A13-o2

Evidence of chronic neuronal injury in adolescents with chronic post-concussive symptoms as detected by whole-brain spatial mapping and a voxel-wise statistical approach.

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Purpose

- Approximately 14% of school age children with mild traumatic brain injury (TBI) including sports-related concussions (SRC) remain symptomatic 3 months after injury [(1-2)].
- Previous studies have shown regions of white matter diffusivity changes and hypoperfusion in symptomatic patients in the chronic phase of mild TBI [(3-6)]; however data in the pediatric population remains limited.
- Using both a voxel-wise statistical mapping and region of interest (ROI) approaches, we investigated the anatomical distribution of white matter diffusivity and hypoperfusion in chronic symptomatic pediatric subjects.

Methods

- Images were acquire on a 3T Siemens TIM Trio with a 12 ch head coil
- 3D T1-MPRAGE, 30 direction DTI, and DSC images were acquired on all subjects
- DTI maps (fractional anisotropy, FA; axial diffusivity, AD; radial diffusivity, RD; mean diffusivity, MD) were generated using Camino
- DSC maps (relative cerebral blood blow, rCBF) were generated using the Bayesian model in Olea Sphere 3.0 (Olea Medical).
- A pediatric template of 3D T1 weighted images was created using ANTs (http://stnava.github.io/ANTs/)
- All subjects T1 images were registered to this common template space using ANTs
- DTI B_0 images and DSC images were registered to the subject's T1 image using ANTs
- DTI maps and DSC maps were transformed into the common template space using the warp files generated by the two registrations steps above
- FSL Randomise was run with 5000 iterations to look for significant differences in rCBF, FA, AD, RD, and MD between controls and subjects
- Regions of interest defined on the pediatric template were used to look at regional changes in rCBF

Patient Demographics

	Subject (n = 26)	Control (DTI n =24, DSC n=12)
Age mean (SD), years	15 (2.42)	15 (2.69)
Age range, years	8 - 17	12 - 18
Gender (male/female)	12/26	11/24
Time after injury		
mean (SD), months	6.5 (4.4)	
Range, months	0.5 - 12.5	
Mechanism of injury %		
Sports-related	62 (16/26)	
Fall	27 (7/26)	
MVA	11 (3/26)	
Symptoms %		
Cognitive	58 (15/26)	
Behavioral	42 (11/26)	
Headache	81 (21/26)	

Results

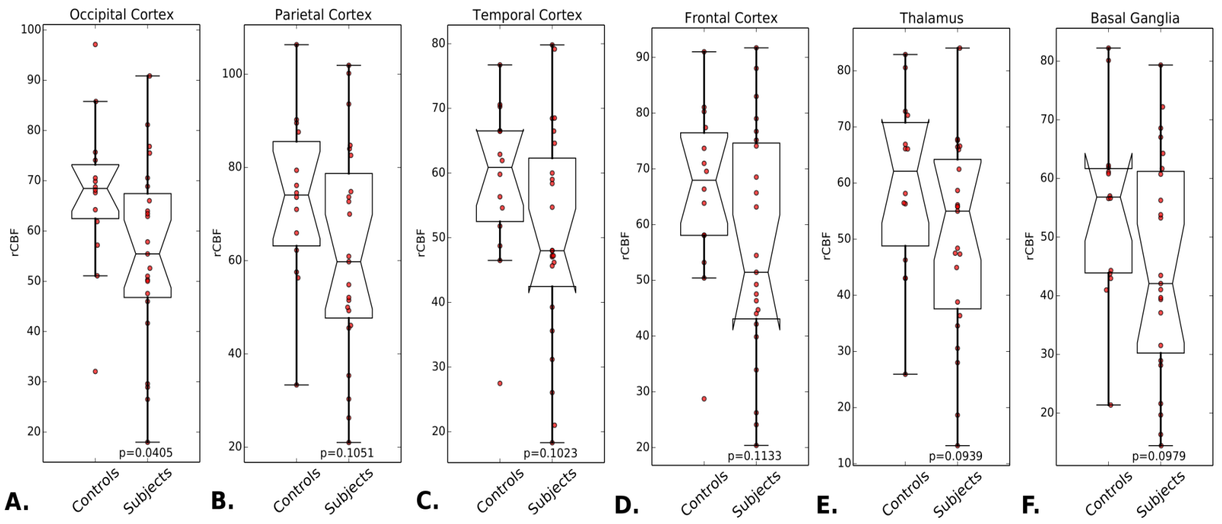

Fig 1. Blood flow in concussion subjects was reduced in all regions, with the occipital cortex showing significance (p=0.04, 2-tailed t-test).

