Abstract #07626 ISMRM ABSTRACT

[USGOV] Assessment of Voxelwise Longitudinal Changes in Tissue Microstructure Measured with MAP-MRI following mTBI

Primary: Neuro - Traumatic Brain Injury **Secondary:** Diffusion - DWI/DTI/DKI **Presentation:** Digital Poster, Oral, PowerPitch Oral, Traditional Poster
Keywords: TRAUMATIC BRAIN INJURY CLINICAL APPLICATION DIFFUSION-WEIGHTED MRI LONGITUDINAL STUDIES MAP-MRI

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Impact

Longitudinal monitoring of within-subject MAP-MRI changes may provide a more comprehensive means to study pathological alterations that evolve at multiple timepoints following mTBI, where current cross-sectional studies of image-based biomarkers lack the sensitivity and specificity to predict outcome.

Synopsis

Motivation: Radiological assessments of mild traumatic brain injury (mTBI) are often limited in their ability to detect subtle alterations in tissue due to largely cross-sectional study designs that obscure signal changes in heterogenous patient populations.

Goals: A multi-center, longitudinal mean apparent propagator MRI (MAP-MRI) study is proposed to address these limitations and perform assessments at a voxel-wise level.

Approach: Voxel-based maps of within-subject differences in the propagator and MAP-MRI metrics were evaluated at three time differentials up to 90 days post-mTBI.

Results: Changes in diffusion propagator metrics generally had signal change on the order of five percent while anisotropy influenced the distance between propagators.

Introduction

Mild traumatic brain injury (mTBI) is a signature injury in civilian and military populations, which is characterized by smicrostructural tissue changes such as edema, gliosis, and axonal injury[1-3]. Longitudinal MRI studies could provide valuable insights into the progression of subtlr spatiotemporal changes in radiological outcomes that are typically obscured due to cross sectional study designs[4]. Mean apparent propagator (MAP) MRI[5] quantifies the 3D net displacement distribution of water molecules using clinical acquisitions[6]. We aim to refine a MAP-MRI analysis pipeline to aid in characterizing the spatiotemporal evolution of tissue microstructure changes following mTBI.

Methods

A pilot dataset was selected from MR images (3T GE Signa MR750, 32 channel RF coil, Nova Medical) that were previously acquired[7] from 2015-2018 across six sites in mTBI patients (aged 15-50; Glasgow Coma Scale ≥ 13) and neurologically healthy controls (age 15-50). Patients were scanned at four encounters (E_1 - <72 hours; E_2 – 5-10 days; E_3 – 12-16 days; E_4 - 83-97 days) post-trauma. 2D axial diffusion weighted MRI data (single spin echo, matrix: 96x96x21, FOV= 24cm, slice thickness = 2.5mm, α= 90°, TR/TE = 2,600ms/~77ms three shells-25,40,75 directions per shell with b-values 800,1200,2800 s/mm^2, 7 interspersed b=0 s/mm^2 weighted volumes, scan time = 6:56 min) was corrected for motion/eddy current distortion and skull-stripped[9]. The sagittal 3D T1-weighted MP-RAGE (matrix: 284x284x180, FOV = 25.6cm, slice thickness = 0.9mm, α= 8° TR/TE/TI = 8.1ms/3.3ms/1100ms, scan time = 4:33 min).

The pipeline (Figure 1) implemented for longitudinal MAP-MRI analysis provided a sample size of 95 participants (64 controls/31 mTBI). Patients were excluded from analysis through an automated outlier detection algorithm that examined signal dropout across axial, coronal and sagittal slices. Diffusion data across the encounters were registered on a within-subject basis by using the T2-weighted image from the final encounter (E_4) as the structural reference for

