In vivo CSI of glutamate in the monkey brain

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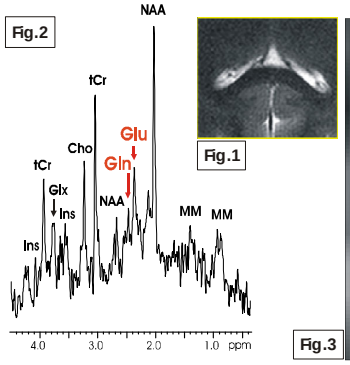
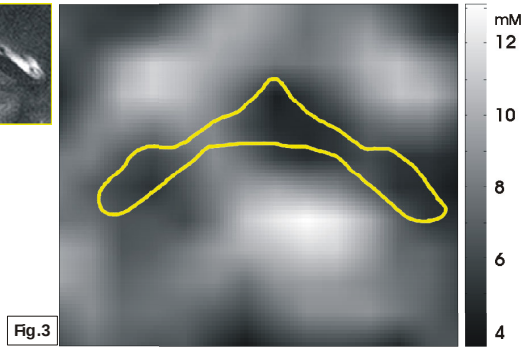
Glutamate is the main excitatory neurotransmitter in the CNS and plays together with glutamine an important role in brain physiology. A quantitative spatially resolved analysis of glutamate separated from glutamine is therefore of particular neuroscientific interest. In a startup study the feasibility of glutamate chemical shift imaging (CSI) is demonstrated in the ventricle region of a macaque monkey, where large differing metabolite concentrations are expected for brain tissue vs. the ventricles filled with CSF. Preliminary results of a CSI study with a very high spatial resolution in the millimeter range are reported from the occipital lobe focusing on NAA in gray vs. white matter.

METHODS: Measurements were done on a *vertical* 7T/60cm Bruker Biospec system [1]. The setup, handling, and anaesthesia of the macaque monkey was described previously [2]. 80mm and 30mm surface coils were used [3]. Shimming with FASTMAP led to a water line width of 13Hz (0.043 ppm) in the selected 28x28x4mm^3 axial slice through the ventricles. For CSI, a STEAM sequence was used with a conventional 8x8 phase encoding scheme, leading to a nominal in-plane resolution of 3.5x3.5mm^2 (TE/TM/TR=10/10/4000ms, NA=35). Water suppression was achieved by a VAPOR module. Mild Gaussian apodization and spatial zero filling up to 16x16 was applied before Fourier transformation. Quantification was done voxelwise with LCModel, assuming 10mM total creatine in brain matter.

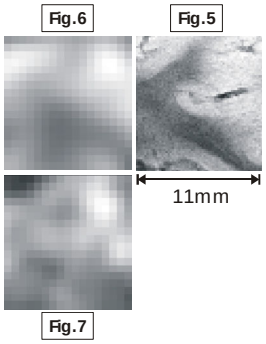
The acquisition parameters in the high-resolution study were TE/TM/TR=6/10/4000ms, CSI FOV: 16x2x16mm^3, phase encoding matrix: 13x13, leading to a nominal in-plane resolution of 1.1mm. Water line width in the selected volume was 17Hz. Data were hamming filtered and spatially zero filled to a 25x25 matrix.

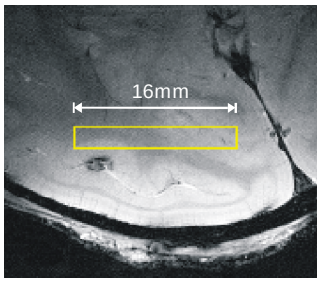
RESULTS & DISCUSSION: The anatomical scout image in Fig.1 (MSME, TE=100ms) is zoomed on the CSI FOV. In a typical brain matter CSI voxel, the spectral separation of the glutamate and glutamine multiplets at 2.35 and 2.45ppm is obvious (Fig.2). A smoothed glutamate map is shown in Fig. 3 with the reduced FOV of 21x24.5mm^2. The Cramer-Rao bounds were in the range of 6-10% and metabolite line widths were 7-11Hz in the brain tissue. The ventricle anatomy is depicted by a yellow contour line that fits well with the expected low glutamate concentrations in the ventricles.





For cortical brain regions in the vicinity of the skull surface, significant sensitivity enhancements could be achieved by the use of a combination coil setup (T: half-volume saddle coil, R: 30mm surface coil). This translates to an improved spatial resolution and significantly smaller CSI slice geometries (yellow frame, Fig. 4). Figure 5 shows the center cantle of a 16x2x16mm^3 'coronal' STEAM voxel, used for CSI. The gray vs. white matter maps with a in-plane resolution of 1.1mm (Fig.6: water, Fig.7: NAA) were measured with one single water acquisition and the average of only 9 CSI scans with focus on NAA.





In most CSI studies insufficient sensitivity or long TE values do not permit the quantification of glutamate+glutamine. Typically glutamate and glutamine can not be separated due to limited spectral dispersion/resolution. In this study, utilizing high magnetic field, we were able to separate glutamate and glutamine and measured a pure CSI glutamate map in the primate. Utilizing the enhanced spectral dispersion and sensitivity at high magnetic fields, these results demonstrate that many brain metabolites are able to be resolved and mapped with CSI methods. CSI of the brain can thereby meet the neuroscientific requirements regarding the spatial resolution, which are defined by brain structures in millimeter dimensions and below.

[1] ISMRM 1877, 2089 (2003), [2] Nature Neurosci. 2, 555 (1999), [3] MAGMA 15, 425 (2002)

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