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Fast high-resolution metabolite mapping on a preclinical 14.1T scanner using ^{1}H-FID-MRSI

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Synopsis

^{1}H-MRSI enables a simultaneous acquisition of MR-spectra from multiple spatial locations inside the brain. While ^{1}H-MRSI is increasingly used in the human brain, its implementation in preclinical setting is limited because of the smaller size of rodent brain. At UHF for humans, ^{1}H-FID-MRSI acquisitions are increasingly used (T_2 and J-evolution minimization, increased SNR). We present the first implementation of fast ^{1}H-FID-MRSI in the rat brain at 14.1T and exploit its potential for an increased brain coverage, reliable and accurate quantification results and metabolic maps. Our results set the grounds for a wider application of ^{1}H-FID-MRSI in the preclinical setting.

Introduction

Magnetic resonance spectroscopic imaging (MRSI) enables a simultaneous non-invasive acquisition of MR spectra from multiple spatial locations inside the brain. Even though the ability of this technique to map the metabolic regional differences in vivo is very valuable for both clinical and biomedical research, its routine application remains challenging due to several issues (e.g. low signal-to-noise ratio (SNR), long acquisition times etc.). The availability of ultra-high magnetic fields (UHF), advanced pulse sequences and new encoding methods improved the quality and speed of MRSI[1,2]. At UHF in the clinical setting pulse-acquire free induction decay (^{1}H-FID-MRSI) acquisitions are increasingly used[2]. FID-MRSI acquisition minimizes the T_2 relaxation and J-evolution, therefore increasing the SNR. It also reduces the chemical shift displacement errors and sensitivity to B_0 inhomogeneities[2–5]. Moreover, this simple sequence design permits a considerable acquisition time reduction by decreasing the repetition time (TR) while using optimal Ernst's flip angle.

While ^{1}H-MRSI is increasingly used in the human brain, it is not yet widely applied in the preclinical setting mostly because of difficulties related to the small rodent brain[6]. The resulting low SNR arises from a very small nominal voxel size in rodents (e.g. 0.75x0.75x2mm^3 in a 32x32 matrix)[7] while in the human brain the nominal voxel size remains fairly big even at high spatial resolution (e.g. 1.7x1.7x10mm^3, for 128x128 matrix)[8]. There are additional challenges in terms of shimming of large volumes with many tissue interfaces, long measurement times (e.g 120min)[7,9,10], water suppression artifacts and lipid contamination[6].

In this study, the advantages of pulse-acquire ^{1}H-FID-MRSI acquisitions are combined with the UHF of 14.1T to obtain increased SNR and spatial resolution for the first time in the rodent brain.

Methods

The data were acquired in the rat brain (n=4) at 14.1T (Bruker/Magnex Scientific) using a homemade transmit/receive quadrature surface coil. T_2-weighted Turbo-RARE images were acquired in coronal and axial direction to position the MRSI slice for shimming, acquisition and for map overlays (20 slices, TR=3000ms, NA=2, RAREfactor=6).

For the high-resolution two-dimensional fast ^{1}H-MRSI a slice selective pulse acquire sequence was used in combination with VAPOR[11] water suppression and 6 saturation slabs to minimize the lipid contamination (FID ^{1}H-MRSI, Figure.1A). The MRSI slice was centered on the hippocampus, with 2mm slice thickness and FOV of 24x24mm^2 (Figure.2up). The matrix size was 31x31 leading to a nominal voxel size of 0.77x0.77x2mm^3. The following acquisition parameters were used: acquisition bandwidth of 7kHz, 1024 spectral data points, Cartesian k-space sampling, 8 dummy scans, TE=1.3ms, TR=813ms leading to total measurement time of 13min. The excitation pulse was adjusted to the Ernst angle of 52^o (0.5ms). First and second order shims were adjusted using MAPSHIM, first in an ellipsoid covering the full brain then in a voxel of 10x10x2mm^3 centered on the MRSI slice. Two datasets with one and two averages were acquired.

