Simultaneous Detection of 17 Brain Metabolites at 3T by JPRESS & ProFit

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Introduction

In clinical spectroscopy it is essential to obtain quantitative estimates of the metabolite concentrations present within the measured volume of interest (VOI). Particularly in ^{1}H brain spectra, many resonances from various metabolites form a crowded spectrum with severe spectral overlap of the individual signals. One possible method to reduce the spectral overlap in human brain ^{1}H spectra at 3T is to employ two-dimensional spectroscopy sequences. This allows spreading the spectral information across two frequency dimensions and as consequence reduces the undesired spectral overlap. A 2D j-resolved sequence based on PRESS localization (JPRESS) was proposed by Schulte et al. [1] for in-vivo detection of brain metabolites at 3T. Furthermore a corresponding software tool called ProFit [2] was developed to process and quantify the acquired data accordingly. To address some of the persisting shortcomings of the original ProFit version a thoroughly revised ProFit 2.0 implementation was developed [3] that allows for inclusion of a macromolecular basis set along with an additional spline baseline fit, a self-deconvolution based line shape model and largely extended and more flexible prior-knowledge handling. In this work the new ProFit 2.0 version was tested and validated using simulated data sets matching common in-vivo SNR, line shape and macromolecule content and in-vivo data.

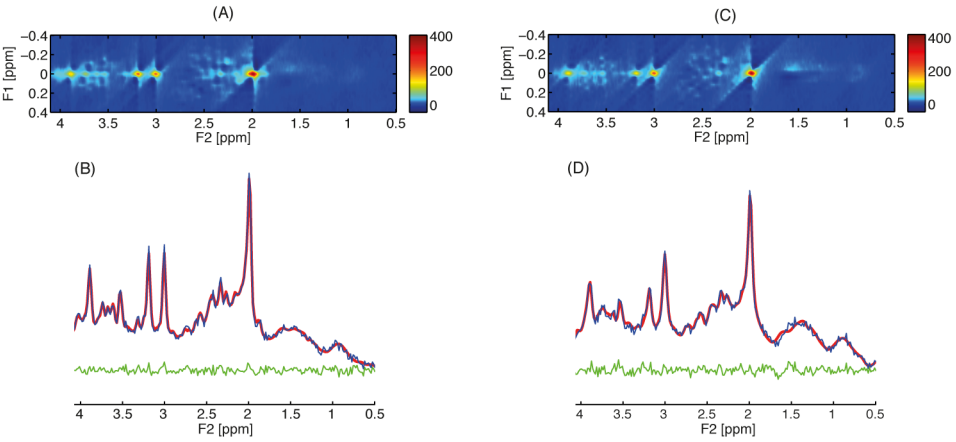

Fig. 1: (A) shows the 2D spectrum of one simulated data set together with the corresponding projection along t_1 (B). The plots in (C) and (D) illustrate a typical in-vivo spectrum, showing the 2D spectrum (C) and the projection (D). The blue line in (B) & (D) represent the data, red indicates the fit as produced by ProFit 2.0 and green shows the fit residual in both cases.

Materials & Methods

A virtual brain data set including 18 metabolites was simulated using the GAMMA [4] library. The starting echo time was set to 24ms while in the indirect dimension 100 steps with 2ms echo time increase were simulated. To mimic realistic line widths approximate relaxation rates were taken from literature [5–7] where available or otherwise set to similar values as other metabolites. Typical relative concentrations were also defined according to literature values [8–10]. Subsequently these signals were combined into 20 inter-subject data sets with individual Gaussian random noise that resembles typical in-vivo signal-to-noise (SNR) situations. To emulate inter-subject or simple acquisition variations concentration values were varied ±10% from the typical values, zero order phase was distorted in the range of ±5 deg and the spectra were shifted arbitrarily between ±4 Hz in the direct and in the indirect dimension. Realistic inhomogeneous line broadening was achieved by randomly applying the normalized lineshape envelopes extracted from 11 measured water scans to the simulated spectra. Additionally a macromolecular baseline signal was added to each data set. The macromolecular contribution was also randomly sampled from a pool of 10 measured and subsequently smoothed metabolite nulled JPRESS spectra from the visual cortex. Additionally ten more 2D JPRESS spectra were acquired from one healthy volunteer on a Philips 3T system using a transmit/receive birdcage coil. The voxel size was set to 25x20x20mm and the VOI was placed in the visual cortex. The minimum achievable echo time was TE=24ms and the TR=2000ms. Both sets of data were fitted using the same basis set including the identical measured macromolecular contribution and the same configuration of fit iterations.

Results & Discussion

Using the settings described above the simulated spectra could closely be matched to in-vivo quality as can be seen in the comparison of measured and simulated data sets (Fig. 1). The correlation analysis of the simulated data shows excellent agreement between true and fitted values for most metabolites (Tab. 1). More specifically eight metabolites show correlation coefficients R>0.9, five metabolites R>0.8, four additional ones R>0.7 and finally two metabolites R>0.5. The in-vivo reproducibility measurements show stable concentration estimates (Fig. 2A) and most importantly, the mean CRLBs of all metabolites except acetate (41.6±22%) stay well below 20%. This leads to the **conclusion** that JPRESS at 3T together with ProFit 2.0 enables the reliable detection and quantification of 17 brain metabolites in-vivo.

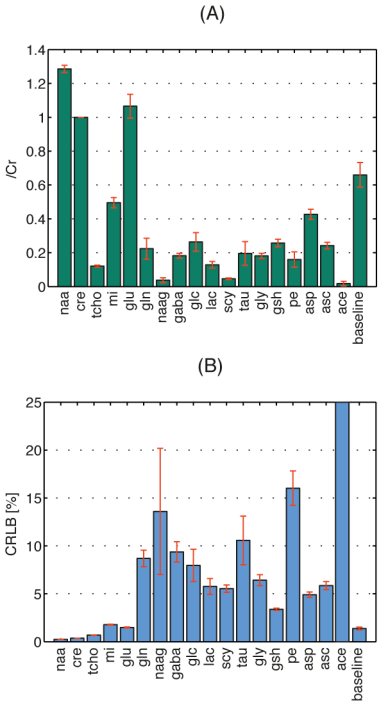

Fig. 2: The bars in (A) show the mean concentration to creatine ratios obtained from the 10 intra-subject measurements while the error bars represent the standard deviation. In part (B) the mean and standard deviation of the resulting CRLBs are shown. The mean CRLBs of ace exceeded the axis scaling (41.6±22%).

References

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Tab. 1: The results of the correlation analysis for the 20 simulated data set are shown, indicating excellent agreement between true and fitted concentration estimates.

	naa	cre	tcho	mi	glu	gln	naag	gaba	glc	lac	scy	tau	gly	gsh	pe	asp	asc	ace	mm
R	0.97	0.99	0.99	0.92	0.95	0.91	0.89	0.75	0.58	0.92	0.87	0.73	0.82	0.91	0.8	0.72	0.52	0.70	0.88