Modeling of 3-dimensional MR spectra of human brain: simultaneous determination of T_1, T_2, and concentrations based on combined 2DJ inversion-recovery spectroscopy

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Introduction

Full quantitation of in vivo MR spectra of the human brain is challenging because it requires not only the determination of peak areas in a single spectrum, but also the determination of individual metabolite T_1's and T_2's, as well as the macromolecular baseline. Simultaneous determination of all these factors in single individuals is usually too time-consuming, particularly in a clinical setting. Hence, group data for T_1, T_2 and baseline are used instead. One approach for more efficient use of measurement time is the acquisition and simultaneous evaluation of complementary MR spectra, as proposed by linear combination (LC) modeling of 2D data arrays obtained from e.g. 2DJ, inversion recovery, or saturation recovery spectra [1-6]. In this work, a method is proposed for the determination of metabolite intensities with built-in relaxation corrections, as well as determination of T_1 and T_2 times, and optionally the macromolecular baseline. This is achieved by simultaneous modeling of a combined dataset, called 2DJ-IR, consisting of a 2DJ series and a set of inversion recovery (IR) spectra.

Methods

Data acquisition: 2DJ spectra were recorded using a localization sequence based on PRESS with incrementing TE. Instead of water suppression, an alternating two step metabolite inversion method [7] was used that provides both metabolite spectra (undistorted by water suppression effects), as well as equivalent water reference data simultaneously (2 s TR, 24 TE's from 20 ms to 307.5 ms in steps of 12.5 ms, 16 scans per TE). IR data was obtained with the same basic metabolite-inversion PRESS sequence at a single TE but including a global adiabatic pre-inversion pulse with variable IR delay times (TI) (TE 20 ms, TR 2 s, TI's 30, 200, 450, 575, 700, 825, 1200 ms, 48 scans per TI). Total measurement time for MRS was < 20 min. Experimental data was obtained from ten healthy volunteers investigated on a Siemens 3T TRIO system with a transmit/receive head coil. For this initial evaluation, a relatively large ROI of 25x25x25 mm^3 was chosen in the occipital cortex.
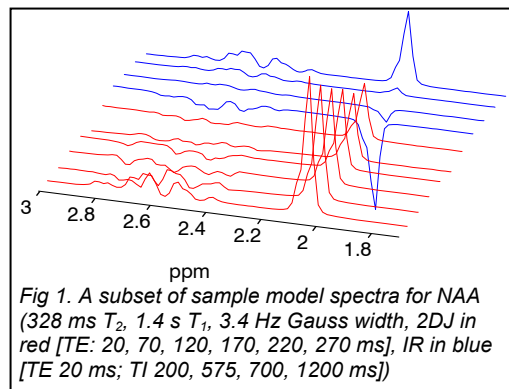

Fig 1. A subset of sample model spectra for NAA (328 ms T_2, 1.4 s T_1, 3.4 Hz Gauss width, 2DJ in red [TE: 20, 70, 120, 170, 220, 270 ms], IR in blue [TE 20 ms; TI 200, 575, 700, 1200 ms])

Data processing: Pre-processing to obtain separate water data and eddy-corrected metabolite spectra was performed in MATLAB, followed by LC model fitting using FiTAID (Fitting Tool for Arrays of Interrelated Datasets) extended for fitting in 3D space (1D spectrum, T_1, T_2) [6]. The data was fitted as a pseudo 2D array of 31 spectra (24 TE's and 7 TI's). Sets of metabolite spectra simulated for ideal PRESS [8] at the required TE's were used as bases. Samples are presented for NAA in Fig. 1. 17 metabolites were included. Voigt lineshapes, where the Lorentz width is deduced from the T_2, were used. A parameter-restricted least squares fit was performed in frequency domain (0 to 4.2 ppm). Different prior knowledge relations between metabolites and multiple fit strategy steps were tested. Macromolecules were modeled as a combination of Voigt lines with fixed offset and common line widths. The following amplitude relationship was applied along the rows of the array in order to fit T_1 and T_2:

$$S \propto \exp(-TE/T_2) \left[1 - \exp(TI/T_1) + \cos\beta \left\{ \exp(TI/T_1) - 2\exp\left(-\frac{2TR - TE - TE1}{2T_1}\right) + 2\exp\left(-\frac{2TR - TE1}{2T_1}\right) - \exp(-TR/T_1) \right\} \right]$$

where TE_1 was 10 ms and β is 180º for IR data and 0º for the 2DJ data.

Results

The dedicated acquisition sequence without water suppression yielded multi-echo and multi IR spectra of excellent quality (average Gauss-linewidth for metabolites of 4.0 Hz) that could be fitted well by the dedicated fitting tool, as illustrated in Fig. 2. The following metabolites could be determined with mean Cramer Rao Bounds (CRB) in single scans < 30%: GPC, total NA, NAAG, creatine, glutamate, aspartate, glutamine, GSH, myo-inositol, scyllo-inositol, and taurine. Interindividual variation was considerably larger than the CRB for most metabolites. To reduce ambiguity, in the present evaluation only 5 different T_1's and T_2's were introduced (NAA, Cr CH$_2$, Cr CH$_3$, CH$_3$ of cholines, other protons). Interindividual CV was 8 – 47 % for T_1, and 13 - 44 % for T_2 respectively (CRBs for T_1 ranged from 60 to 300ms, for T_2 from 6 to 30 ms). Metabolite contents as well as relaxation times agreed well with expectations based on the literature.
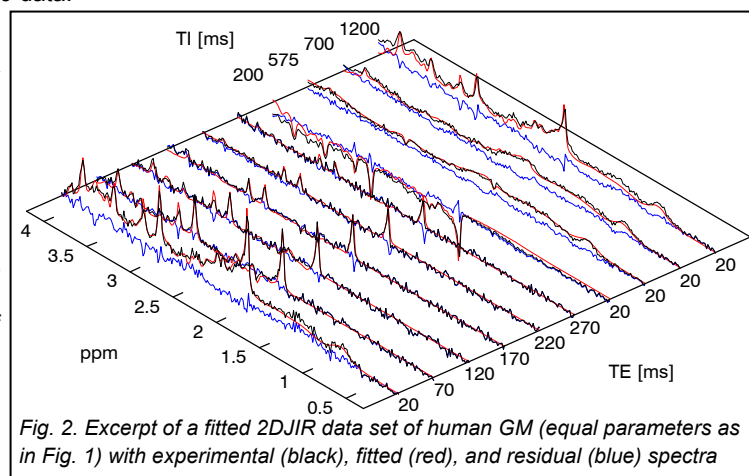

Fig. 2. Excerpt of a fitted 2DJIR data set of human GM (equal parameters as in Fig. 1) with experimental (black), fitted (red), and residual (blue) spectra

Conclusions

2DJ-IR acquisitions and subsequent simultaneous 3D modeling allowed for the determination of metabolite contents and individual T_1 and T_2 relaxation times. Due to the relationship between 2DJ and IR spectra, the area parameters as determined by this method are inherently relaxation-corrected and can be directly interpreted as concentration ratios.

References

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