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Identification of microstructural subdomains by diffusion MRI microscopy in the perilesional cortex following controlled cortical impact in the mouse

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Abstract:
Objectives: Following focal brain trauma, multiple and evolving cellular and tissue changes affect the microstructure of the perilesional brain tissue. Some of these changes indicate damage while others are associated with a protective or regenerative response. The purpose of this work was to use high resolution diffusion MRI of ex-vivo mouse brains taken at variable times following controlled cortical impact (CCI) to identify distinct MRI markers of tissue changes, validate them with histology in the same brains and characterize their spatial pattern and evolution after injury. Methods: A total of 19 perfusion-fixed mouse brains were obtained following mild CCI at 24 hours, 1 week, 4 weeks or 12 weeks, controls were surgically naive. For each brain, 297 diffusion weighted MRI volumes were collected with b-values ranging from 100 to 10,000 s/mm2. The resolution of these images was 100 microns isotropic. Standard diffusion tensor imaging (DTI) maps of fractional anisotropy (FA) and mean diffusion (MD) were calculated as well as mean apparent propagator (MAP) index maps, including return to the origin probability (RTOP), which probes water restriction. Histological processing is ongoing. Results: Both DTI and MAP-MRI revealed spatially distinct and highly reproducible abnormalities in the perilesional cortex (PLCX) following injury. Abnormal MD values were most prominent at 24 hours post-CCI with a central region of high MD surrounded by a region of low MD that extended for several mm. At the edge of this low MD region there was a distinct thin band of high RTOP. At later time points MD was low and RTOP was high in a thin band near

the cavity. FA abnormalities were non-overlapping with MD and RTOP abnormalities. At 24 hours, FA was low on the side of injury, but at 1 week a distinct patch of increased FA was evident. At 4 and 12 weeks all brains demonstrated a region of high FA that encapsulated the cavity and extended several mm in all directions. Tissue orientation within this region was radial to the cavity wall and comparison with glial fibrillary protein (GFAP) indicated only partial overlap of oriented astrocytes and high FA. Conclusions: We have used high-resolution diffusion MRI to identify subregions within the perilesional cortex that differ in diffusion based metrics. In particular, MD, FA and RTOP appear to offer complementary and non-overlapping information about the altered structural environment. Ongoing histological validation promises to better define the source of diffusion changes in the identified subdomains. In this study, diffusion MRI microscopy has demonstrated sensitivity to the spatial organization of cellular changes that follow brain injury.
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