Glutamate and GABA Imaging at 7 Tesla

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Purpose – Glutamate and GABA are a pair of important neurotransmitters that play a key role in neuropsychiatric diseases. In these studies, we aim to imaging the Glutamte and GABA specifically using chemical exchange saturation transfer technique(*1, 2*) at 7 Tesla. In addition, we optimized the pre-saturation power respectively and further demonstrated the application in ischemic stroke model in vivo.

Methods – MRI : MRI experiments were conducted under an Agilent 7T animal MRI system with a standard volume coil for RF transmission and reception. Glutamate and GABA imaging were obtained by the standard EPI-CEST sequence. We set offset frequency at 3.0 ppm and 2.75 ppm for Glutamate and GABA respectively. Other parameters: pre-saturation time=3000 ms, TR/TE=4000/2.5 ms, slices=1, slice thickness=2mm, NEX=1 or 32, FOV=34*34 mm^2, imaging matrix=64*64 and bandwidth=50 kHz. The pre-saturation power was varied from 0.5 μT to 8 μT with interval of 0.5 μT. Z-spectra and MTR asymmetric analysis were obtained in Matlab. Phantom: Glutamate, GABA, Choline, Creatine and inositol phantoms were prepared to optimize the pre-saturation power for CEST imaging, and the pH were titrated to 7.0. MACO: Five adult male Sprague Dawley rats were underwent permanent middle cerebral artery occlusion by thread embolism, following the protocol approved by local institutional ethics committee. T2-weighted imaging (TR/TE=2000/30 ms, NA=8) and ADC maps (TR/TE=2000/34 ms, NA=8) with b-value of 1000 s/mm2 were acquired for reference.

Results and Discussion – Fig. 1 shows the CEST MTRasym imaging from Glutamate and GABA phantoms, with amine proton CEST effect at 3 ppm and 2.75 ppm, respectively. Moreover, they can be distinguishable from other metabolites. We also evaluated the pre-saturation for optimization (Fig. 2). Both the Glutamate and GABA CEST effect increased with power and peaked at about 5.5 μT to 7.5 μT. The speeds of them appear first quick back slow trend, so we empirically use 6 μT for reasonable pre-saturation power when consider the specific absorption rate. We further obtained in vivo CEST data in MACO SD rat brains using the optimized glutamate CEST parameters (Fig. 3). The spatial resolution and sensitivity were sufficient so that the apparent CEST contrast between the ischemic region and normal region could be well delineated. Specifically, Glutamate CEST effect was measured using the asymmetry analysis, with the CEST effect being -7.7±0.9% and -5.3±0.9% for ischemic lesions and lateral normal regions, respectively. In summary, because Glutamate and GABA CEST imaging show good sensitivity and specificity, they remain promising for translational CEST imaging at high field strength and clinical applications.

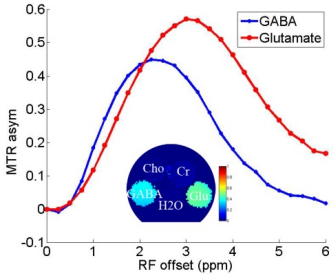

Fig. 1 MTRasym of Phantoms

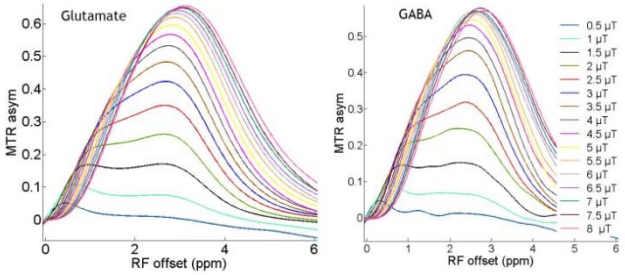

Fig. 2 Optimize pre-saturation power for Glu and GABA

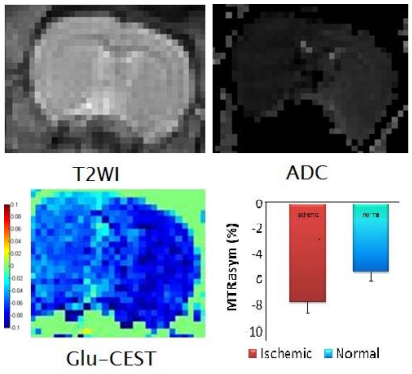

Fig. 3 Glu-CEST imaging at MACO

References –1. K. Ward, Journal of Magnetic Resonance 143, 79 (2000). 2. K. J. Cai et al., Nature Medicine 18, 302 (Feb, 2012).