Age Related Differences in Myelin Content Assessed Using Myelin Water Fraction Imaging

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Purpose: The corpus callosum is a commissural structure connecting the two cerebral hemispheres. In addition to the topographic arrangement, the distribution of axon diameters varies with larger diameter axons found in the splenium and predominantly small diameter axons in the genu. Larger diameter fibers are more heavily myelinated than small diameter axons and therefore the distribution of myelin content follows a similar pattern. Differences in the content of myelin in white matter tracts containing axons of the association cortices have been hypothesized to contribute to age related differences in cognition. Imaging markers sensitive to myelin content of axons in white matter may aid in elucidating the mechanisms of age related differences in cognition. In this preliminary study, we apply a 3D GRASE multi-echo sequence to investigate the myelin content in the genu and splenium in a cohort of young and old individuals.

Methods: Subjects in this study are part of a longitudinal study of healthy aging, which included 13 participants, all females except for 1 male and ranged in age from 18 to 71 years old (mean: 44.7±21.2). The young age-group was defined as 18 to 39 yrs old (N=7) and the old age-group ranged from 58 to 71 yrs old (N=6). All images were collected on 3.0T Siemens Verio system. A multi-echo sequence using 3D-GRASE with 32 echoes, inter-echo spacing = 11 ms, TR = 1,110 ms, 192x144 matrix in the axial plane, field of view = 220x165 mm^2, and 24 slices of 5 mm thick was collected. Additionally, a 1x1x1.34mm^3 resolution T_1-weighted structural images in the coronal plane were collected using MPRAGE. The T_1–weighted images were down-sampled to 1.15mm^2x2.5mm and were co-registered to a MNI template (of equal resolution), using FNIRT. Multi-echo data was sinc interpolated to 2.5mm thick slices using FLIRT. The interpolated multi-echo data was co-registered to the down-sampled T_1–weighted images using FLIRT with 6 degrees of freedom. For each region of interest two regions were sampled and were identified in MNI space using FSL (Figure 1). These regions were projected back to subject space and were used to extract the multi-echo data. Regularized NNLS was used to fit the multi-echo data with 40 logarithmically spaced T_2 values from 10-2,000 ms. The short compartment was defined as 10-40 ms (Figure 2). The generalized linear model was used to predict MWF values with age group, ROI, and age group x ROI entered as predictors. We hypothesized that independent of age group MWF would be higher in the splenium compared to the genu.

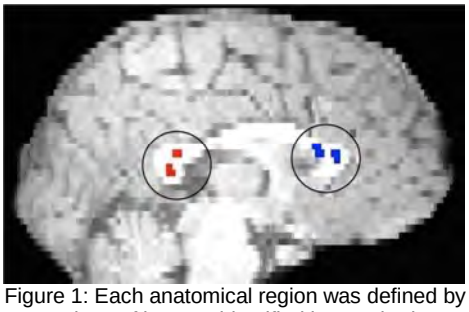

Figure 1: Each anatomical region was defined by two regions of interest identified in standard space. These regions were projected into the subject space using FNIRT. This figure demonstrates the projection of regions of interest from standard space to subject space in one subject.

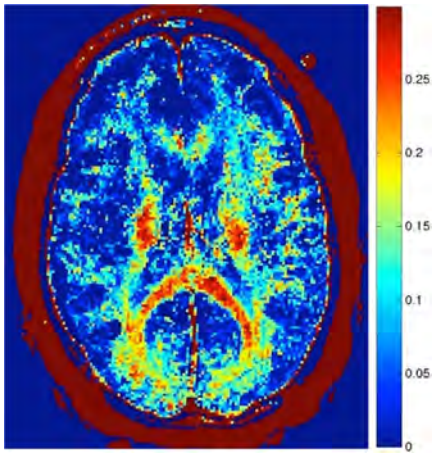

Figure 2: MWF image from the same subject as in Figure 1. The intensity reflects greater myelin content. Note the greater myelin content in the splenium as compared to the genu.

Results: The age group x ROI interaction was significant (p = 0.013). In both the younger and older groups MWF in the genu was significantly less than in the splenium (p < 0.012 and p < 0.0001, respectively) (Figure 3). MWF in the genu was not statistically different between the young and older groups (p = 0.16), however MWF in the splenium was greater in the older group (p = 0.0005).

Conclusions: We demonstrate that multi-compartment T_2 modeling recapitulates the known pattern of myelin content in the genu and splenium of the corpus callousm. Furthermore, we demonstrate that 3D GRASE combined with multi-compartment T_2 modeling is sensitive to age differences in a healthy older cohort and maybe used to characterize myelin content changes in normative aging.

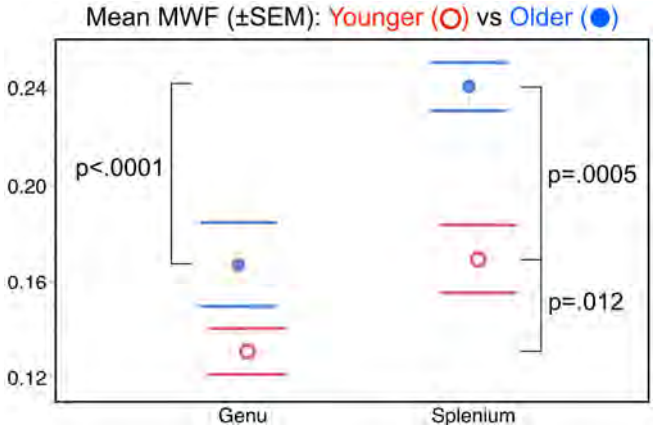

Figure 3: MWF in the genu is less than in the splenium in both age groups. MWF is significantly greater in the splenium of the older age group.

1. Aboitiz, F., Scheibel, A.B., Fisher, R.S., & Zaidel, E. *Brain Research* **11**, 143-153 (1992).
2. Mackay, A., Whittall, K., Adler, J, Li, David et al. *Magnetic Resonance in Medicine* **31**, 673-677 (1994)