In vivo early MRI and MRS at 9.4T of combined hypoxia-hypotension and traumatic brain injury in the rat

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INTRODUCTION

Following traumatic brain injury (TBI), hypoxia and hypotension are frequent and damaging secondary insults. Physiopathology of vulnerable brain concept needs more understanding to consider possible treatment. Post-traumatic dysfunction of brain energy metabolism could play a central role in brain oedema formation and in delayed neuronal cell death.

The aim of this work is to characterize the traumatic injury by MRI (T2, diffusion tensor[1], angiography) and MRS experiments *in vivo* on rat brain. The final aim is to understand the role of secondary insults like hypoxia and hypotension in the development of post-traumatic brain oedema.

Using an animal model of diffuse TBI combined with hypoxia - hypotension (HH), we will focus on post-traumatic brain oedema development using MRI combined with MRS, as well as consequences of post-traumatic perturbations on brain energy metabolism using cerebral microdialysis.

MATERIAL AND METHODS

Head trauma was performed according to the method described by Marmarou [2] with a loss of a 450 gr weight from a height of 1.80 meter. Hypoxia and hypotension (HH) were induced 45 min after trauma by ventilating rats with O_2 : N_2 mixture 10%: 90% followed by a controlled haemorrhage to decrease mean arterial pressure (MAP) to 40 mmHg via a rapid arterial blood withdrawal. After 15 minutes, the whole blood volume was restored to the animal (1-2 min) and hypoxia was stopped by ventilating animal with room air and oxygen (1 L/min). Cerebral monitoring (interstitial lactate) was performed using microdialysis placed in the right thalamus using stereotaxic frame.

MR experiments were performed 1h30 min after trauma (sham n=5, trauma+HH n=4, trauma n=3) in a horizontal 9.4T spectrometer (94/21 USR Bruker Biospec, Wissembourg, France). A quadrature birdcage coil (Bruker) with 72mm inner diameter was used. A stereotaxic head holder was used to fix the animals and anaesthetize them with isoflurane (1.5%) in an O_2/N_2O 1:1 mixture at 0.7l/min. Respiration and temperature were monitored.

Preparatory axial images were recorded using axial multislice RARE images. T2 maps were computed using weighted axial MR image using a 16 echoes MSME sequence : FOV = 5x5cm^2, matrix = 256x256, slice thickness 1 mm, experimental time = 17 min. Measurement of vascular cerebral blood network was performed by MR angiography (MRA) using FLASH sequence: FOV = 5x5cm^2, matrix = 256 x 256, TR/TE = 12/3.5 ms, 120 axial slices thickness 0.4 mm, experimental time = 13 min. Angiograms were produced by generating maximum intensity projections (MIP). DTI experiments were recorded using EPI acquisition, 4 b values with b = 50, 500, 1000, 1500 s/mm^2, 6 directions, FOV= 5x5cm^2, slice thickness = 2mm, experimental time = 10 min. Image analysis and processing were performed with the Paravision software. For MRS, PRESS localized spectra were recorded on right hippocampus region centered at -3mm from bregma : Voxel 5x5x5mm^3, TR/TE = 4000/12ms, acquisition points 2048, SW=10ppm, VAPOR water suppression, experimental duration 34min. Spectra were computed with JMRUI software .

RESULTS AND DISCUSSION

Traumatic rat brain with hypoxia - hypotension compared with sham rats presented signs of oedematous brain damage with hyperintense signals visible on T2 weighted images (*Figure 1)*. On HH trauma rats, T2 maps confirmed the perturbations located in the specific oedematous cortical or sub cortical region showing a statistic significant ($p<0.05$) increase of T2 values. On the other hand, vascular blood flow perturbations displayed unaltered MRA signals meaning that the main vascular regime would remain intact. In cortical and thalamic ROIs, DTI maps showed increased values of trace D, e1 eigenvalue with a statistical p value of 0.05 (*Figure 2*) and heterogeneously perturbated anisotropy factor maps. Metabolic measurements by microdialysis *(Figure 3)* showed an increase of lactate for HH traumatic rats. MRS depicted an increase of lactate, lipids/Cr ratios, a decrease of Ins/Cr ratio, no significant changes of Choline, Glu, Gln, Taurine/Cr ratios.

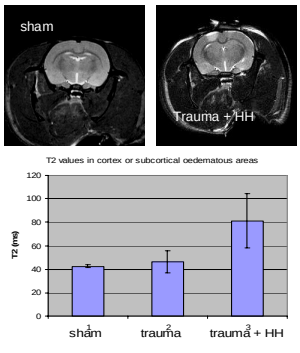

Fig 1 : T2-w images and quantifications of traumatic HH rat brain

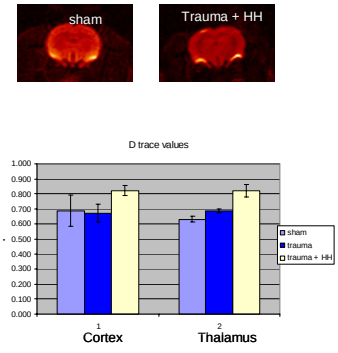

Fig 2 : DTI images and table of Dtrace parameters

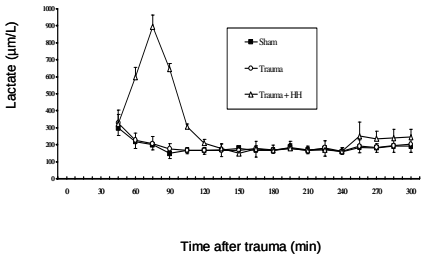

Fig 3 : Microdialysis : Lactate increased for HH traumatic rats

CONCLUSION

This study shows that traumatic brain injury could be characterized by MRI (T2 and DTI methods) and that HH increased the severity of the injury.

REFERENCES [1] Xu J et al. J. Neurotrauma 2007, 24, 753-765. [2] Marmarou A et al., 1994, J Neurosurg 80:291-300.