Quantitative MRI and MRS at five to eleven months after traumatic brain injury in rat

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Introduction

Traumatic brain injury (TBI) is one of the most prevalent causes of morbidity and mortality in young persons. The MRI and MRS investigation of spatio-temporal changes in morphology, tissue water-homeostasis and metabolism may provide an insight into long-term consequences of TBI and guide medical intervention. It was recently shown that MRI parameters obtained in the acute and chronic phases after TBI correlate with the long-term functional and histological outcome [1]. These follow-up studies lasted for 6 months and indicated ongoing pathological processes even at 6 months after onset of TBI. The objective of the present study was to investigate if these progressive changes still continue at 5-11 months after onset of TBI and could be detected by quantitative MRI and MRS.

Methods

TBI was induced in 20 adult male Spraque Dawley rats (350-400 g) by fluid percussion as described previously [2]. Ten sham operated rats served as controls. MRI data were acquired in 4.7T Magnex magnet interfaced to Varian Inova console. Quadrature half volume rf-coil was used as transmitter and receiver. Rats were anaesthetised with 1% halothane. MRI was performed 7 months and 11 months, and MRS 5months and 10 months after onset of TBI. Volumetric changes were detected using T_2-wt adiabatic spin echo multi-slice sequence (TE=70ms, TR=3s, 128*256pts, FOV 3*3cm^2, thk=0.75mm, 19 slices covering rat cerebrum). T_2, $T_{1\rho}$ and the 1/3 of the trace of diffusion tensor (D_{av}) were quantified from a single slice using a fast-spin-echo sequence with BIR-4 refocusing pulses (TR=3.0s, echo spacing=10ms, 16 echoes, 128*256pts, FOV=3*3cm^2, thk=1.5mm; T_2: TE=20, 38, 52, 76ms; $T_{1\rho}$: spin lock times=18, 38, 58, 78ms, B_{1SL}=0.8G; diffusion: b-values=90, 496, 1014s/mm²). The single voxel spectroscopy data were obtained with adiabatic spin-echo pulse sequence, LASER [3] (TE = 2ms , TR = 4s , np = 3336, sw = 2500 Hz, nt = 512) incorporating VAPOR water suppression scheme, after FASTMAP shimming. Voxels (2.5mm*3mm*3mm) were placed in both the ipsilateral and contralateral hippocampus. The spectral analysis was performed using LC model and only results with SD% < 20 were included in further analysis. All values are given as relative concentrations to Cr +PCr peak, because water could not be used as a reference. Statistical comparisons were performed using Student's paired t-test. All results are indicated as mean +/- SEM.

Results

Quantitative MRI: Volumetric MRI did not show further increase in the volume of the lesion from 7 months to 11 months. The combined volume of lesion and ipsilateral ventricle was 94±41mm^3 and 10±5mm^3 for TBI and sham animals, respectively. In the ipsilateral cortex adjacent to primary lesion area, quantitative MRI parameters $T_{1\rho}$, T_2 and D_{av} remained at the same elevated level both at 7 and 11 months. Interestingly, in the hippocampal sub-structures all measured MRI parameters $T_{1\rho}$, T_2 and D_{av} showed relatively small but statistically significant changes.

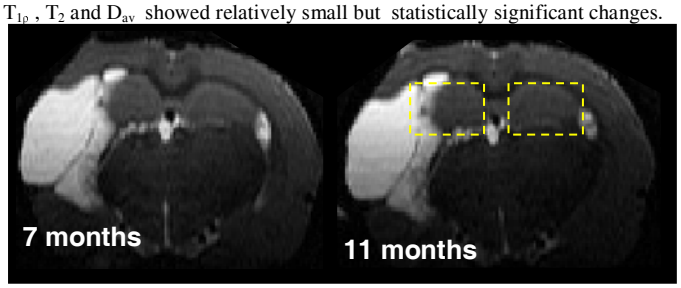


Fig1. *A T2-wt image of typical lesion 7 and 11 months after induction of TBI. Locations of hippocampal MRS voxels are indicated.*

