A longitudinal evaluation of diffusion kurtosis imaging in patients with mild traumatic brain injury

Jesse A Stokum[1], Jiachen Zhuo[1], Jacqueline Janowich[1], and Rao Gullapalli[1]

[1]Magnetic Resonance Research Center, Department of Radiology & Nuclear Medicine, University of Maryland School of Medicine, Baltimore, MD, United States
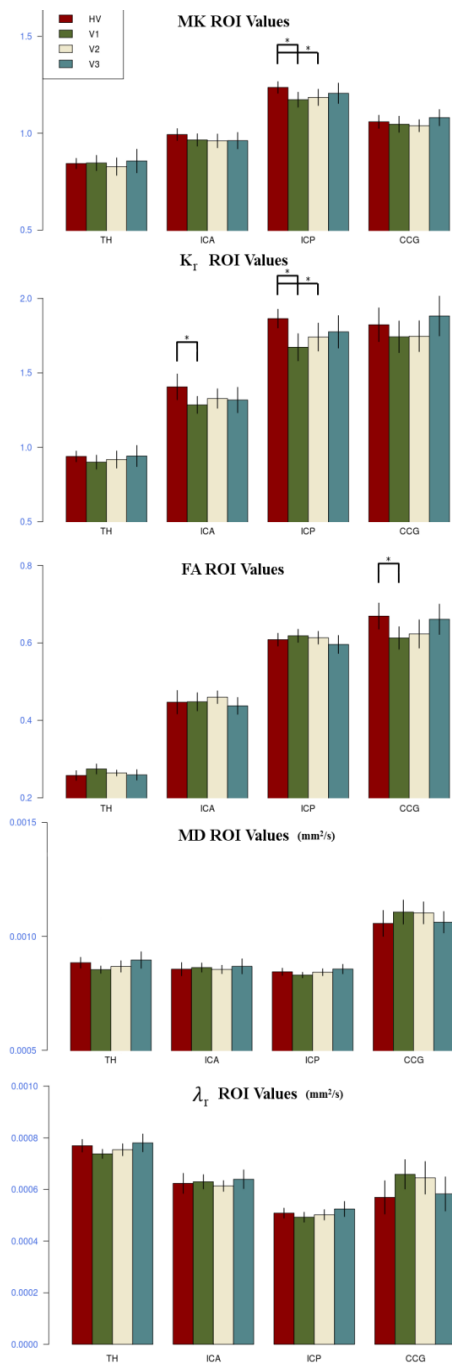
Figure 1: Mean ROI DTI/DKI values over visit 1-3. TH=thalamus, ICA=anterior internal capsule, ICP=posterior internal capsule, CCG=genu of corpus callosum. Bars indicate difference from controls. HV = healthy volunteers, V1 = visit 1, V2 = visit 2, V3 = visit 3.

Introduction

In patients with mild traumatic brain injury (mTBI), presence vs absence of pathological findings in CT and MRI underestimates long-term cognitive outcome[1] and traumatic axonal injury[2]. Diffusion tensor imaging (DTI) has been shown to be sensitive in depicting white matter injury in TBI patients. More recently diffusion kurtosis imaging (DKI) has been shown to be more sensitive to subtle microstructural changes and may complement information provided by DTI especially in gray matter regions[3,4]. In this prospective study, we examine DTI and DKI parameter changes in several gray and white matter regions across three time points (<10 days, 1 month, and 6 months) in mTBI patients and their relationship to the patients' cognitive status.

