Evaluating the feasibility of quantifying longitudinal microstructural changes in mild traumatic brain injury (mTBI) with MAP-MRI

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Synopsis

Mean Apparent Propagator (MAP) MRI, an expansion of diffusion tensor imaging (DTI), explicitly measures the distribution of net 3D displacements of diffusing water molecules, providing better delineation of crossing white matter fiber tracts. This characteristic may be useful in characterizing unseen microstructural damage in patients with mild traumatic brain injuries whose clinical imaging scans are otherwise normal. An image processing pipeline for using mean apparent propagator (MAP) MRI to analyze diffusion weighted images in mTBI patients has been validated in healthy controls and shown to generate reliable data for patient brain scans.

Introduction

Conventional diffusion tensor imaging (DTI) is a promising method for evaluating traumatic brain injury (TBI), but DTI-derived parameters have been shown to be inconsistently correlated with clinical symptoms/course, especially in mild cases[1]. DTI uses a Gaussian model to quantify the diffusion of water molecules in the brain, which does not specifically describe restricted diffusion processes due to microstructural features such as cell membranes, organelles, and lipid compartments. Mean Apparent Propagator (MAP) MRI explicitly measures the distribution of net 3D displacements of diffusing water molecules without assuming a Gaussian model[2]. MAP-MRI provides better delineation of crossing white matter fiber tracts, and has been shown to be feasible in evaluating healthy controls[3], Parkinson's disease[4], temporal lobe epilepsy[5], brain masses[6], and ischemic stroke[7]. Mild TBI (mTBI) has been difficult to characterize with structural imaging due to variations in injury severity, location, and clinical course[8]. Group analysis can obfuscate significant changes on an individual level; the clinical and scientific utility of brain imaging lies in longitudinal comparison[9]. We aim to develop a robust pipeline by which MAP-MRI parameters can be calculated and analyzed in patients with mTBI to describe the evolution of microstructural brain injury compared to their clinical symptoms, setting the stage to evaluate the potential clinical utility of MAP-MRI parameters to characterize healthy and injured states of the brain.

Methods

Patients were recruited between age between 15-50 years and a clinical diagnosis of mTBI with Glasgow Coma Scale (GCS) ≥ 13. mTBI was defined as a low-velocity injury that results in clinical symptoms. Patients were enrolled at either Encounter 1 (E1), within 72 h, or Encounter 2 (E2), 5–10 days post-trauma. They returned for a maximum of 4 encounters over 3 months. Encounter 3 (E3) occurred at 15–29 days and Encounter 4 (E4) at 83–97 days. MR images were collected on 3T GE Signa MR750 scanners with a 32-channel brain radiofrequency coil (Nova Medical) from 2014-2015. Images acquired included sagittal MP-RAGE 3D T1 (matrix: 284x284x180, FOV = 25.6cm, slice thickness = 0.9mm, flip angle = 8 degrees, TR/TE/TI = 8.1ms/3.3ms/1100ms, scan time = 4:33); sagittal 3D T2 FLAIR (matrix: 256x256x164, FOV = 25.6cm, slice thickness = 1.0mm, ETL = 200, TE/TR = 119ms/6800ms, scan time = 5:50) ; axial diffusion MRI (single spin echo, matrix: 96x96x21, FOV= 24cm, slice thickness = 2.5mm, flip angle = 90 degrees, TR/TE = 2,600ms/~77ms 140 directions distributed on three shells-25,40,75 directions per shell-with b-values 800,1200,2800 mm2/s with 7 interspersed T2 volumes, scan time = 6:56);
Controls underwent neurological assessments and MR imaging at initial and follow-up visits between 7-90 days, with an average of 3 weeks between the initial and follow up encounters. A subset of available healthy control images was then selected to validate the pipeline, consisting of 5 separate individuals, each with scans corresponding to the initial and follow up visit. Diffusion weighted images (DWI) were registered to the corresponding T_2W (B0) image and corrected for motion/eddy current distortion[10] and skull-stripped[11]. MAP-MRI and DTI parameters were calculated from the corrected DWI data. Segmentation and cortical parcellation maps were generated on the T_1W MP-RAGE scan[12] and registered to the diffusion image space13. The entire image processing and analysis pipeline is depicted in Figure 1. ROI analysis for the segments of interest were performed with Matlab. Test-retest variability was compared for propagator anisotropy (PA) and fractional anisotropy (FA) in three regions of the brain: cerebral white matter (WM), thalamus, the rostrum/splenium of the corpus callosum, and the entorhinal cortex.Longitudinal analysis at the timepoints described was also performed for the areas listed above for a representative patient and matched control.

Results

Representative MAP-MRI images from one healthy control as compared to their DTI counterparts are shown in Figure 2. Repeat scans of healthy controls showed minimal variability between E1 and E2 in the MAP-MRI PA image, comparable to the corresponding DTI FA image in cerebral white matter, thalamus, and entorhinal cortex (Figure 3). The PA images showed decreased variability in the rostrum/splenium of the corpus callosum as compared to the FA. In Figure 4, scans from a mTBI patient (who was not fully recovered by the end of the study) at encounters 2, 3, and 4. are shown alongside those from a matched control.

