Post-Traumatic Mean Apparent Propagator MRI: Reaching Beyond Gaussian Diffusion to Image Cortex Abnormalities Following Injury in the Mouse Brain.

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Diffusion MRI is a useful tool to investigate post-traumatic abnormalities in microstructure. Standard approaches, such as diffusion tensor imaging (DTI), require the assumption that diffusion is Gaussian, however in brain tissue the true microstructural environment is far more complex. Recent methods including mean apparent propagator (MAP) MRI provide a framework that characterizes the non-Gaussian components of water diffusion and thereby provide a new set of MRI "stains" to detect and better describe brain abnormalities that may not be evident from Gaussian approaches. In this work, we have applied MAP-MRI to characterize post-traumatic cortex abnormalities in the mouse brain.

METHODS

A total of 13 perfusion-fixed mouse brains were obtained at different time-points following CCI (24 hours, 1 week, 4 weeks, 12 weeks and uninjured) and imaged using a 7T Bruker microimaging system. For each specimen, image volumes were acquired with 100-micron isotropic resolution using 3D-EPI and the following diffusion weighted shells were collected: b(# directions)=1700(32), 3800(32), 6700(56) and 10,000(87) s/mm2.

Each set of images was processed using the TORTOISE pipeline for realignment, artifact correction and DTI modeling. The diffusion displacement profile was modeled using the MAP-MRI algorithm implemented in IDL and quantitative maps for return to the origin, axis and plane probabilities (RTOP, RTAP and RTPP, respectively), non-Gaussianity (NG), and propagator anisotropy (PA) were computed. ROI analysis of cortical regions and visualization of orientation distribution function (ODF) glyphs were performed.

RESULTS AND DISCUSSION

DTI abnormalities confirmed previous descriptions and included increased diffusion of the perilesional cortex (PLCX) in the 24 hour group and reduced diffusion in later time-point groups. The FA in the PLCX was increased as early as 1 week and persisted for all later time points. The cortical FA in distant regions was also elevated at 4 and 12 week time points.

The RTOP and related metrics may be interpreted as a measure of water restriction or inverse pore size, with higher values indicative of greater restriction. In the PLCX, RTOP was low at 24 hours and increased at all later time points, suggesting long term microstructural change toward greater restriction of water in this region.

The NG and related metrics report the deviation of the diffusion propagator from Gaussian diffusion and may increase with several factors including the presence of multiple compartments and complex arrangement of oriented structures. This measure

demonstrated a more complicated spatial pattern than the others, but was found to be modestly increased in the PLCX for all injured groups.

Another notable finding was a linear-shaped abnormality appearing in the frontal cortex bilaterally and penetrating form the cortical surface through the white matter. Between 1 and 6 instances per brain were observed for 4/6 brains from the 4 and 12 week groups, however no brains from earlier time points demonstrated this abnormality. The T2W image was unremarkable for this marker and DTI metrics showed low and isotropic diffusion. An interesting feature of this pathology was remarkably high NG and RTOP values suggesting highly restricted water diffusion.

In addition to the above scalar values, MAP MRI provides a richer description of the three-dimentional shape of the diffusion propagator than that provided by the diffusion ellipsoid obtained from DTI analysis. Visualization of ODF glyphs in the cortical tissue demonstrated a spatially dependent and changing complexity of the microstructural environment following CCI. For example, the ODF profile in previously determined “prolate” and “oblate” subdomains of the perilesional tissue were confirmed by the underlying ODF profile and the complexity of the ODF glyphs was demonstrably increased from 1 to 4 weeks post-CCI.

CONCLUSION

This work is an important first step in translating recent advances in higher-order diffusion modeling to identification of new markers in experimental models of brain injury. While ongoing histological validation of DTI and MAP-MRI indices will undoubtedly improve our understanding of the underlying mechanisms, the extension of diffusion MRI analysis beyond a Gaussian framework appears to be useful in the investigation of post-traumatic tissue change.