Methods

36 patients with mTBI (Glasgow coma scale ≥ 14) and 17 healthy controls (mean age = 23.2±5.4, 14 males) participated in this study. This study was approved by the institutional IRB. For patients, 3 imaging visits at 10 days post injury (n=20: mean age = 38.3±14.7, 19 males), at 1 month (n=20: mean age = 38.3±16.5, 16 males), and at 6 months (n=16: mean age = 41.1±18.2, 11 males) were completed. A battery of neurocognitive tests using the American Neurological Assessment Metrics (ANAM) was administered including, but not limited to, code substitution delay (CSD), match to sample (MTS), math processing (MATH), and procedural reaction time (PRT). Diffusion weighted images were obtained with b = 1000, 2000 s/mm^2 at 30 diffusion directions, 6 volumes at b = 0 s/mm^2, 2 averages, resolution = $2.7mm^3$, TE/TR = 93ms/6000ms. Motion and eddy correction, brain extraction, and smoothing (kernel size = 3mm) were performed. DKI reconstruction yielded mean kurtosis (MK), radial kurtosis (K_r), mean diffusivity (MD), fractional anisotropy (FA), and radial diffusion (λ_r). Mean DKI and DTI values were extracted from 4 hand drawn regions of interest (ROIs) on thalamus (TH), anterior (ICA) and posterior internal capsule (ICP), and genu of corpus callosum (GCC).

Unpaired t-tests (α = 0.05) corrected with false discovery rate (q = 0.05) were used to detect the departure of each parameter/visit/ROI combination from healthy-control range. Partial Spearman rank correlation coefficients controlled for age were used to measure correlation of DKI parameters and neurocognitive test reaction times.

Results

DKI parameters in the internal capsule show initial decrease compared to healthy controls followed by normalization over the six month follow-up. Specifically, MK is decreased in patients compared to healthy controls in posterior internal capsule at visit 1 (p = 0.023) and visit 2 (p = 0.044) but increases to a healthy range by 6 months. K_r is reduced in patients compared to healthy controls in anterior internal capsule at visit 1 (p = 0.045) and in posterior internal capsule at visit 1 (p = 0.003) and visit 2 (p = 0.029). These regions return to healthy range by visit 2 and 3, respectively.

DTI measurements show no change in internal capsule. FA is decreased in patients compared to healthy controls in genu of corpus callosum at visit 1 (p = 0.027) and returns to normal values by one month.

ROI \ Cognitive Test	CSD	MTS	MATH	PRT
MK ICP	-0.24 (p=0.1)	-0.1 (p=0.52)	0.035 (p=0.82)	**-0.33 (p=0.02)**
K_r ICP	**-0.36 (p=0.01)**	-0.16 (p=0.28)	-0.09 (p=0.54)	**-0.35 (p=0.02)**

Table 1: Partial Spearman rank correlation coefficients (controlled for age) and p-values between mean K_r in posterior internal capsule and the 4 neurocognitive tests.

Patient reaction times trend towards an initial increase followed by return to baseline over the three visits. Spearman rank correlation coefficients (Table 1) show a significant negative correlation between both DKI parameters in posterior internal capsule and the procedural reaction time. A negative correlation between K_r in posterior internal capsule and code substitution delay was also detected after correcting for age.

Discussion and Conclusion

DKI parameters (MK and K_r) in internal capsule show initial decreases, followed by an increase to healthy levels by 6 months. Although a trend of reduced K_r was apparent in the thalamus and genu of corpus callosum, this trend was not significant. Conversely, DTI shows little change from baseline at any time point. The greater sensitivity of K_r over λ_r in a white matter region such as ICP may be due to the higher sensitivity of kurtosis to the intra- and extra-axonal exchange rate, as evident by the multi-compartment model[5]. Increased radial water exchange resulting from myelin breakdown has been shown to produce decreased K_r and MK[4] and may be more sensitive compared to λ_r.

Internal capsule shows trends in DKI that are inversely correlated with cognitive testing reaction times. MK and K_r are correlated with reaction times, suggesting that the recovery mechanisms responsible for returning cognitive processing speed to near pre-trauma levels is partially composed of or accompanied by changes in tissue complexity.

We conclude that DKI parameters (MK and K_r) in internal capsule are reduced following mTBI and that changes in DKI are associated with improvements in cognitive task reaction time.

References

[1]Adams JH, et al. Ann Neurol. 1982; 12: 557-63.
[2]Arfanakis K, et al. Neuroradiol 2002; 23:794-802.
[3]Grossman EJ, et al. J Neurotrauma 2011; 15: Epub ahead of print
[4]Zhuo J, et al. Neuroimage. 2012; 59: 467-77.
[5] Jensen JH, Helpern JA. NMR in Biomedicine 2009; 23: 698-710.