Mapping glucose and lactate concentrations with microliter resolution in rat brain using short-echo-time spectroscopic imaging

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Introduction: Short-echo-time (TE) proton spectroscopic imaging is capable not only to map the spatial distribution of NAA, creatine, choline, glutamate/glutamine and myo-inositol but also of metabolites having lower concentrations and/or giving more complex spectral patterns. Glucose (Glc) and lactate (Lac) are compounds which are closely related to energy production in the brain tissue. The spatial distribution of these compounds in brain with microliter resolution (1) can provide information about the function of various brain structures or about brain tumor metabolism (2). The aim of this study was to test the feasibility of measuring distribution of Glc and Lac in the brain of a healthy rat at different plasma Glc levels using short-TE spectroscopic imaging.

Experimental: The data were obtained from brain of two adult Sprague-Dawley rats. For inducing hyperglycemia, 20 % Glc solution was infused into the femoral vein at a rate of 0.8 – 2 mL/hour. Plasma Glc levels were measured using an Analox GM7 analyzer (Analox Instruments, MA, USA) and were increased from 6.4 mmol/L (normoglycemia) to 15.0 mmol/L. Metabolic maps were obtained on an actively shielded 9.4 T/31 cm spectrometer (Varian/Magnex Scientific) using a SPECIAL spectroscopy sequence (TR/TE = 2000/2.8 ms) with phase encoding in the horizontal plane (1). A home-built 14 mm diameter quadrature coil was used as a transceiver. Field homogeneity was adjusted by FASTMAP (3). The size of the excited VOI was 9×2×10 mm^3. Two acquisitions were collected for each of the 32×32 phase encoding steps using FOV of 24 mm×24 mm, giving a nominal voxel size of 0.75×0.75×2 mm^3 (1.1 μL). The *k*-space data were then filtered with an optimized Hanning function in two spatial domains, thus giving the effective spatial resolution of 1.7 μL (1). Absolute concentrations of metabolites were calculated from the spectra of individual voxels using LCModel (4). Reference water signals were measured using the same protocol without water suppression and with TR=1.5 s. The total measurement time, including both metabolite and water scans, was 2 hours.

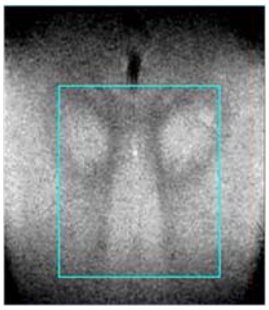

Fig. 1. Position of the VOI in the rat brain

Results: Fig. 1 shows a VOI, which was phase encoded into 10×12 voxels (Fig. 2). The VOI included mostly hippocampi, striatum and frontal cortex. Total creatine (Cr) was used as an indicator of the measurement stability. Its mean concentration (7.7 – 7.8 mmol/kg) did not change at different plasma Glc concentrations and its distribution was also very stable, with higher levels in hippocampus and cortex than in striatum. With increasing plasma Glc level to 11.1 mmol/L, the mean Glc concentration remained almost the same (from 2.7 to 2.6 mmol/kg) whereas the Lac concentration increased from 1.7 to 2.3 mmol/kg. With further increasing plasma Glc to 15.0 mml/L, the brain Glc concentration raised to 4.8 mmol/kg, whereas Lac slightly dropped to 2.1 mmol/kg. The mean brain Glc concentrations at different plasma Glc levels fell in the range found by ^{13}C spectroscopy (5). The spatial distribution of Glc and Lac did not vary substantially with Glc infusion: Glc seemed to be highest in cortex, Lac was higher in striatum and hippocampus than in cortex.

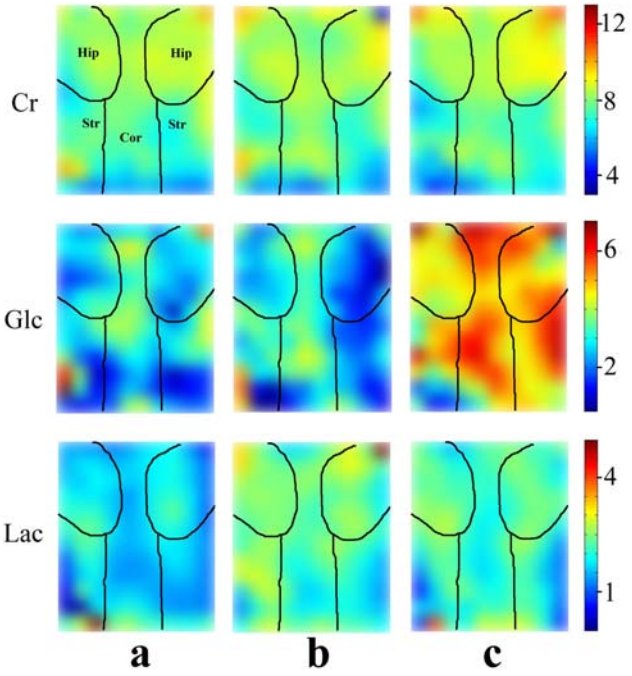

Fig. 2. Metabolic maps of Cr, Glc and Lac in the brain region depicted in Fig.1 at Glc plasma concentrations of 6.4 (**a**), 11.1 (**b**) and 15.0 (**c**) mmol/L. The numbers on the color scales denote absolute brain concentrations in mmol/kg of tissue. Spectra from the outermost voxels were potentially affected by chemical shift displacement errors of the excitation scheme.

Discussion and Conclusions: The stable concentration of total creatine suggests an absence of systematic biases during the experiment. Relatively small changes in metabolite concentrations can be clearly seen in their maps. The observed differences in various brain regions agree well with those obtained by single voxel spectroscopy (6). This preliminary study indicates that short-TE proton spectroscopic imaging can be used to measure the spatial distribution of low-concentration metabolites or those with complicated spectral patterns in rat brain with a resolution comparable to PET.

Acknowledgments

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