Discussion/Conclusions

The MAP-MRI images of healthy controls show improved contrast between grey and white matter areas, as well as increased delineation of WM

tracts, when compared to their DTI counterparts. This pipeline was shown to perform well on externally acquired data, with test-retest variability comparable or improved upon from conventional DTI in both subcortical and cortical structures. MAP-MRI is a promising method by which microstructural changes in patients with mTBI can be evaluated, showing improved test-retest variability in WM tracts compared to FA. Improved conspicuity of WM tracts can be used to assess subtle changes in these brain structures over time. With this image and analysis pipeline in place, further work is now needed to analyze longitudinal changes in specific WM tracts and their projections throughout the brain, rather than performing ROI analysis of discrete brain structures. Additionally, MAP-MRI can be used to derive microstructural parameters from many dMRI techniques including DTI and diffusion kurtosis imaging (DKI)[14] .

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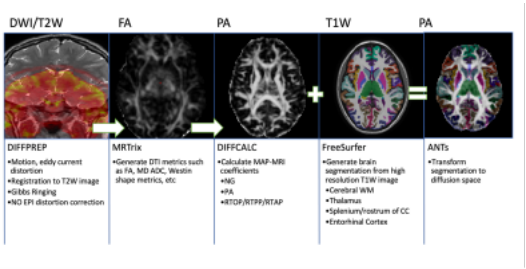
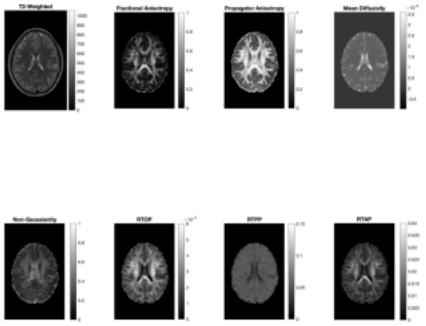
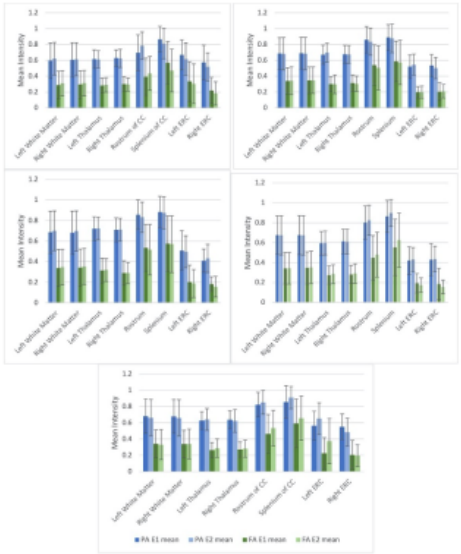
Figures



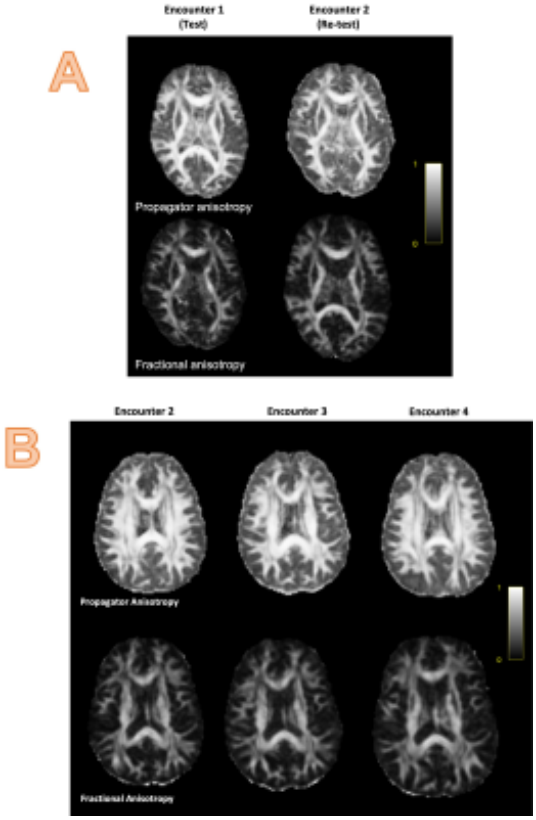
Schematic of MAP-MRI image processing pipeline.



Representative T2W, DTI, and MAP-MRI images from a healthy control. DTI parameters shown include fractional anisotropy and mean diffusivity. MAP-MRI parameters depicted include propagator anisotropy (PA), non-gaussianity (NG), return to origin probability (RTOP), return to axis probability (RTAP), and return to plane probability (RTPP). The images show improved grey-white matter contrast and delineation of white matter tracts, especially in the PA/RTOP/NG images.



Test-retest variability for 5 control subjects scanned at two separate encounters (E1 and E2). Propagator anisotropy (PA) and fractional anisotropy (FA) were compared for left cerebral white matter, right cerebral white matter, left thalamus, right thalamus, rostrum of the corpus callosum (CC), splenium of the corpus callosum (CC), left entorhinal cortex (ERC) and right entorhinal cortex (ERC). Test retest variability was comparable in all control subjects for cerebral white matter, thalamus, and entorhinal cortex, and improved for corpus callosum.



Longitudinal propagator isotropy data and fractional anisotropy data for matched control (A) and patient (B). The patient had Sport Concussion Assessment Tool (SCAT2) composite scores of 53, 51, 28 at each encounter respectively and exited the study unrecovered. The increased resolution in white matter tracts provides more information for deeper analysis.