Quantitative MRI correlates with long-term functional outcome 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 investigation of spatio-temporal changes in morphology and tissue water-homeostasis may provide an insight into long-term consequences of TBI and guide medical intervention. In the present study quantitative MRI parameters obtained in the acute and chronic phase after TBI were correlated with the long-term functional outcome assessed by behavioral testing.

Methods

TBI was induced to 14 Spraque Dawley rats by fluid percussion as described previously [1]. Five sham operated and 4 intact 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 in transmit/receive –mode. Rats were anaesthetised with 1% halothane and MRI was performed 3 hours, 3 days, 9 days, 23 days, 2 months, 3 months and 6 months after induction 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 functional outcome was evaluated using Morris Water maze and fear conditioning tests after 7 months. Correlation analysis between MRI and behavioral testing was performed using Spearman test.

Results

TBI resulted in a T_2 hyperintense lesion, in ipsilateral cortex and hippocampus, that progressively increased in size over the following 6-months. Because of large variation between individual animals the rats were divided into 3 groups according to 23-day lesion volume (the sum of T_2 hyperintense tissue and ipsilateral ventricle volumes) as follows: 'severe' (n=3) > 30 mm^3 > 'moderate' (n=8) > 10 mm^3 > 'mild' (n=3), for further analysis. Hippocampal $T_{1\rho}$ and T_2 times were elevated on day 3 in ipsilateral hippocampus ($T_{1\rho}$ 8%, 8% and 5%; T_2 6%, 4% and 0% for severe, moderate and mild-groups, respectively) after which they normalized. Interestingly, relaxation times showed secondary increase after 3 months. In T_2 this secondary increase levelled off 5% above the control-level in most of the TBI-animals, but $T_{1\rho}$ gradually increased throughout the rest of the 6-months observation period in all TBI-animals. D_{av} showed no changes in acute or subacute phase but became elevated after 2 months showing progressive increase thereafter (Fig.1).

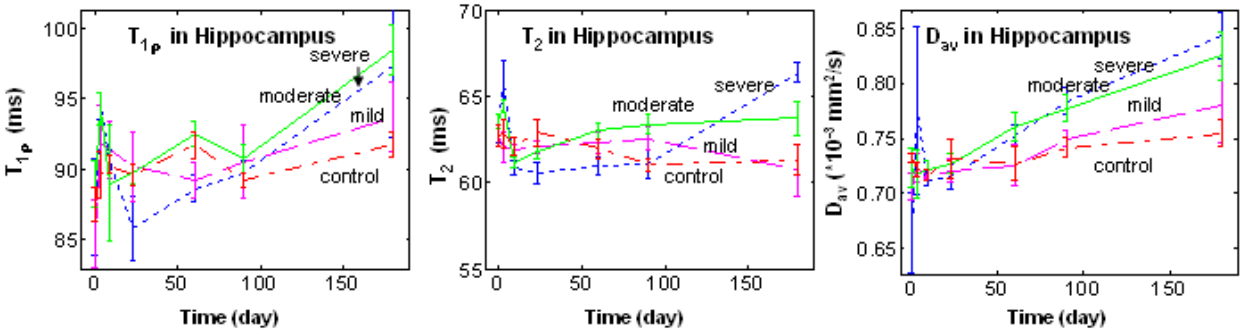

Fig 1: $T_{1\rho}$, T_2 and D_{av} in ipsilateral hippocampus. The MRI-parameters showed progressive changes during 6 months after TBI indicating on-going tissue changes.

The Morris water maze test performed at 7 months measures spatial learning, which is related the function of hippocampus. According to the swimming latencies the TBI-animals had impaired learning ability (the average of the relative latency changes between day 1- day 2 and day 1- day 3) compared to the controls. The MRI parameters measured in different time points were correlated with the learning ability (Table 1). As expected, the lesion volume at 6 months correlated with the learning ability. Interestingly, the lesion volume at 23 days after TBI already predicted the extent of later atrophy, and also correlated with the learning ability at 7 months. D_{av} in hippocampus and cortex and $T_{1\rho}$ and T_2 in cortex at 6 months also correlated with learning impairment. Surprisingly, also some of the quantitative MRI parameters measured as early as 3 hours -3 days after TBI correlated significantly with Morris water maze testing. D_{av} in ipsilateral hippocampus and cortex 3 hours after TBI, as well as T_2 in cortex 3 days after TBI correlated with the learning ability 6 months later. The fear conditioning test, which predominantly measures the amygdala function, showed no correlations between MRI parameters measured from hippocampus and cortex areas with the freezing times, as expected.

CORRELATION BETWEEN MRI PARAMETERS AND WATER MAZE TEST SCORES										
MRI parameter	Time after TBI	ROI = ipsilateral hippocampus			ROI = contralat. hippocampus			ROI = ipsilat. cortex		
		r-value	p-value	Sig.	r-value	p-value	Sig.	r-value	p-value	Sig.
D_{av}	3 hours	-0.674	0.002	*	0.498	0.030	*	0.575	0.010	*
	3days	0.249	0.303	-	0.315	0.189	-	0.177	0.468	-
	6 months	-0.537	0.018	*	-0.197	0.420	-	0.627	0.004	**
$T_{1\rho}$	3 hours	-0.309	0.198	-	-0.125	0.611	-	-0.355	0.135	-
	3days	-0.388	0.101	-	0.045	0.856	-	-0.426	0.069	-
	6 months	-0.275	0.255	-	-0.133	0.589	-	-0.543	0.016	*
T_2	3 hours	0.154	0.530	-	-0.044	0.858	-	0.298	0.215	-
	3days	-0.566	0.012	*	-0.204	0.401	-	-0.471	0.042	*
	6 months	-0.445	0.056	-	-0.169	0.488	-	-0.498	0.030	*
Volume	23 days	Lesion volume			-0.526	0.021	*			
	6 months				-0.484	0.036	*			

Table 1: The correlations between MRI parameters and 'spatial learning ability' calculated from the swimming latencies in Morris water maze test.

Conclusion

Traumatic head injury results a progressive alterations in the brain that last for months after initial impact and can be followed using MRI. Volumetric and quantitative MRI results obtained in the acute and subacute phase 3 hours - 23 days after induction of TBI correlated with the functional outcome of the animals 7 months later. This provides evidence that MRI may facilitate the prediction of the functional outcome after TBI.

References: [1] Kharatisvili et al. 2003.

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