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Diffusion tensor “MRI-microscopy” of structural abnormalities in the mouse cortex at 4 and 12 weeks following CCI.

Diffusion tensor MRI (DTI) at high spatial and diffusion weighting resolution was performed in the fixed mouse brain to investigate the presence and nature of microstructural abnormalities at 4 and 12 weeks following controlled cortical impact (CCI).

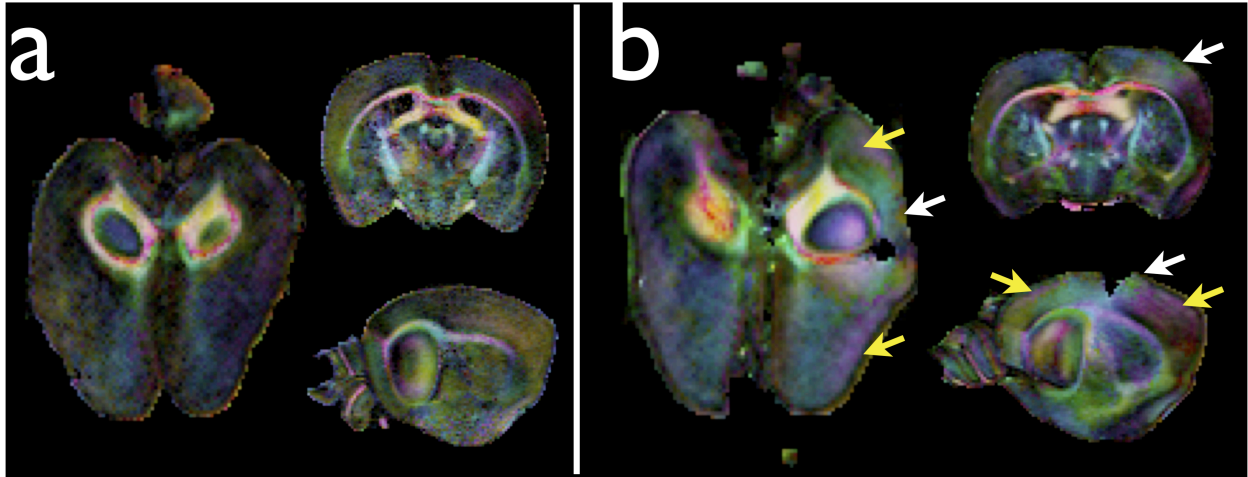
DTI images were acquired at 7T using a 3D-EPI sequence to obtain 452 image volumes per scan with isotropic spatial resolution of 100 microns and diffusion weighted shells of  $b = 400, 1700, 3800, 6700$  and  $10,000 \text{ s/mm}^2$  for perfusion fixed mouse brains taken 4 or 12 weeks following mild CCI as well as for a control brain.

Both the raw diffusion weighted images and processed DTI maps, were of remarkably high quality and several notable abnormalities were observed at both time points following CCI, including:

- 1) A peri-lesional region of tissue with abnormally increased anisotropy was observed approximately 1mm in extent from the cavity wall with principal orientation radial to the cavity wall.
- 2) In cortical regions on the same side of injury, but not near the lesion, anisotropy was also abnormally elevated. It was greatest for the 12 week specimen.

The degree of detail demonstrated in high resolution DTI maps of the injured mouse brain has revealed previously unobserved microstructural abnormalities that exist following CCI. Ongoing work is to reproduce these observations, characterize additional time points and examine the underlying mechanisms by comparison to histology. This work demonstrates the utility of DTI “microscopy” for basic research and its promise for developing TBI-related imaging biomarkers.

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**Figure** Hi-resolution DTI maps of control (a) and CCI injured (b) mouse brains. DEC maps show fractional anisotropy (brightness) and tissue orientation (color), which are abnormal for the cortex of the CCI injured brain on the side of injury both in the perilesional area (white arrows) as well as in more distant cortical regions (yellow arrows).