Diffusion tensor imaging shows decreased diffusivities in the developing brain after mild trauma

P. V. Bayly[1], E. E. Black[1], S-K. Song[2]

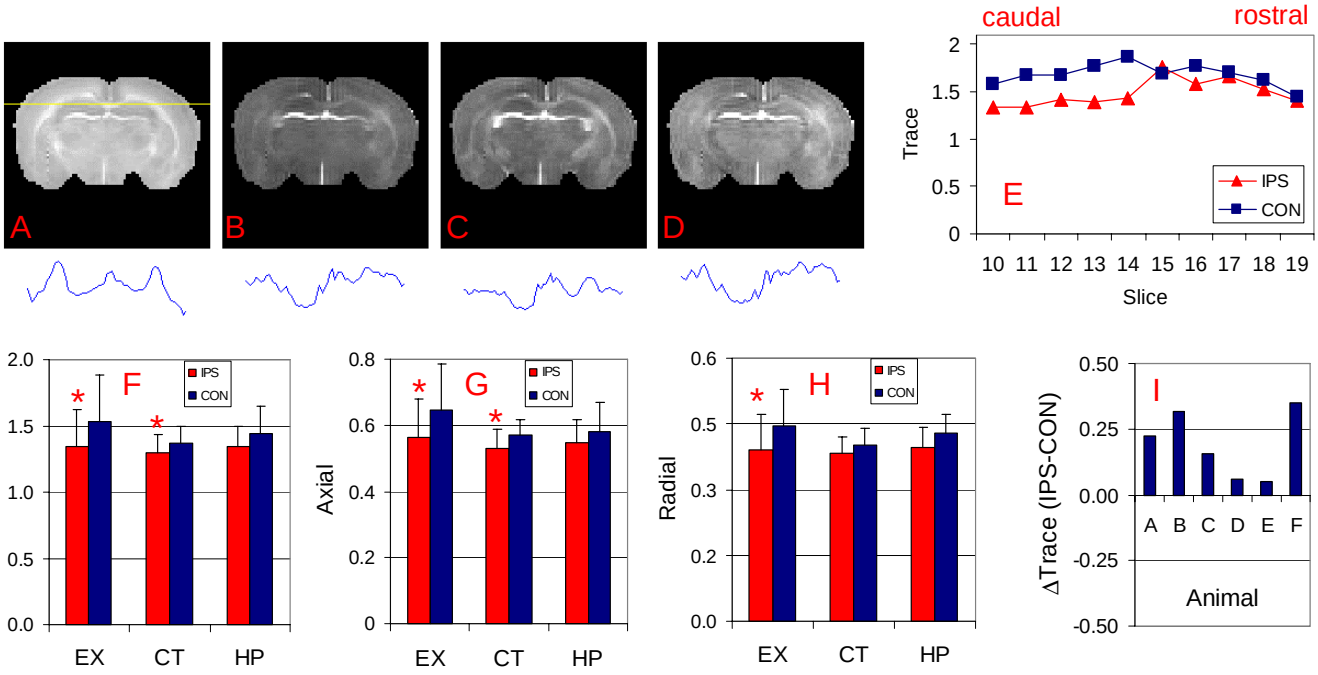
[1]Mechanical Engineering, Washington University, St. Louis, MO, United States, [2]Radiology, Washington University School of Medicine, St. Louis, MO, United States

Background: Children 6 yrs and younger suffer traumatic brain injury (TBI) more frequently than any other age group [1]. Prior work in the 7-day post-natal (P7) rat pup [1] suggests that the infant brain is sensitive to trauma, exhibiting a massive wave of apoptotic cell death 20-24 hr post-injury. Changes in axial and radial diffusivity characterize axonal injury and demyelination after various insults in the adult brain[2]. Here we use diffusion tensor imaging (DTI) to measure changes in water diffusivity 24 hr post-TBI in the P7 rat.

Methods: An electromagnetic impact device (myNeuroLab.com) was mounted on the arm of a stereotaxic instrument. Isoflurane was used to induce (5%,1min) and maintain (2%,~10min) anesthesia. The animal was placed in a molded plastic head support. A midline incision was made and the scalp reflected to expose the skull. The 3mm-dia impact tip was centered stereotaxically 3 mm anterior to lambda, 2mm lateral to midline. A single impact of 2 mm depth and 2.5 m/s speed was given. At 24 hr post-injury the animal was deeply anesthetized and perfused with a glutaraldehyde fixative. All procedures were in compliance with NIH guidelines for animal care and use. Fixed brains were imaged *ex vivo* using a 1-cm inner dia solenoid coil in a 4.7T magnet (Oxford 200/330). A multi-slice spin-echo imaging sequence modified by addition of the Stejskal-Tanner diffusion-sensitizing gradient pair was used to acquire a series of diffusion-weighted images. Repetition time TR=3 s; echo time TE=38 ms; inter-pulse interval Δ=12 ms; pulse duration δ=4 ms; slice thickness=0.5 mm; data matrix 256x256 (zero-filled to 512x512); FOV=4x4 cm. Diffusion gradients were applied along six directions: [Gx,Gy,Gz]={[1,1,0],[1,0,1],[0,1,1],[-1,1,0],[0,-1,1],[1,0,-1]}. Two *b* values, *b*=0 and *b*=1.813 ms/μm2 were used. The six independent elements of the diffusion tensor were calculated in each image. The resulting tensor was diagonalized and the axial diffusivity $\lambda_{\parallel}$, the radial diffusivity $\lambda_{\perp}$, the trace (Tr) and relative anisotropy (RA) were computed. Symmetric regions of interest (ROI) in the external capsule (EX), cortex (CT) and hippocampus (HP) were analyzed on both ipsilateral and contralateral sides in the four slices caudal to the rostral limit of the hippocampus. These slices were from the region directly under the site of impact.

Results: Representative images are shown in Figs. A-D. Diffusivity, both axial and radial, decreased on the injured side of the brain under the impact site (Figs. E-H). These changes were statistically significant in the external capsule and cortex (*= p<0.05 in Figs. F-H, Student's paired t-test). The drop in diffusivity was consistently present (Fig. I), though variable in amplitude, among animals.

Discussion: Decrease in water diffusivity is consistently observed with DTI after traumatic injury in the infant rat. The cause of these changes has not been determined; the etiology may be different in the infant than in the adult. Comparative histology of corresponding sections is planned. DTI appears to have potential for non-invasive monitoring of TBI, and clarification of degeneration mechanisms.



Figures: (A-D) Images and linear profiles from one animal in a plane under the impact site. (A) Unweighted (*b*=0) image; (B) Trace; (C) Axial diffusivity; (D) Radial diffusivity; (E) Trace vs. location: slices 11-14 are directly under the impact site. (F-H) Regional averages of diffusion markers: EX=ext. capsule; CT=cortex; HP=hippocampus (*=p<0.05). (I) Subject-specific differences in trace.

References: [1] Bittigau P, et al, Ann Neurol 45:724-735 (1999); [2] Song et al, Neuroimage, 20:1714-1722 (2003).