motion and eddy current distortion corrections in TORTOISE[8]. In parallel, the T1-weighted volume from E_4 was used to perform tissue segmentation in Freesurfer[9]. Segmentation maps were transformed to the native diffusion space and smaller regions were combined and eroded in 3D using a custom script in Matlab to generate eleven segmented regions of interest (ROIs) – corpus callosum, left cortical white matter, right cortical white matter, thalami, putamen, caudate, amygdala, hippocampi, pallidum, left cortical gray matter and right cortical gray matter. Following estimation of the diffusion tensor and associated metrics (fractional anisotropy - FA, mean, axial and radial diffusivities), the propagator and associated metrics including propagator anisotropy (PA), return-to-origin probability (RTOP) and Non-Gaussianity were estimated with reference to the diffusion tensor from the final visit. The percent difference between DTI and MAP-MRI metrics at each visit relative to E_4 with respect to the mean across all encounters and absolute distance between the propagators at each visit relative to E_4 were computed on a voxel-wise basis for each participant. The median values of the difference (MAP-MRI metrics) and the absolute distances (propagator-derived) within each ROI were used as the summary statistic for each participant.

Results

Figure 2 shows the thresholded percent difference in DTI and MAP-MRI metrics in an exemplar control and mTBI subject at three time intervals (E_1vE_4, E_2vE_4, E_3vE_4). Percent changes in PA were near zero in large white matter tracts and had similar magnitude and direction in gray matter, while other tensor and diffusion propagator parameters were more variable across voxels. Figure 3 shows absolute distance (total variation) between the diffusion propagator and the mean distance across the same time difference intervals in the same participants as Figure 2. The distance was largest in white matter tracts such as the corpus callosum and corticospinal tract.

Discussion and Conclusions

Percent change in PA were most stable when measured in white matter. Voxel-based distance between diffusion propagators tended to be largest in these tracts in control and mTBI subjects and is likely driven by anisotropic microstructure and fiber orientation. Additional regions that were prone to variation can be attributed to CSF and cardiac pulsation.

This work illustrates an approach to perform longitudinal assessment of alterations in MAP-MRI parameters, as well as direct assessment of distances of the propagator between visits after mTBI. Our revised pipeline includes a within-subject registration that enables voxel-based computation of differences between the diffusion propagator and associated metrics. Future directions include application of this pipeline to datasets that are better suited for MAP-MRI estimation, and the use of the longitudinally registered metrics in the development of a convolutional neural network for direct image-based differentiation between mTBI patients and controls.

Acknowledgements

This work was supported by the Intramural Research Program (IRP) of the Eunice Kennedy Shriver National Institute of Child Health and Human Development and partially funded by the Department of War in the Military Traumatic Brain Injury Initiative (MTBI2) under award 309698-4.01-65310. Disclaimer The authors have no conflicts of interest to disclose. The views, information or content, and conclusions presented do not necessarily represent the official position or policy of, nor should any official endorsement be inferred on the part of, the Uniformed Services University, the Department of War, the U.S. Government or the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.