All spectra were quantified using LCModel. The metabolites were simulated using NMRScope-B (18 metabolites) from jMRUI[12], using published values of J-coupling constants and chemical shifts[13,14] and the pulse-acquire sequence with the same parameters as for the in vivo ^{1}H-MRSI metabolite acquisitions (Figure.1B). The macromolecule (MM) spectrum was acquired using a double inversion recovery STEAM (TI$_1$=2200ms, TI$_2$=850ms) sequence in the voxel of 10x10x2mm^3 centered on the MRSI slice. The metabolite residuals were removed with AMARES[15]. To match the acquisition delay (1st order phase evolution due to the acquisition delay of 1.3ms) to the one of the metabolites in the basis-set the first points of the FID were removed, and this final MM signal was added to the basis-set (Figure.1B). To improve the quantification robustness, the water signal was used for phase correction and the metabolite signals were decontaminated from skull lipids using the metabolite-lipid spectral orthogonality approach[16].

Results

The LCModel quantifications, using the created basis-set, provided reliable quality fits for the data obtained with both one and two averages (Figure.2). The resulting Cramér-Rao lower bounds (CRB's) were sufficiently low (<40%) for the metabolites of interest leading to accurate metabolic maps. The shim adjustments using MAPSHIM proved to be efficient when shimming in big areas, which translated into good quality spectra in a large number of nominal voxels in the matrix. Therefore, a good brain coverage was achieved extending also towards the edges of the brain and was not limited to a standard rectangular volume. Metabolic maps overlaid to the corresponding anatomical image for NAA, Glu, GPC+PCho and GABA are shown in Figure.3. Although the metabolic maps obtained from the acquisition with two averages provided a better contrast, the maps kept the same pattern when using one average proving that this very fast acquisition leads a satisfactory output.

Discussion and conclusion

We presented the first implementation of fast ^{1}H-FID-MRSI in the rat brain at 14.1T which provided an increased brain coverage, reliable and accurate quantification results and metabolic maps. Our results set the grounds for a wider application of ^{1}H-FID-MRSI in the preclinical setting with a potential for further improvement and acceleration. Further improvements will be investigated regarding the efficiency of lipid suppression, improvements in the homogeneity and coverage of the surface coil. In parallel, further reducing TR and implementing a concentric rings encoding would allow a faster acquisition.

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Figures

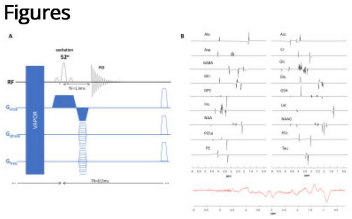
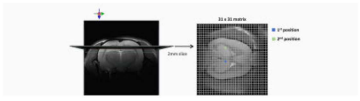


Figure.1: (A) A schematic drawing of the ^{1}H-FID-MRSI sequence used for data acquisition. (B) The metabolites simulated using NMRScope-B (18 metabolites) from jMRUI (up) and the MM included in the basis set. The MM spectrum was acquired with double inversion recovery STEAM and the residual metabolites were removed with AMARES from jMRUI.



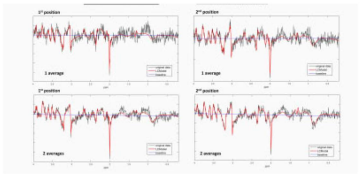


Figure.2: The slice position and the spatial resolution are shown on the figure up. The quality of LCModel quantification is shown for spectra from two different positions in the matrix with one and two averages.

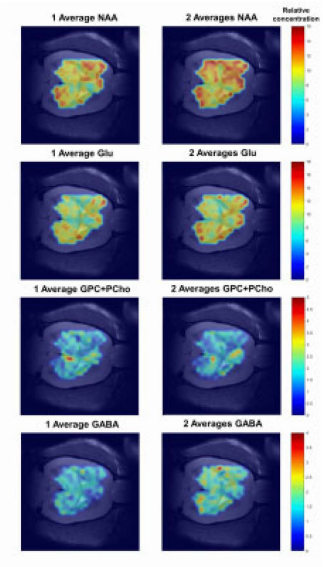


Figure.3: Metabolic maps obtained from the LCModel quantification results of the data acquired with one average (on the left) and two averages (on the right). The metabolic maps were superimposed to the corresponding anatomical image using an in house written MATLAB script. The scales correspond to LCModel outputs when referenced to tCr by setting its concentration to $8_{mmol/kgww}$.