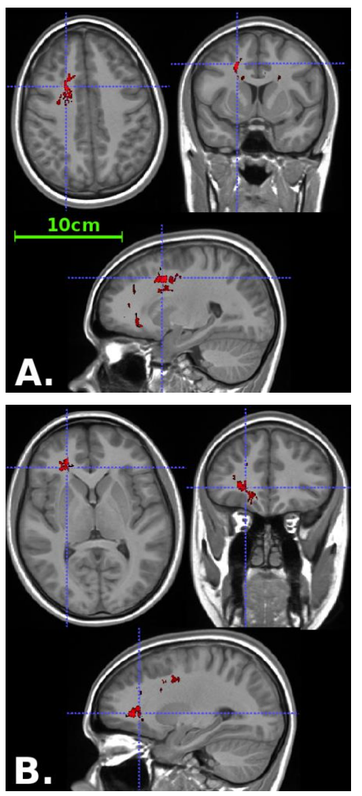

Fig 2. Regions with a significant increase ($p < 0.05$) in AD were identified in two main clusters in the superior A) and inferior B) right frontal white matter.

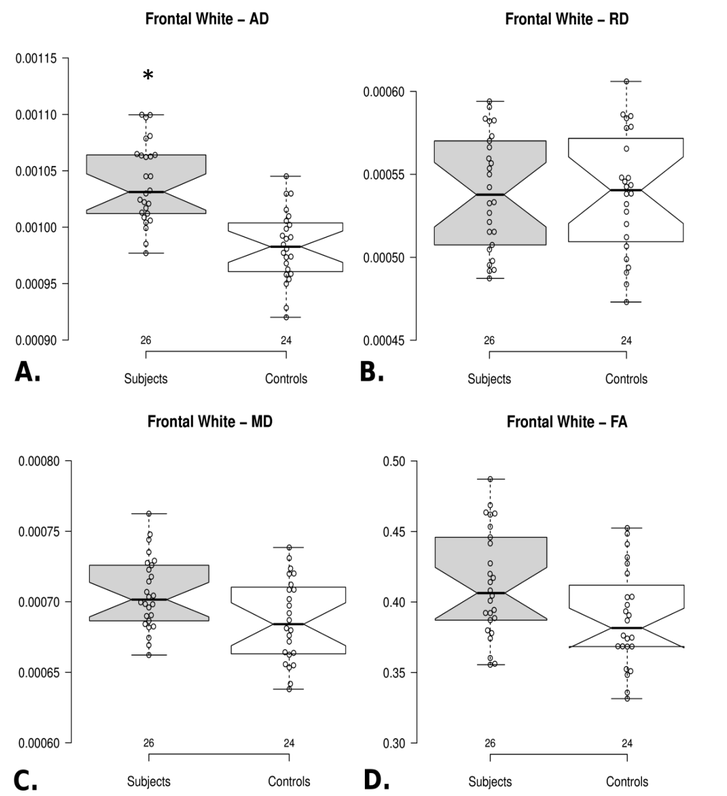

Fig 3. DTI parameters from an ROI drawn to encompass the area of significant change (Fig 2A) and surrounding tissue. The significant changes in AD (A), were associated with non-significant increases in both MD (C) and FA (D). RD (B) shows no change.

Results Summary

- Hypoperfusion (reduced rCBF) was seen in all regions, with significant changes in the occipital grey matter (Fig 1, $p < 0.05$) suggesting a diffuse reduction of metabolism or neuronal loss.
- Cluster voxel-wise analysis of the DTI maps showed clusters of elevated AD in the right frontal white matter (Fig 2, $p < 0.05$).
- ROI analysis confirmed the significant increase in AD with corresponding increases in FA and MD but not RD (Fig 3).

Conclusions

- Changes in rCBF appear to be driven by a subset of patients with significantly reduced blood flow, with the remaining patients showing no change. Future studies will attempt to associate symptoms, time post injury, or other factors to the patients that show significant decreases.
- In our cohort DTI changes are due to increased AD, with AD showing greater sensitivity than FA or MD. This could indicate swelling of axons.
- These findings may reflect long term changes to the neurovascular unit following concussion, which likely contributes to posttraumatic headaches and long term cognitive and behavior deficits.

References: 1. Ponsford et al. 1999;14(4):360-375. 2. Barlow et al. 2010;126(2):e374-381. 3. Ge et al. 2009;23:666-674. 4. Bonne et al. 2003;124:141-152. 5. Grossman et al. 2013;34(5): 951-957. 6. Bartnik-Olson et al. 2014; 31(17):1497-506.