Anatomically matched MRS voxel reveal NAA concentration differences between cortical gray and corpus callosum white matter in the mouse brain

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Introduction: Localized proton MR spectroscopy (MRS) enables in vivo neurochemical profiling of brain substructures. Therewith it is feasible to disentangle metabolic processes which differently involve gray and white structures and provide a deeper understanding of physiologic and pathologic processes. The extended experimental options in animals and a myriad of genetically modified mouse lines may contribute to fill the gap between basic research and human diseases. The lower fraction of white matter in mice compared to those in human, however, hinders an exclusive quantification of metabolites from white matter structure such as the corpus callosum by conventional rectangular volume of interest approaches.

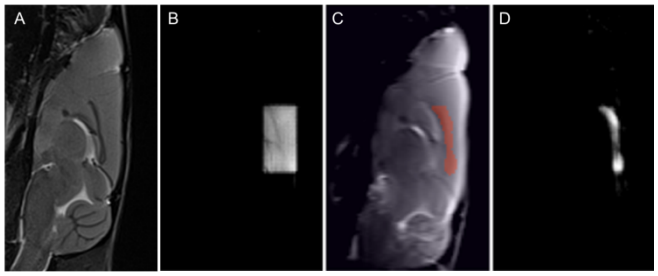

Figure 1

Thus, little is known about possible differences of metabolite concentrations in mice gray and white matter. The aim of the present study was to use a recently developed localization method based on 2D-selective RF excitations (2DRF) (1, 2) to measure anatomically matched MRS voxel of the corpus callosum and cortical gray matter to compare their NAA concentrations.

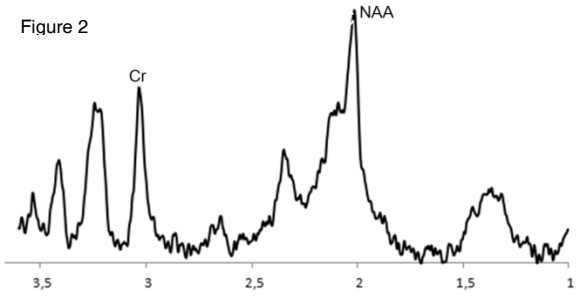

Figure 2

Material & Methods: Healthy female adult mice (C57BL/6, n = 6) were anesthetized by isoflurane (1.75% in ambient air) and positive pressure ventilated via an endotracheal tube. MR measurements were performed on a 7 T small animal system (Bruker ClinScan) using a standard 4-channel mice head coil. For proper positioning of volumes-of-interest T2-weighted images (2D TSE, TR/TE= 3140/41 ms, resolution 100×100 μm^2, slice thickness 500 µm) were obtained in axial, coronal and sagittal orientation. Localized proton MRS of anatomically defined voxel was achieved using half-Fourier 2D-selective RF excitations based on a PROPELLER trajectory (2). For each mouse individual excitation profiles covering the corpus callosum (CC) were defined by segmentation of the CC in a sagittal T2 weighted image. A second profile with the same volume but covering only cortex was defined adjacent to the CC. For comparison conventional PRESS spectra of 2 cuboidal volumes (3,9 x 3,7 x 0,7 mm^3) were acquired. One of these voxels was placed in a way that a maximal portion of the CC was inside this cube. The second voxel contained only cortical structures. All spectra were obtained with an echo time of 12 ms and a repetition time of 2 s.

Metabolite quantification involved spectral evaluation by LCModel (Version 6.3-0G, Provencher, 1993) using a simulated basis data set acting on the assumption of a PRESS acquisition scheme. Results with Cramer-Rao lower bounds above 20% were excluded from further analyses.

	2DRF						PRESS					
	CC			Cortex			CC			Cortex		
Animal	SNR	NAA	NAA(rel)	SNR	NAA	NAA(rel)	SNR	NAA	NAA(rel)	SNR	NAA	NAA(rel)
1	3	1.75	0.93	3	3.81	1.18	10	4.26	0.89	12	4.29	0.95
2	5	1.90	0.89	5	2.17	1.02	10	4.10	0.94	13	4.67	0.86
3	4	1.52	0.93	5	2.92	1.03	13	4.75	0.92	9	3.73	0.90
4	5	1.67	0.94	5	5.14	1.08	13	5.03	0.99	13	4.05	0.87
5	3	1.40	0.90	4	3.58	1.26	10	3.71	0.87	11	4.23	0.87
6	4	1.67	0.99	4	3.74	1.18	10	4.26	0.92	13	4.77	1.02
Average	**4.0**	**1.652**	**0.928**	**4.3**	**3.561**	**1.126**	**11.0**	**4.352**	**0.921**	**11.8**	**4.289**	**0.912**

Table 1

Results: Fig 1 shows the corpus callosum in sagittal slice through a mouse brain (Fig.1A), the excited volumes using the 2D selective RF excitations visualized with an imaging variant of the 2DRF MRS sequence (Fig.1B: 2x2x4 mm^3 cuboidal voxel, Fig. 1D: a profile obtained from the sagittal T2 weighted MR image covering only the corpus callosum). On average 25% of the 2x2x4 mm^3 cuboidal volume shown in Fig.1B voxel represent the CC resulting in only 4 mm^3. In Fig. 2, a spectrum acquired using the 2DRF to excite the CC is presented. Table 1 contains absolute and relative (normalized to creatine) NAA values for both regions and methods. While the inclusion or exclusion of the CC in a conventional PRESS voxel did not change the observed NAA concentration, the measurements with the anatomically matched voxels clearly reveal a NAA reduction in the CC compared to cortical gray matter (Fig. 3).

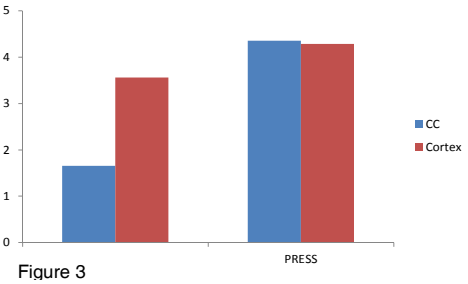

Figure 3

Conclusion: Segmented spatially 2D-selective RF excitations in single-voxel MR spectroscopy to acquire anatomically defined volumes in mice brain are a promising tool to improve the specificity of MRS to different cerebral compounds. Using this technique we demonstrated for the first time reduced NAA values in white matter compared in gray matter structures of mice.

References: [1] Pauly et al. JMRI 81, 43-56 (1989) [2] Busch M & Finsterbusch J, MRM 68, 1383-1389 (2012)