Temporal changes of cerebral blood perfusion and diffusion kurtosis parameters in the thalamus following mild Traumatic Brain Injury

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Background:

Traumatic brain injury (TBI) accounts for 1.5 million injuries in the United States each year, and veterans' advocates believe that between 10 and 20% of Iraq veterans have some level of TBI. Non-invasive monitoring of cerebral blood flow (CBF) may reflect local alterations of blood perfusion and may help in the therapeutic management of TBI patients.[2-3] Neuroimaging tools such as arterial spin labeling (ASL), which uses arterial blood as an endogenous tracer, may provide insights into the subtle changes following injury and serve as an effective imaging marker to monitor novel rehabilitative efforts.[7] On the other hand, diffusion kurtosis imaging (DKI) is a measure for diffusion heterogeneity[9] and has been shown to be sensitive to tissue microstructure changes in the grey matter following TBI[9]. The aim of this study is to investigate regional CBF changes at three time points up to six months following mild TBI, and their relationship to tissue microstructure changes measured by DKI and patient's cognitive functioning.

Methods:

TBI patients were recruited in the acute stage of injury from the Adam Crawley Shock Trauma Center at the University of Maryland, Baltimore as part of the MagNeT Study (**Ma**gnetic **R**esonance Imaging of **N**euro**T**rauma). 18 mTBI patients (admission Glasgow Coma Scale > 13, age: 39.21 ± 17.94) and 34 control individuals (age: 40.22 ± 14.70) were included in this study. Patients were scanned within 10 days of injury, 1 month and 6 months post injury. Participants underwent pulsed arterial spin labeling (pASL) (TE=11ms, TR=2500ms, FOV=230mm, resolution 64×64, 16 slices, sl.th.=5mm, 45 pairs of labeled and control volumes) and T1-weighted MPRAGE imaging (TE=3.44ms, TR=2250ms, TI=900ms, flip angle=9º, resolution = 256×256×96, FOV=22cm, sl. th.=1.5mm), and DKI imaging (b = 1000, 2000 s/mm2, 30 diffusion directions, 2 averages, resolution = 2.7mm3, TE/TR = 93ms/6000ms) as part of a larger MRI protocol on a 3-Tesla Siemens MRI scanner. If able, each mTBI patient was subject to a battery of computerized cognitive assessments using the Automated Neuropsychological Assessment Metrics (ANAM), which measures speed and accuracy of attention, memory, and thinking ability. The weighted throughput scores on accuracy and reaction time from these cognitive assessments was used to correlate with imaging measures. ASL images were motion corrected and CBF maps were generated using in-house developed MATLAB program.[6] DKI images were motion corrected and smoothed (kernel size = 3mm) in SPM8 before fitting for fractional anisotropy (FA), mean diffusivity (MD) and mean kurtosis (MK) maps[9]. For each individual, five regions of interest were identified for ASL images: frontal lobe, occipital lobe, parietal lobe, temporal lobe and thalamus; and thalamus was identified for the DKI maps. A gray matter mask from the segmentation of the T1-MPRAGE was used to mask each ROI. ANOVA was carried out to test temporal changes in each measure, followed by independent two-tailed t-test to compare each time-point to the values obtained from the control subjects.

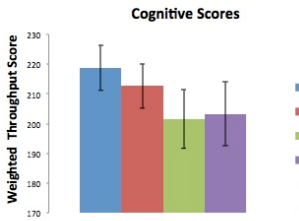

Fig. 1

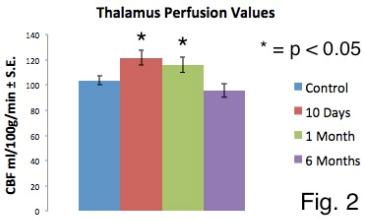

Fig. 2

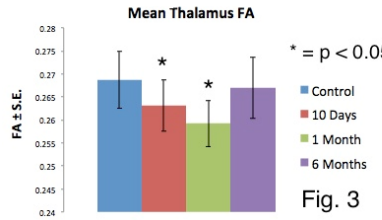

Fig. 3

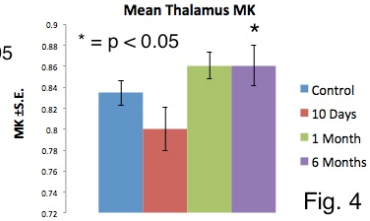

Fig. 4

Results:

No significant temporal changes in cognitive scores in mTBI patients (p = 0.462, Fig 1), as well as the overall lobe CBF values were found (frontal lobe: p = 0.462, parietal lobe: p = 0.662, temporal lobe: p = 0.192, occipital lobe: p = 0.172). However, significant temporal changes in CBF were observed in the thalamus (p = 0.004, Fig 2). The thalamus was significantly hyperperfused at the 10 day time point (p=0.015) and 1 month time point (p=0.088) but normalized by the 6 month time point (p=0.240). FA was significantly reduced in the thalamus at 10 days (p=0.037) and 1 month (p = 0.041) and eventually returned to control values by 6 months (p = 0.139), as shown in Fig 3. MK in the thalamus was relatively unchanged at the 10 day visit (p = 0.564) and 1 month (p = 0.176). However, MK was significantly increased at 6 months (p = 0.041, Fig 4. MD changes were non-significant at any time points.

Discussion:

Our data suggests an initial hyperperfusion mechanism in the thalamus, probably as a therapeutic response to injury followed by a normalizing pattern to normal values by 6 months even in the absence of any measureable cognitive changes. Hyperperfusion in the brain in early stages post TBI has been reported in relation to poor outcome because increases in CBF beyond matching metabolic demand relate to vasoparalysis with consecutive increases in intra-cranial pressure (ICP)[5] Our study suggests the existence of hyperperfusion even among the mTBI patients which takes course towards normal values by 6 months. The temporal CBF changes in the thalamus also corresponded to FA changes in the regions, indicating that disrupted tissue microstructure may be responsible for the increased perfusion. Interestingly, increased MK was observed at 6 months post injury when other measures normalized, which may indicate an increased glial cell activity in response to healing[9] that remains active for longer periods of time.

Conclusion:

The brain's repair mechanism is complex, and investigating the results of the different imaging modalities might explain how an mTBI patient maintains stable cognitive performance throughout the 6-month timeline. The findings validate arterial spin labeling and diffusion kurtosis imaging as a viable diagnostic method and reliable marker for the therapeutic management of mTBI patients.

References:

[1] Kim et al, 2012 [2] Chen, et al, 2012 [3] Chen, et al, 2008 [4] Glenn, et al, 2003 [5] Kim, et al. 2010 [6] Wang J et al., 2003 [7] Zauner et al, Head Injury 1997 [8] Jensen and Helpen, 2010 [9] Zhuo et al., 2012.