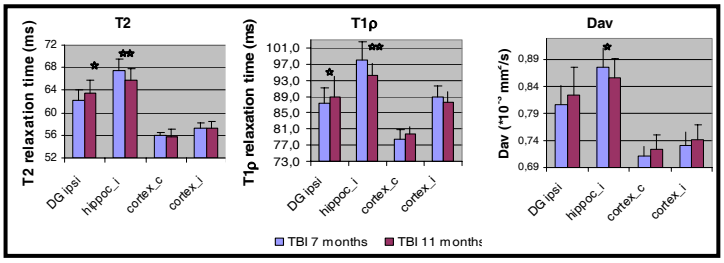
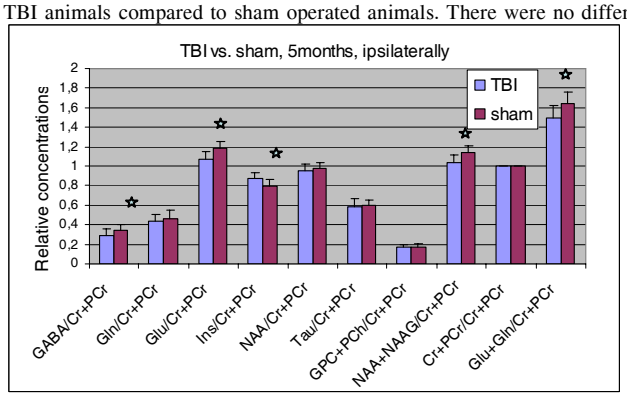


Fig 2. *T1ρ , T2 and Dav of ipsilateral dentate gyrus (DG ipsi), ipsilateral hippocampus (hippoc_i), ipsilateral cortex (cortex_i) and contralateral cortex (cortex_c) , 7 and 11 months after induction of TBI. Statistically significant changes between 7 and 11 months were evaluated using Student's t-test, * p<0.05.*

MRS: At five months, MRS data indicated decreased GABA, Glu, NAAG, NAA+NAAG and Glu+Gln and increased Ins in ipsilateral hippocampus of TBI animals compared to sham operated animals. There were no differences between TBI animals and shams in the contralateral side. The only significant change ($p<0.05$) from 5 months to 10 months was the further decrease of Glu.



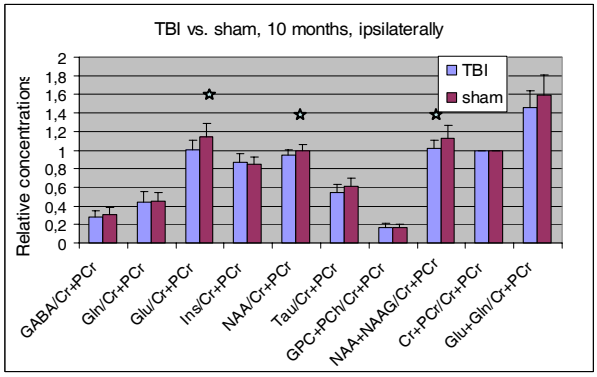


Fig 3. *Relative concentrations of different metabolites relative to Cr+PCr peak. Statistically significant differences are indicated as * <0.05.*

Conclusion

Traumatic head injury results in progressive alterations in the brain that can be followed using MRI. The alterations are known to last for months after initial impact. This study provides evidence that even though the lesion size does not increase anymore in late chronic state at 7 to 11 months after TBI, there are still some progressive MRI detectable alterations in hippocampus area. These may be associated with either ongoing neurodegeneration, gliosis or neuronal plasticity as response to trauma. MRS data showed several metabolic abnormalities in TBI animals, mainly ipsilaterally to the impact site. Many of these abnormalities, such as decreased NAA generally associated with decreased neuronal number and increased Ins associated with inflammation/gliosis have, also been seen in chronic human head trauma MRS studies [4]. This provides further evidence that the present animal model mimics human disease, not only in the structural but also in the metabolic level.

References: [1] ISMRM proceedings 2005 and 2006, [2] Kharatisvili et al. 2003, [3] Garwood, de la Barre 2003, [4] Shutter et al 2006

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