USPIO-enhanced MRI at 7T in a mouse model of focal cerebral ischemia

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Rationales and objectives: Inflammatory processes are involved in the pathophysiology of stroke. Non invasive monitoring of activated macrophages in the brain using Ultrasmall superparamagnetic particles of iron oxide (USPIO)-enhanced MRI may provide relevant information in this setting. [1;2]. The purpose of the present study was to monitor the course of inflammatory process in a mouse model of focal cerebral ischemia.

Methods: Permanent middle cerebral artery occlusion (pMCAO) was induced in 8 male wild-type mice by electrocoagulation. Three of them received i.v. injection of AMI-227 USPIO (Sinerem®, Guerbet SA, Paris) at the dose of 2 mmol Fe/kg 4h after pMCAO. Five control animals were also included. Three were operated but did not received USPIOs and two recieved USPIO without pMCAO surgery. All mice were scanned 1h, 2 days and 3 days post-injury using multiparametric MRI (T2, gradient-echo imaging, multiecho sequence for T2 quantification, diffusion for ADC quantification) at a field strenght of 7-T. Multiparametric MRI was performed immediately after administration of contrast agent in order to assess permeability to USPIO. Animals were sacrified after the last MR examination and brains prepared for immuno-histological analysis.

Results: Regions of increased T2 were observed in all animals as soon as 1h post-ischemia before USPIO was administered. The area of reduced ADC matched the region of T2 increase. Immediatly after administration of AMI-227 all mice showed USPIO accumulation in the boundary zone of the lesion which appeared hypointense in the gradient-echo (Figure 1B, arrow) and T2-weighted images. Strongly hypointense region became visible within the corpus callosum contralateral to the lesion and in the caudate putamen in the ischemic hemisphere on day 2 and 3 (Figure 1C and 1D, arrow). In contrast, no signal change was noted in three healthy animals with injection of USPIOs nor in two stroke-induced animals without injection of USPIOs.

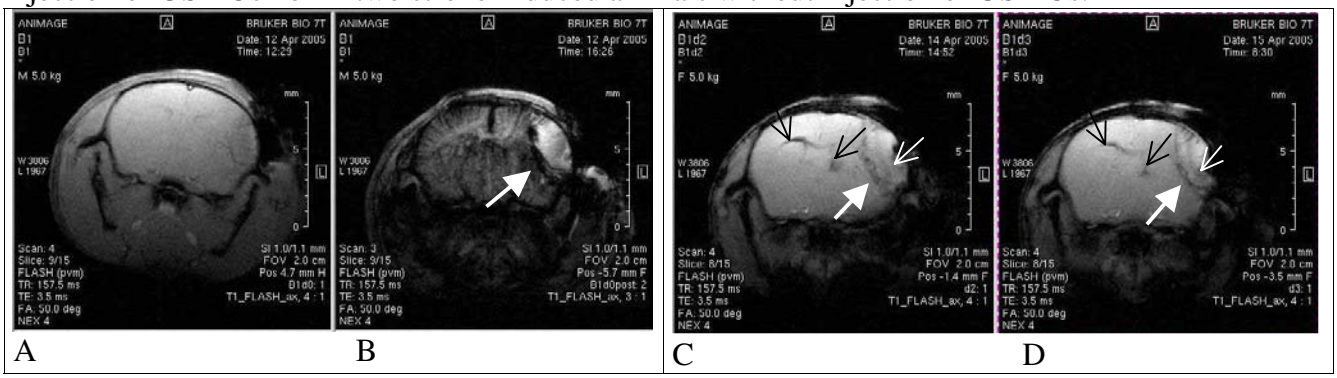

Figure 1- Coronal gradient-echo images of mouse brain A) 1h; B) 4h i.e. following USPIO administration; C) 48h and D) 72h post-pMCAO. Arrows show the signal void due to USPIO accumulation.

Conclusion: Peripheric accumulation of USPIO around to the lesion could be due to the blood-brain-barrier insult, conversely hyposignal contralateral to the lesion may result from a different mechanism. Further pathological investigations are needed to investigate this process. To our knowledge, this study provides the first USPIO-enhanced MRI data in stroke-induced mice, raising the possibility of dynamic assessment of inflammatory process related to ischemic damage in genetically engineered mice.

References:

[1] Rausch et al. Magn Reson Med, 46 (2001) 1018-22.

[2] Saleh et al. NMR Biomed, 17 (2004) 163-9.