Evaluation of Diffusion Kurtosis Imaging in Hypomyelinated Mouse Models

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Target Audience: Researchers in diffusion MRI and MRI relaxometry; neurologists and neuroscientists

Purpose

Diffusion kurtosis imaging (DKI) is an extension of diffusion tensor imaging (DTI) with the potential of providing additional information about white matter microstructure, including its state of myelination[1,2]. Further evaluation of the utility of DKI as a tool for evaluating white matter myelin can be done through comparison with other previously established methods of characterizing myelin. In this study, DKI measures are compared with myelin-related measures derived from multi-exponential T_2 (MET2) and quantitative magnetization transfer (qMT) in two knockout mouse models, tuberous sclerosis complex (TSC) and Rictor CKO, known to result in hypomyelination[3,4].

Methods

Normal (N=3), TSC (N=2), and Rictor CKO (N=3) P60 mice were euthanized and perfusion-fixed with 2.5/2% glutaraldehyde/paraformaldehyde + 1 mM Gd-DTPA in phosphate-buffered saline (PBS)[5]. Mouse brains were excised and post-fixed, and then washed in PBS + 1mM Gd for ≥1 week before imaging. Imaging was performed on a 15.2T 11-cm bore Bruker scanner with FOV = 19.2 x 14.4 x 10.8 mm^3 and matrix size = 128 x 96 x 72 for an isotropic resolution of 150 µm. The DKI scan used a 3D diffusion-weighted fast spin-echo sequence with TR/TE/ESP = 200/19.0/7.1 ms and ETL = 4. Pulsed-gradient diffusion weighting was achieved with δ/Δ = 5/12 ms, b = 0, 3000, 6000 s/mm^2, 30 directions, and 2 signal averages with gradient polarity reversal for a scan time of ≈ 12h. Diffusion and kurtosis tensors were estimated voxel-wise using a constrained linear least-squares approach[6], and then fractional anisotropy (FA), mean, axial, and radial diffusivity (MD, AD, and RD), and mean, axial, and radial kurtosis (MK, AK, and RK) were calculated. MET2 data were acquired using a 3D Extended Phase Graph (EPG)-compliant multi-spin echo sequence with a scan time of ≈ 6h. T_2 spectra were estimated voxel-wise using an EPG-signal model for B_1 insensitive fitting[7] and myelin water fraction (MWF) was extracted. 3D qMT data were collected using a selective inversion-recovery (SIR) fast spin-echo sequence[8] requiring a scan time of ≈ 3.5h and macromolecular pool size ratio (PSR) was estimated voxel-wise. White matter ROIs were manually delineated on 2D cross-sections and group ROI means of each DKI parameter were correlated with both MWF and PSR.

Results and Discussion

Figure 1 shows correlation plots between DKI indices and both MWF and PSR for white matter ROIs in normal and Rictor CKO mouse brains. MK has the strongest correlation with MWF and RK has the strongest correlation with PSR across white matter ROIs compared with other diffusion parameters. This indicates that DKI indices, specifically MK and RK, correspond better with MWF and PSR overall than conventional DTI parameters and could lead to improved myelin characterization. Additionally, DKI was able to detect changes in both the TSC and the Rictor CKO mouse models as they showed decreases in FA, MK, and RK and an increase in RD.

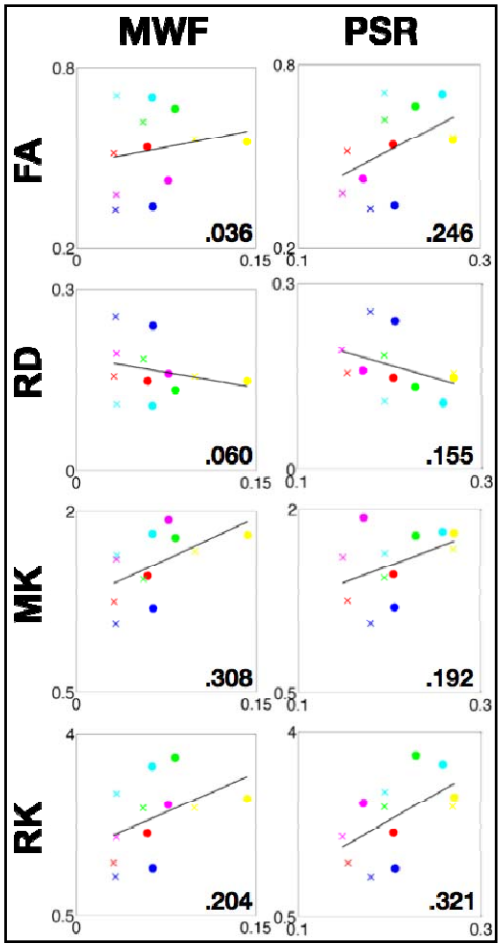

Figure 1. Correlations between DKI parameters and both MWF and PSR. Control means are represented with circles, CKO means are represented with x's. R^2 is shown in the lower righthand corner of each plot. Group means were calculated across 6 ROIs: EC = External Capsule (blue), FI = Fimbria of the Hippocampus (green), F = Fornix (red), AC = Anterior Commissure (cyan), CC = Corpus Callosum (magenta), and IC = Internal Capsule (yellow)

Conclusion

This study utilized hypomyelinated mouse models to evaluate the potential of DKI in the assessment of myelin content. Comparison of DKI parameters to MWF, PSR, and histology provides valuable insight into the relationship between DKI metrics and myelination.

References

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