In vivo Magnetic Resonance Spectroscopy (MRS) studies of brain metabolism during ammonia infusion

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^{15}N is an alternative approach to ^{13}C MRS in studying glutamate-glutamine metabolism. In vitro observations suggested that during hyperammonemia, alterations in brain metabolites other than Gln can occur. The aim of the study was: 1) to directly measure the Vsyn (glutamine synthetase rate) and V_{GDH} (net glutamate dehydrogenase rate) under ^{15}N-labeled ammonia infusion; 2) to image for the first time the in vivo effect of hyperammonemia per se on 12 metabolites in different brain regions. Experiments were performed on a 9.4T MRI system using SD rats. NH_4Cl was infused (4.5mmol/h/kg) for 9-10h. ^{15}N and ^{1}H spectra were acquired and a neuroglial two-compartment model was fitted simultaneously to the total Gln, 5-^{15}NGln and 2-^{15}NGlu+Gln curves. Vsyn, V_{GDH} and neurotransmission rate (V_{nt}) were measured (0.24±0.03, 0.030±0.001 and 0.21±0.03µmol/min/g, respectively). Metabolic maps were obtained using short-echo-time proton-spectroscopic-imaging and the linear-fit of the time-evolution of Gln gave the map of the net glutamine synthesis flux (Vsyn-V_{nt}=0.039±0.007 in cortex and 0.024±0.007µmol/min/g in hippocampus). Combining localized in vivo ^{15}N with ^{1}HMRS we measured for the first time along with Vsyn, V_{nt} and V_{GDH} in the rat brain. High resolution metabolic maps enabled to observe the in vivo spatial distribution of 12 metabolites in various brain structures under hyperammonemia. No changes were observed except for Gln increase (17.7±1.4mmol/kgww). We also imaged for the first time Vsyn-V_{nt} in vivo in the rat brain and showed that it was significantly higher in cortex than in hippocampus.