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Characterizing microstructural alterations in a mTBI ratmodel: a multi-shell diffusion MRI analysis

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Introduction

Traumatic brain injury (TBI) is the leading cause of acquired disability in young adults [1]. Most TBI patients have mild TBI (mTBI) and while conventional scans show no evidence of injury, patients can experience chronic cognitive defects. Diffusion imaging is an MRI technique sensitive to diffusion of water molecules in the brain and can detect subtle changes in brain microstructure. Since standard diffusion parameters lack specificity [2], the aim of this study is to better characterize white matter changes with advanced diffusion MRI analysis in a mTBI rat model.

Methods

Nine female Wistar rats sustained mTBI utilizing the Marmarou weight drop model [3]. In brief, the anesthetized rat was positioned under a 450g brass weight on a foam bed. The weight was dropped from a height of 1m guided through a plexiglass column onto a steel helmet fixed on the rat's skull. The bed together with the rat was rapidly pushed aside to prevent a second impact. MRI data were acquired on a 7T-MRI scanner (PharmaScan, Bruker) before, 1 week and 6 months after injury. T2-weighted images were acquired for anatomical reference. Multishell diffusion data were acquired with multiple directions/b-values (b=800, 1500 and 2000 s/mm2; 32, 46 and 64 directions). Diffusion kurtosis tensor estimation was performed on distortion corrected DWI images, and diffusion and kurtosis maps calculated. Maps for white matter metrics were calculated based on a white matter diffusion model. A volume-of-interest analysis was performed in the corpus callosum, hippocampus and cingulum on maps coregistered to a local anatomical template. Subsequently, differences between timepoints were analysed with the Wilcoxon-signed-rank-test in SPSS (significance level: $p<0.05$).

Results

We found increases in AD, AWF, AxEAD and FA 1 week post injury compared to baseline (table 1). No significant differences were found 6 months post injury.

Conclusions

An increased AWF could be explained by axonal swelling, consistent with an increased AD, AxEAD and FA. Because AWF values were increased in all three regions, we can conclude that this metric is very sensitive for changes in microstructure due to mTBI (1 week post injury).

References/acknowledgements

[1]Thurman,JChildNeurol,2016,31:20-7.[2]Jones,NeuroImage,2013,73:239–54.[3]Marmarou,JNeurosci,1994,80: 291-300.

Figure (optional)

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Table 1. Results for the diffusion, kurtosis and white matter metrics of the corpus callosum, cingulum and hippocampus before (pre) (n=9), 1 week (1w) (n=9) and 6 months (6m) (n=3) after impact. Abbreviations: AD, axial diffusivity (10^{-3} mm²/s); AWF, axonal water fraction; AxEAD, axial extra-axonal diffusivity (10^{-3} mm²/s); FA, fractional anisotropy; TORT, tortuosity (10^{5}).

Metric	Corpus Callosum			Cingulum			Hippocampus		
	pre	1w	6m	pre	1w	6m	pre	1w	6m
AD	1.40 ± 0.04	1.47 ± 0.09	1.35 ± 0.07	1.32 ± 0.04	1.30 ± 0.07	1.02 ± 0.03	1.15 ± 0.05	1.19 ± 0.46 *	1.09 ± 0.07
AWF	0.30 ± 0.02	0.36 ± 0.03 *	0.38 ± 0.02	0.31 ± 0.02	0.35 ± 0.02 *	0.37 ± 0.04	0.24 ± 0. 02	0.27 ± 0.01 *	0.29 ± 0.01
AxEAD	1.84 ± 0.09	2.05 ± 0.16	1.23 ± 0.11	1.75 ± 0.08	1.81 ± 0. 12	1.62 ± 0.13	1.43 ± 0.08	1.54 ± 0.69 *	1.38 ± 0.01
FA	0.36 ± 0.04	0.45 ± 0.04 *	0.52 ± 0.02	0.35 ± 0.01	0.39 ± 0.03 *	0.45 ± 0.03	0.20 ± 0.01	0.22 ± 0.03	0.30 ± 0.03
TORT	1.57 ± 0.69	1.58 ± 0.95	2.35 ± 0.16	1.64 ± 0.28	1.50 ± 0.40	2.06 ± 0.04	1.12 ± 0.48	1.46 ± 0.11	1.62 ± 0.07

* $p < 0.05$ with Wilcoxon signed rank test