At high magnetic field, the challenges for multivoxel MRS in murine brains are substantially amplified. In particular, first- and second-order shim correction becomes essential to improve local field homogeneity. Thus, we aimed first to demonstrate the feasibility of acquiring in vivo high-field magnetic resonance spectroscopy (MRS) in mice using dynamic shim updates (DSU) on both shims without any supplementary hardware. The second aim was to apply the DSU approach to in vivo studies of glutamatergic neurons devoid of mitochondrial pyruvate carrier 1 (MPC1) and to their control littermates following i.p. injection of the GABAa receptor (GABA) antagonist pentylenetetrazole (PTZ). Changes in in vivo transcranial metabolite profile might reveal the aberrant glutamatergic function from the normal state.

**Methods**

Animals

Vanderperre et al. (2016) studied transgenic mice with glutamatergic neurons devoid of mitochondrial pyruvate carrier 1 (MPC1) and to their control littermates following i.p. injection of the GABAa receptor (GABA) antagonist pentylenetetrazole (PTZ). Changes in in vivo transcranial metabolite profile might reveal the aberrant glutamatergic function from the normal state.

**Microscopy**

A home-made quadrature surface coil (two geometrically decoupled 12mm-diameter loops) resonating at 600MHz was used for radio-frequency transmission and reception. The head was fixed with two ear pieces and one bite bar, and rectal temperature was maintained at ~36ºC via circulating warm water via silicone tubes. Mice were anesthetized with 3% isoflurane mixed with 1:1 air and oxygen and their breathing rates were thereafter maintained in the range of 80-110bpm by adjusting the percentage of isoflurane (1-2%). 30min before the MRS measurements, mice were administered i.p. 20mg/kg pentylenetetrazole (PTZ), corresponding to half the dose that induced seizures in MPC1−/− mice. All experiments were performed in a horizontal 14.1T scanner, equipped with 400mT/m gradients (200μsec rise time) interfaced to a DirectDrive console (vnmrj, Agilent Inc.). Different scan parameters were obtained in an interleaved fashion from two brain regions, i.e. cortex and hippocampus (2.2×1.2×1.5 mm).

MR methods:

Field homogeneities were optimized using FASTMAP (Fig. 1). Typical 1H MR spectra of cortex (a, yellow voxel) and hippocampus (b, red voxel) of one mouse using DSU. Both spectra are averaged 160 scans and displayed (green). Although the metabolic changes due to the low dose of PTZ under isoflurane anesthesia are not substantial and remain to be explored further, regional differences in Lac, Glu, Ins and Glu were noticeable (Fig. 3a). Since DSU enables interleaved acquisition of both cortex and hippocampus regions, the metabolite difference, e.g. lactate (Lac), offers concurrently studying two important and distinct brain regions in the very same animal upon a small dosage of the GABAa receptor antagonist, i.e. PTZ. A consistent lower GABA level was observed in the hippocampus of MPC1−/− mice after the PTZ injection. Two-way ANOVA was performed on these metabolites with two factors, region with matched subjects and genotype. "r" indicates statistically significant (p<0.05) differences in metabolite levels between the two regions.