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Figures and Tables

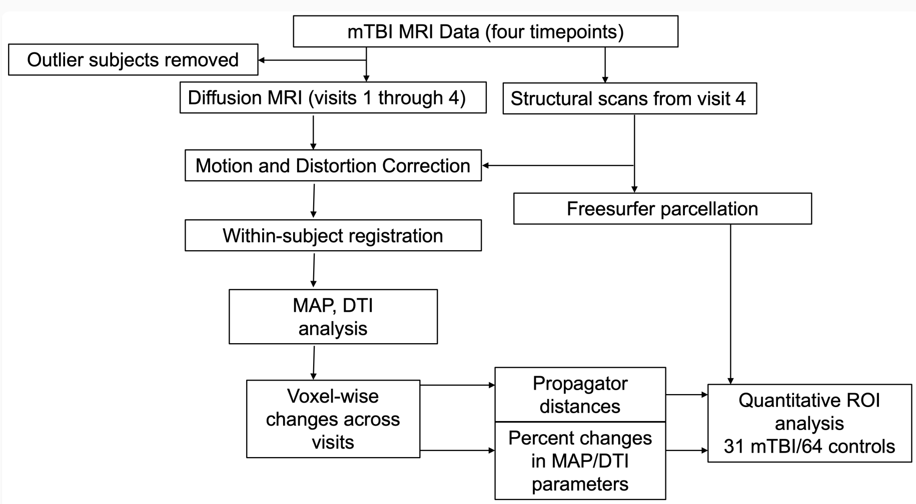

Figure 1: Figure 1. Longitudinal MAP-MRI analysis pipeline for evaluation of spatiotemporal changes following mTBI. *Diffusion MRI data from four timepoints up to 90 days post-injury was registered within-subject to data from the final visit. ROIs were used to summarize spatial patterns of voxel-based differences in the diffusion propagator and diffusion MRI metrics. Abbreviations: mTBI – mild traumatic brain injury; MAP – mean apparent propagator; DTI – diffusion tensor imaging; ROI – region of interest.*

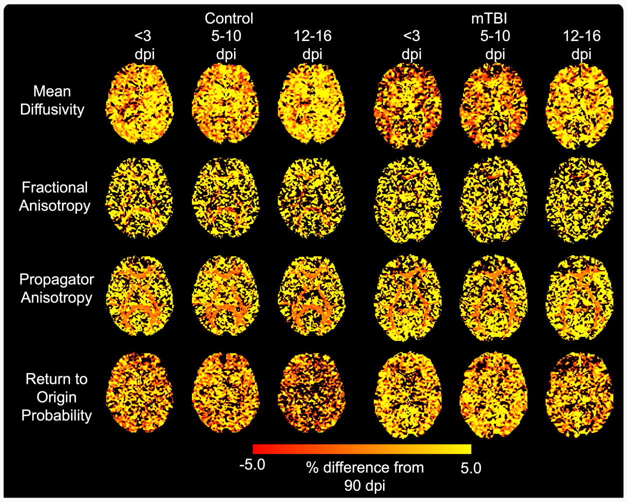

Figure 2: Figure 2. Longitudinal alterations in tissue microstructure revealed by voxel-based percent changes in propagator metrics across encounters. *The voxel-based percent difference of tensor and diffusion propagator metrics at each scan relative to 90 days post injury (dpi) and normalized across all four scans in an exemplar control and mTBI subject. Values are thresholded between -5.0 and 5.0%. Abbreviations: mTBI – mild traumatic brain injury.*

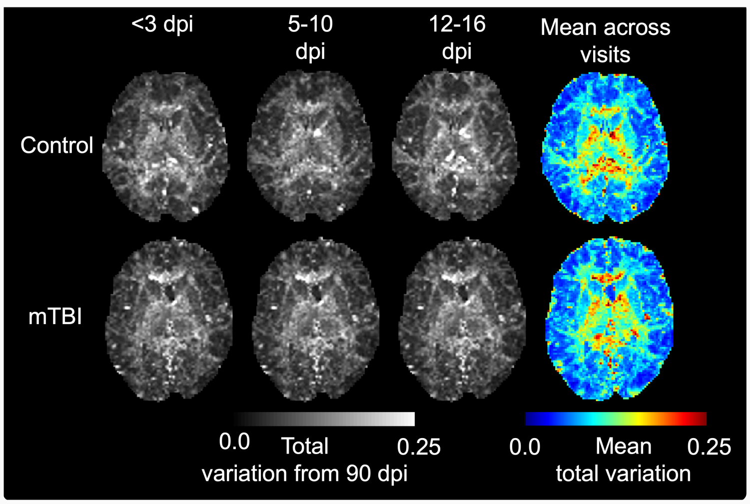

Figure 3: Figure 3. Longitudinal changes in tissue microstructure shown by voxel-based diffusion propagator distance maps across encounters in exemplar participants. *Voxel-based total variation measured the distance between diffusion propagators at three encounters from <3 to 16 days dpi relative to the final encounter (90 dpi) and the mean across visits. Units of total variation are dimensionless. Abbreviations: mTBI - mild traumatic brain injury; dpi - days post injury.*