DTI detects FA changes in the internal capsule and thalamus in rat after traumatic brain injury - comparison with histology

T. P. Laitinen[1], A. Sierra Lopez[1], T. Bolkvadze[1], A. Pitkänen[1], and O. H. Gröhn[1]
[1]Dept. of Neurobiology, A. I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, Finland

Introduction

Lateral fluid percussion induced traumatic brain injury (TBI) is a clinically relevant rat model of closed head TBI in humans [1]. After primary injury, a complex combination of molecular and cellular alterations occurs in the central nervous system [2] leading to functional disabilities such as somatomotor impairment or epilepsy [3]. This study demonstrates the capability of diffusion tensor imaging to detect changes in the thalamus and internal capsule (IC) of rats after TBI.

Methods

TBI was induced in Male Wistar rats (n=9) by lateral fluid percussion injury as described previously by Kharatishvili I. et al. [3]. Age- and weight matched control animals (n=7) were sham operated. Six months after TBI, the animals were perfused transcardially with Na_2S and 4% paraformaldehyde and brains were dissected from the cranium. Prior to DTI, brains were immersed to perfluoro polyether to prevent signal from the solution. DTI experiments were carried out in a 9.4 T magnet interfaced to a Varian console using a quadrature volume RF-coil (Rapid Biomedical GmbH) as transmitter and receiver. Data were acquired using a 3D spin echo sequence (TR=1s, TE=60ms, data matrix 192×74×56 zero padded to 256×144×112, FOV 29.3×17×12.8mm^3). Six 3D images with diffusion weighting (diffusion time 17 ms, b-value 1000s/mm^2) in six orthogonal directions and one image without diffusion weighting were obtained. From the measured images a diffusion tensor was determined and fractional anisotropy (FA) maps and color-coded FA maps were created. Timm-staining and gold chloride-staining for myelin were used to quantify changes in the laterodorsal thalamic nuclei (LD), ventral posterolateral and -medial thalamic nuclei of thalamus (VPM) and in the internal capsule.

Results

The results show a significantly increased ($p<0.01$) FA in ipsilateral ventral posterolateral and -medial thalamic nuclei (VPN) in comparison to contralateral VPN in rats with TBI as well as when compared to ipsilateral VPN in controls (Figs 1 and 2). Also a significant ($p<0.01$) FA decrease was observed in ipsilateral IC of TBI animals in comparison to contralateral IC in rats with TBI and in contrast to ipsilateral IC in control animals (Figs 1 and 2). Also a trend towards elevated FA was observed in ipsilateral LD in rats with TBI in comparison to contralateral LD in TBI animals and ipsilateral LD in controls (Figs 1 and 2). No differences were seen between ipsi- and contralateral LD, VPN and IC in control animals. Histological analysis showed that in LD there are more densely packed neuronal fibers and myelin deficiency in the ipsilateral LD as compared to contralateral LD in TBI rats (Fig 3). Also in ipsilateral VPN there are changes in the neuronal architecture and less myelin than in contralateral VPN (Fig 3) in the animals with TBI. In the IC demyelination is observed in the ipsilateral IC that is not visible in the contralateral IC in TBI animals (Fig 3). The changes in FA are well in line with the histological observations.

Conclusions

Our data show that DTI is able to detect specific areas of increased and decreased FA in thalamus and internal capsule, respectively. Importantly, the changes seen in FA corresponded well to the neurobiological alterations seen with the histological analysis. As DTI provides a completely non-invasive method to be used also in clinical settings, our observations may have implications for the detection of neurobiological changes in patients at risk of functional disabilities after closed head brain trauma.

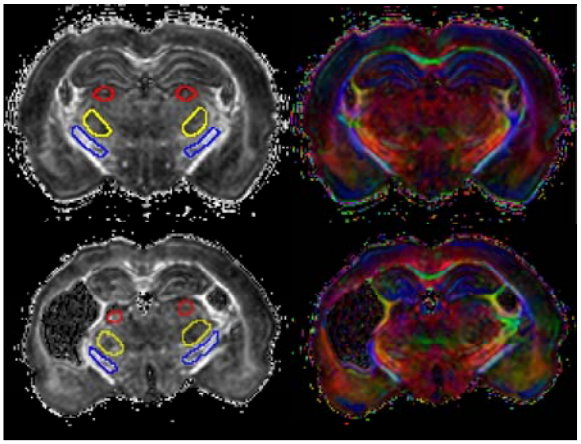

Figure 1. Fractional anisotropy maps (left column) and color-coded FA maps (right column) of a control (top row) and a rat with TBI (bottom row). Regions of interest are outlined on FA-maps: LD in red, VPN in yellow and IC in blue.

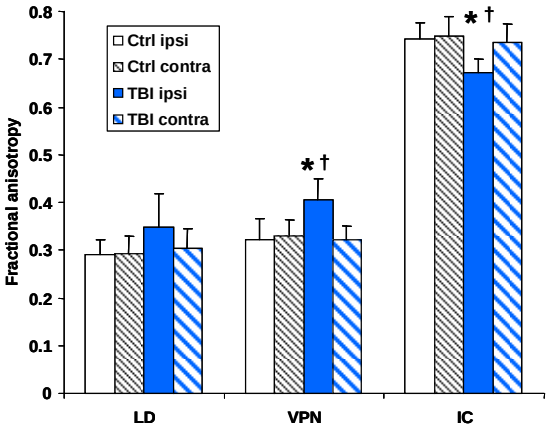

Figure 2. Fractional anisotropy of ipsilateral and contralateral LD, VPN and IC of controls and rats with TBI. Values are expressed as mean ± STD. * $p<0.01$ as compared to contralateral area in rats with TBI. † $p<0.01$ in comparison to ipsilateral area in control animals.

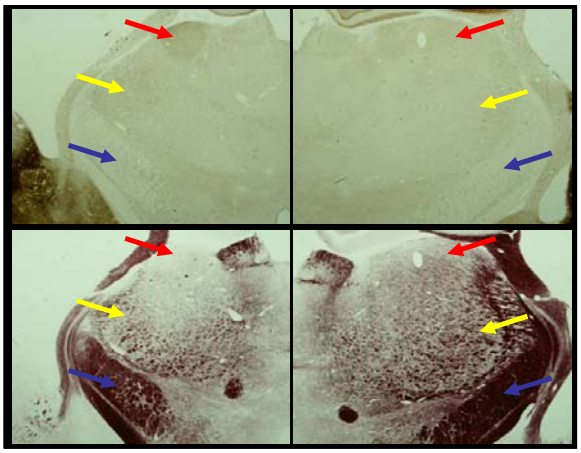

Figure 3. Timm-stained (top row) and myelin-stained (bottom row) histological sections from the ipsi- (left) and contralateral (right) thalami of a rat with TBI. LD is marked with red arrows, VPN in yellow and IC in blue

References
[1] McIntosh TK et al. *Neuroscience* (1989) **28**: 233-244
[2] Karhunen H. et al. *Neurochem. Res.* (2005) **30**:1529-1542
[3] Kharatishvili I. et al. *Neuroscience* (2006) **140**:685-697