

Can next-generation diffusion MRI metrics of anisotropy provide new biomarkers of TBI?

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Introduction

A new class of non-Gaussian diffusion MRI methods has emerged in recent years that promises to extend the utility of diffusion imaging for basic research and potentially clinical use. These new methods may be particularly relevant for the study of TBI given the robust changes to the tissue microenvironment and anatomical organization of the brain that follow injury. From these models, numerous scalar metrics are generated, each quantitatively describing water diffusion in a different way. An important subset of these metrics across all modeling approaches describes the geometrical features of tissue (e.g. anisotropy, dispersion). The best known example is the fractional anisotropy (FA) metric of DTI, which has already been shown to change sensitively following TBI in humans and animal models. Newer modeling approaches and anisotropy/dispersion metrics (namely: kurtosis FA - KFA, propagator anisotropy - PA and orientation dispersion index - ODI) may confer greater sensitivity and/or specificity than FA, however these newer metrics will also have different vulnerability to noise and experimental design (e.g. DWI sampling scheme). In the context of TBI research, we must understand if more advanced diffusion models can offer new information and biomarkers. Furthermore, we must also know the relationship of the newer metrics to the quality and experimental design of the DWI data. The objective of this abstract is to compare anisotropy metrics and markers from diffusion tensor imaging (DTI), diffusion kurtosis imaging (DKI), mean apparent propagator MRI (MAP-MRI) and neurite orientation and dispersion distribution imaging (NODDI) in same high-quality ex-vivo diffusion data sets from mouse and ferret brains following injury.

Methods

High-resolution ex-vivo DWI data sets with comprehensive diffusion sampling were selected from studies of mild controlled cortical impact (CCI) in the mouse (n=16) and ferret (n=10). For each species, brains were obtained and imaged ex-vivo for control and 24h-4weeks post-CCI. Diffusion MRI acquisition was performed at 7T using a 3DEPI pulse sequence. The spatial resolution for mouse and ferret imaging was 100 and 250 micron isotropic respectively and the diffusion parameters were $b=100-10,000$ s/mm² and included 297 DWI volumes. The TORTOISE software package was implemented for pre-processing corrections and then four models were applied to the data sets: DTI with TORTOISE, DKI with the DKE software, MAP-MRI with custom IDL software and NODDI using the NODDI Matlab toolbox. To inspect the effects of noise and experimental design on the different models in a subset of brains, the corrected data sets were subject to either noise manipulation or subsampling and the models re-run.

To determine and describe abnormalities in anisotropy metrics of FA, KFA, PA and ODI, two main analysis approaches were used: 1. individual whole brain 2D histograms to directly compare KFA, PA and ODI with FA and 2. voxelwise group comparisons between each time point and the control group.

Results and Discussion

The analysis of anisotropy metric abnormalities following CCI in the mouse and ferret brain across diffusion models has provided a systematic foundation to understand the benefits and costs of advanced diffusion modeling in TBI research. Several initial observations of this work suggest that KFA, PA and ODI each report information that is different from FA both in the normal brain and the injured brain. For example, ODI appears to be more specific to tissue architecture while PA is more specific to microstructural features of tissue. In voxelwise analysis of the injured brain, both similarities and differences were found between the newer anisotropy metrics and FA underscoring both the complexity and promise of these metrics to identify and describe abnormalities. Importantly, we also found each modeling approach to be differentially vulnerable to the effects of image quality and experimental design with consequences for the utility and effective implementation of the different models. While no single model or metric can fully describe all tissue environments, a better understanding across modeling approaches will provide more effective diffusion MRI tools for TBI research.