Localized ^{1}H MR Spectroscopy in the Primary Visual Cortex (V1) of the Macaque Monkey

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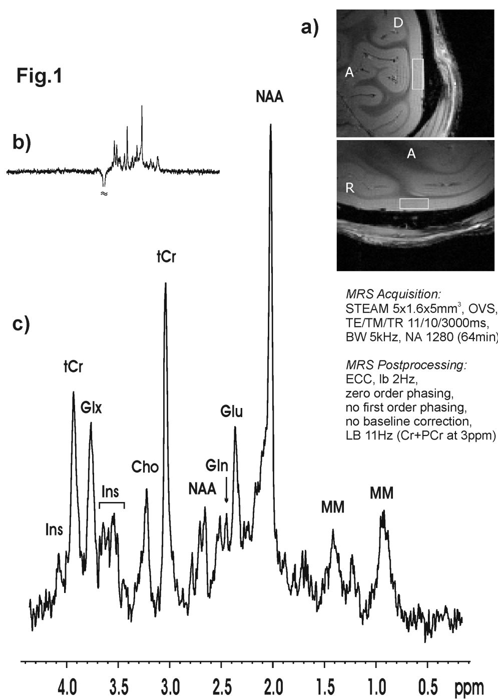
The primary visual cortex (V1) is one of the elementary targets, when visual function and cortical reorganization are investigated. Neurotransmitters like glutamate (Glu), glutamine (Gln), and γ-aminobutyric acid (GABA) or substances of the brain's energy metabolism like creatine (Cr) and phosphocreatine (PCr) are thought to be key compounds for a deeper understanding of the underlying processes. The feasibility of ^{1}H MR spectroscopy (MRS) from small volumes exclusively positioned within V1 of the macaque monkey in direct vicinity to the cranial bone was shown previously [1]. ^{1}H MRS was used in the monkey model to achieve an independent quantification of Glu and Gln non-invasively from cortex gray matter tissue without partial volume contaminations. A dedicated 7 T MR setup and home-built RF coils were applied to maximize the reproducibility of the experimental conditions and the amount of attainable signal from the MRS voxel placed to V1 gray matter of the macaque monkey which has a thickness of 1.5-1.7 mm only. Magnetic field distortions were analyzed and quantified and a shimming strategy for MRS in V1 was developed. The minimization of quantification errors and the desired separation of Cr from PCr, however, required further methodological improvements for a maximized spectral quality. Here, we present the result from a complete study including optimizations of shimming, outer volume suppression (OVS) and RF pulse design.



METHODS: Measurements were made on a vertical 7T/60cm Bruker Biospec system [2], temporarily equipped with a Siemens AC44 head gradient insert (40 mT/m, <200 μs). A home-built saddle coil and a Bruker 30-mm surface coil were used for excitation and reception, respectively. The setup and anesthesia of the macaque monkey (n=3, 12 sessions) has been described previously [3]. For single voxel spectroscopy, a STEAM sequence was used (TE/TM/TR=11/10/3000 ms) with VAPOR water suppression. The MRS voxel (5x1.6x5 mm^3, 40 μL, Fig.1a) was selected by sinusoidal filtered sinc pulses with 5 side lobes to minimize errors of the spatial selection profile. With 1.3/4.0/1.3 ms the RF pulses were short enough to force maximum gradient amplitudes thereby minimizing the chemical shift displacement in the 2-4 ppm range to <0.2 mm. A train of 20 hyperbolic secant pulses was used for OVS at an isotropic gap size of 1 mm only. Since the second order shim requirements exceeded the capabilities of the currently installed shim device by far, a combined passive and active shimming approach was applied (see separate abstract, this meeting). Passive shimming reduced the main field distortions significantly within a 1 cm^3 cube volume from cortex adjacent to V1. Subsequently, the high accuracy adjustment of the first and second order shims was done actively via the FASTMAP algorithm on the same voxel. For optimized shimming of the spectroscopy voxel, the linear shim terms were refined locally by an iterative optimization procedure [1].

RESULTS: High quality MRS from the macaque V1 was achieved by an improvement of the MRS sequence with respect to the particular task and target brain region. Due to proper sequence adjustment, high quality spatial selection profiles and OVS slices with minimal gap to the MRS voxel no contaminations from the surroundings of the STEAM voxel, for instance from the cranial bone marrow were observed that could lead to baseline alterations (Fig.1b). Except for some residual water, there was no signal outside the spectral region of the metabolites. Spectra were eddy current corrected, however, first order phasing or baseline correction was not required (Fig.1c). Linewidths of 12-14 Hz for the water peak and 10.5-12.5 Hz for the Cr+PCr peak at 3 ppm were reproducibly achieved. A Cr+PCr linewidth of 11 Hz and reasonable signal-to-noise ratio in the presented study allowed among others the independent quantification of GABA, Glu, Gln, Cr, and PCr with Cramér-Rao lower bounds below 20% (see Table).

metabolite	conc. (CR)	
GPC	0.6	(17)
GSH	2.1	(12)
GABA	2.6	(14)
Gln	2.9	(18)
PCr	3.9	(16)
Cr	4.1	(15)
Asp	4.7	(13)
Ins	5.3	(7)
NAA	9.4	(5)
Glu	10.5	(5)
Cr+PCr	8.0	(4)
NAA+NAAG	10.6	(3)
Glu+Gln	13.4	(5)

DISCUSSION: Based on the methodological improvements the attained ^{1}H MRS signal strength and excellent spectral quality enabled the independent quantification of GABA, Glu, Gln, Cr and PCr in a small and highly localized voxel of macaque V1 at 7 T without partial volume contaminations from higher functional areas. In particular, the spectral separation of Cr and PCr required minimal linewidth and maximum overall quality of the spectra. These results provide the technical basis for neuroscientific studies on changes of the metabolite concentrations as a function of sensory stimulation and plasticity.

[1] ISMRM 2040 (2004), [2] Magn Reson Imaging 22, 1361 (2004), [3] Nature Neuroscience 2, 555 (1999)