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Correlating quantitative MR changes with pathological changes in the white matter of the cuprizone mouse model of demyelination

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Mouse brain white matter (WM) damage following the administration of cuprizone was studied weekly using diffusion tensor imaging, quantitative magnetization transfer imaging, T2-weighted MRI (T2w), and electron microscopy (EM). A previous study examined correlations between MR metrics and EM measures after 6 weeks of feeding. The addition of weekly *ex vivo* tissue analysis allows for a more complete understanding of the correlations between MR metrics and EM measures of tissue pathology.

Signal inversion is apparent in the T2w images as the number of weeks of cuprizone feeding increased. A decreased magnetization transfer ratio (MTR) is observed in the WM regions of the cuprizone mouse as cuprizone feeding continued. Many changes are observed in the *ex vivo* data including directionality changes in the external capsule in the directional encoded map of diffusion tensor imaging from weeks 1 to 6. From the EM images, myelinated axons are apparent in both cuprizone and control mice. Cuprizone is associated with oligodendroglial swelling and apoptosis.

The significant change between control and cuprizone mice in the corpus callosum peaks in T2w at week 3 whereas it peaks at week 4 in MTR. The first large change in T2w occurs between weeks 2 and 3 in the external capsule and between weeks 3 and 4 in the MTR. Radial diffusivity appears to be different between control and cuprizone mice even in week 1. The weekly changes in radial diffusivity follow a different time course than MTR and T2 in the cuprizone mouse.

The different time courses of the MR metrics suggest that T2, MTR and diffusivity are sensitive to different pathological features in WM. ANOVA will be used to determine when significant changes occur in MRI metrics. EM analysis of the tissue is in progress for correlations with WM pathology. Visually it can be seen in the EM images at week 3 that the control and cuprizone corpus callosum show a similar amount of myelinated axons. Our results are consistent with EM from other studies suggesting MTR likely reflects demyelination. The addition of the weekly *ex vivo* tissue analysis allows for a more complete understanding of the correlations between MR metrics and EM measures of tissue pathology.

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