Changes of Mobile Lipids in Rat Brain after Transient Focal Ischemia Observed by Long Echo-Time *In Vivo* ^{1}H Magnetic Resonance Spectroscopy

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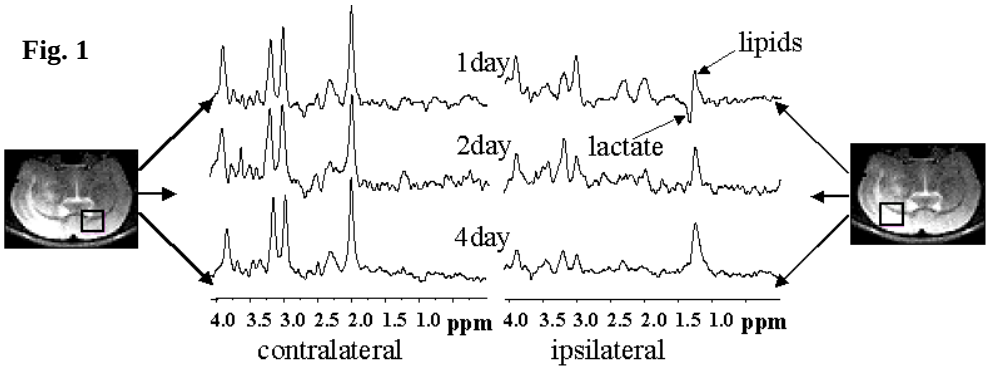
Introduction: Magnetic resonance visible lipids (MRVL) in brain have been the subject of many recent studies in view of that they may provide valuable information for the diagnosis and the prognosis of certain neurological diseases, such as brain tumor and stroke. It has been shown that increases in the MRVL (e.g. fatty acyl signal at =1.22 ppm) in brain tumor tissues are associated with either apoptosis or necrosis[1,2]. Increases in the MRVL were also observed in stroke patients[3] and ischemic rat brain slices[4], probably as a manifestation of activated inflammation reactions after cerebral ischemia[3]. Postischemic inflammatory reactions have been shown to be different in the ischemic core and ischemic penumbra, and be the important factors causing expansion and maturation of ischemic infarctions[5,6]. To further investigate the lipid metabolism after cerebral ischemia and its origin, long echo-time *in vivo* ^{1}H MRS was used in this study to monitor the changes of cerebral metabolites, including MRVL, in a rat model of transient middle cerebral artery occlusion (MCAO).

Materials and Methods: The suture model of MCAO (180 min) was induced in 15 male Wistar rats weighting 150~170 g. Rectal temperature of the rats was maintained at 37±1 ^{o}C during ischemia and during the first one and half hours postischemia. All MR experiments were carried out on a 4.7 T/30 cm Bruker Biospec scanner at 1, 2 and 4 days after ischemia. T_2-weighted MRI was used to identify ischemic lesions (TE of 120 ms, TR of 2500 ms and FOV of 3×3 cm^2). Based on the T_2-weighted images, localized *in vivo* ^{1}H MRS was performed using a PRESS sequence with TE of 136 ms, TR of 1000 ms, and 1024 averages. Two spectra were acquired for each rat (one in the contralateral hemisphere, and the other in the ipsilateral hemisphere, whose locations shown in Fig. 1). All spectra were processed and quantified by the software package MRUI.

Results: Figure 1 shows the results from a representative rat. The spectra acquired from the contralateral hemisphere did not change significantly from 1 day to 4 days postischemia. Compared to control, the signal intensities of NAA, total creatine (tCr) and total choline (tCho) in the ipsilateral cortex decreased significantly at 1, 2 and 4 days after ischemia. Both lactate (i.e., inverted signal at 1.33 ppm) and lipids (i.e., positive signal at 1.27 ppm) were observable in the ipsilateral cortex of this particular rat 1 day postischemia. The lactate signal disappeared while the lipids signal increased at 2 and 4 days after ischemia. The percentage of the rats in which lactate signal was observed (i.e., lactate appearance probability) decreased progressively from 1 day to 4 days postischemia, which was the opposite to the lipids appearance probability (Fig. 2). The average lipids signal intensities were about the same at 2 days and 4 days after ischemia, however the 4-day data seemed to have somewhat lower inter-animal variation (Fig. 3).

Discussion and Conclusion: Previous studies using short echo-time ^{1}H MRS have shown that the MRVL increase significantly in the cerebral ischemic lesions of stroke patients and in ischemic rat brain slices[3,4]. Long echo-time *in vivo* ^{1}H MRS was used in this study to monitor the changes of the MRVL in the ischemic rat brain after transient MCAO. It is shown that the MRVL are observable in the ischemic tissues starting from 1 day postischemia, and increase progressively hereafter up to 4 days postischemia. The MRVL observed apparently have long T_2, thus most likely coming from mobile lipids or intra-cytoplasm lipid droplets. The time course of the MRVL change suggests that they might be related to the postischemic inflammatory reactions[4]. If so, observation of the mobile lipids signal could be useful for monitoring the evolution of stroke-related pathological changes. However, further studies using histochemistry are still needed to substantiate such a postulation.

Fig. 1



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References: 1) E. Iorio et al, *Biochim Biophys Acta* 2003; 1634:1-14; 2) S. Zoula et al, *NMR Biomed* 2003; 16:199-212; 3) G. D. Graham et al, *Stroke* 2001; 32:2797-2802; 4) C. Gasparovic et al, *Neurosci Lett* 2001; 301:87-90; 5) T. Mabuhci et al, *Stroke* 2000; 31:1735-1743; 6) E. Lehrmann et al, *J Comp Neurol* 1997; 386:461-476.

Fig. 2

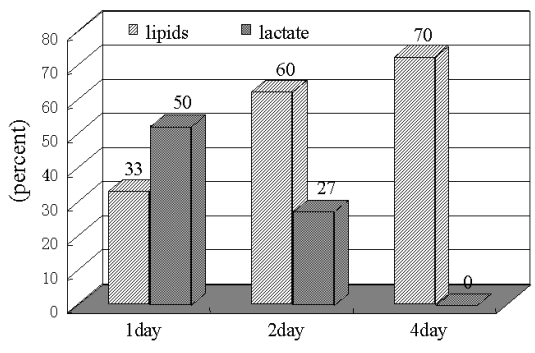

Fig. 3