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. Thereby 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.

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.

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 μm², 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 was defined by segmentation of the CC in a sagittal T2 weighted MR image covering only the corpus callosum (Fig. 1A). On average 25% of the 2x2x4 mm³ excited volumes 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).

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.