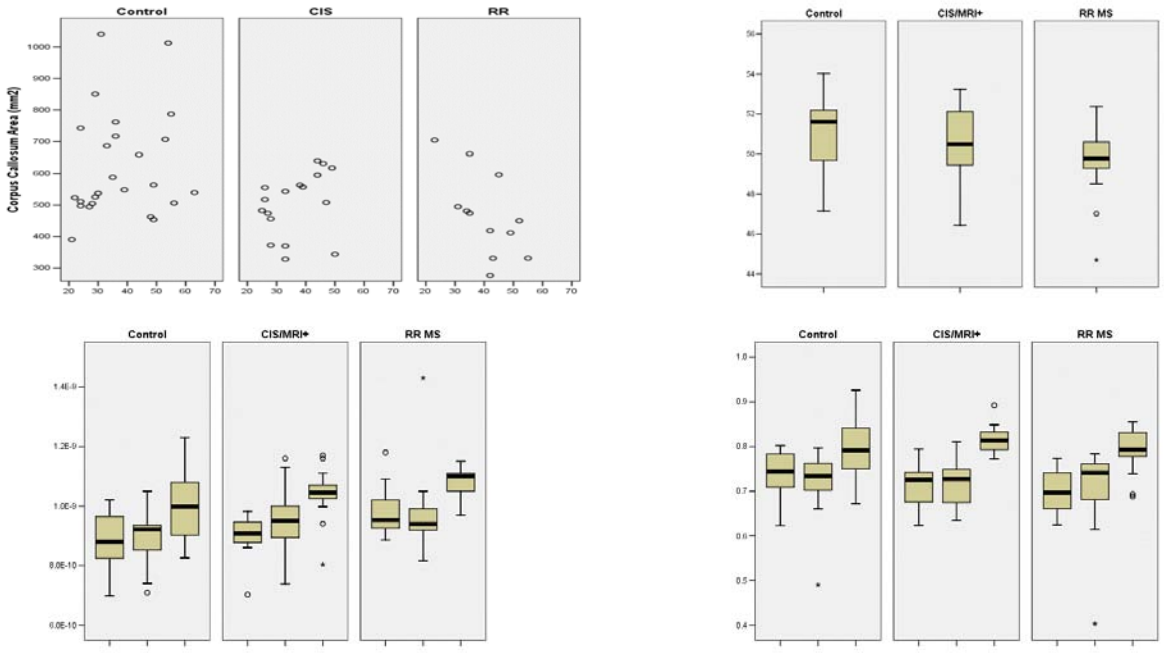
Background: The normal appearing white matter (NAWM) is abnormal in MS by multiple quantitative MRI methodologies on the basis of microscopic pathology and likely related to traversing neuronal fibers injured by distant lesions, but also we believe by artifact induced by partial volume averaging of focal lesions. The corpus callosum provides an ideal test material for evaluating the pathophysiology of early MS, as fiber direction is relatively predictable, the tissue is relatively homogeneous, and early and late injury patterns in MS have been described [1,2].

Purpose: Baseline characterization of corpus callosum from a prospective, longitudinal MRI study of changes from the earliest disease, after a clinically isolated syndrome (CIS) in patients with a positive MRI. We hypothesized that the NAWM carefully selected to be free from conventional MR detected focal MS pathology would be normal.

Methods: Patients were enrolled in a prospective longitudinal study including 17 CIS patients with an MRI showing at least 2 characteristic T2-lesions (CIS/MRI+) placing them at high risk for the development of MS [3]. A normal control group included 26 age and sex matched subjects for the primary comparisons. Secondary comparisons were based on patients with established MS (14 relapsing and 9 secondary progressive). The protocol at 3T included 3mm thick, non-gapped conventional T1/PD/T2 sequences and 3D gradient echo series with and without magnetization transfer (MT) pulse. Diffusion tensor images were acquired using a double spin-echo EPI sequence acquired with 5.1mm slices offset by 1.7 mm , 25 gradient directions and maximal b-value of 1000.

Results: For the CIS/MRI+ group, there was a small decrease in fractional anisotropy (FA) in only one of three segments (genu; p=0.037). The MT ratio of NAWM was not significantly reduced. Greater changes were seen in the RR MS patients, with decreased area (p=0.07 female; p=0.02 male), increased apparent diffusion coefficient (ADC) for three regions (p= 0.036 to 0.008), decreased FA (genu only; p = 0.017), but only borderline (not significant) decreases in MT ratio. Results for the SP MS group were inconsistent presumably reflecting the small sample size.

Discussion: Our results for this "earliest MS" enriched group suggests that apart from the focal pathology, the NAWM is normal or near normal by multiple quantitative MR analyses. As disease progresses, increased abnormality is detected in the NAWM. We know that a sizeable fraction of these callosa contain fibers that are at risk for injury as they connect to distant (non-callosal) focal MS lesions[4], but the pathology from this mechanism is dilute within the mostly normal corpus callosum in early disease. Longitudinal studies of these patients will provide a sensitive system to evaluate the pathophysiology of early injury including that from Wallerian degeneration.



Top Left Panel: Corpus callosum area by age and group. Top right panel: Group by MT ratio. Bottom left panel:ADC by Group (left genu; middle body; right splenium). Bottom right panel: FA by Group (left genu; middle body; right splenium).

1. Evangelou N, et al. Regional axonal loss in the corpus callosum correlates with cerebral white matter lesion volume and distribution in multiples clerosis. Brain, 123(9):1845–9, September 2000.
2. Simon JH, et al. Transcallosal bands: a sign of neuronal tract degeneration in early MS? Neurology, 57(10):1888–90, November 2001.
3. CHAMPS Study Group. MRI predictors of early conversion to clinically definite MS. Neurology. 2002 Oct 8; 59(7):998-1005.
4. Simon JH et al. Identification of fibers at risk for degeneration by diffusion tractography in patients at high risk for MS after a clinically isolated syndrome. JMRI, in press.

Supported by grants from the National MS Society (RG 3307-A-1), and General Electric Medical Systems.