Quantitation of Edited GABA Signals

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Introduction

γ-Amino butyric acid (GABA) is an inhibitory neurotransmitter that plays an important role in several brain disorders [1]. Reliable detection of GABA *in vivo*, using ^{1}H Magnetic Resonance Spectroscopy (MRS) is difficult and faces various challenges. Spectral-Editing sequences based on multiple quantum (MQ) filtering techniques enable removal of overlapping signals [2]. Reliable *quantitation* of GABA however, additionally requires advanced signal processing that accommodates sequence-dependence of the edited signals. We propose to use the time-domain quantitation algorithm QUEST [3]. Moreover, we exploit the Cramér-Rao Lower Bounds (CRBs) to predict the precision gain of GABA quantitation. Finally, quantitation with QUEST of ^{1}H *in vitro* double-quantum signals at 300 MHz of a phantom containing a solution of metabolites with concentrations of a normal brain is demonstrated.

Method

Reliable, *in vivo* quantitation of GABA in the brain by ^{1}H MRS is difficult: 1) GABA has a low concentration. 2) Strong overlaps with many, more intense, metabolite resonances such as NAA, Creatine (Cr), Glutamate (Glu) and Glutamine (Gln) occur. We propose: 1) Use of a single-voxel PRESS sequence including a double-quantum (DQ) filter to edit/acquire the GABA signal [2]. DQ filtering is an excellent tool to effectively suppress the large singlet resonances (Cr, Choline (Cho)) overlapping the GABA spectrum. 2) Either Quantum-Mechanical simulation (with the NMR-SCOPE program) or DQ-acquisition of GABA signal and use it as prior knowledge in the QUEST quantitation algorithm. 3) Quantitation of the edited GABA signal with QUEST.

Strong correlations between metabolite signals due to overlaps hamper the quantitation and lead to large CRBs. The latter are reduced when using edited signals which are virtually correlation-free. By comparing the CRBs on the GABA amplitude of the edited PRESS-DQ filtered and conventional PRESS signals respectively, one can predict the *gain* of precision of GABA quantitation attendant on spectral editing.

Results

The experiments were performed *in vitro* on a 300 Mhz Bruker spectrometer using a PRESS-DQ filter sequence. Two phantoms were used, one containing a solution of 1.5 mM GABA and eleven metabolites whose known concentrations correspond to a normal adult human brain, in D_2O, and another containing a solution of only 1.5 mM GABA in D_2O. GABA was well edited, see Figs. 1b and d and 'doublets' are observed at 2.99 ppm and 2.28 ppm. The intense NAA, Cho, Cr singlets are perfectly suppressed as well as most of the metabolite coupled spectral components. After water removal, the edited DQ signal of the solution containing all metabolites (see Fig. 1b) and exhibiting mainly GABA, was quantitated with QUEST. The basis set was made of only the DQ GABA signal, acquired *in vitro* from the GABA solution. Quantitation results are given in Fig. 2. The DQ spectrum of GABA was perfectly estimated. The observed residue is mainly due to the DQ spectra of Glu and Gln. The estimated proportion of GABA signal in the phantom with respect to the metabolite basis set was 1.0 ± 5% a.u which is to be compared with the true value of 1.0 a.u., provided that the error on its concentration was negligible.

At 1.5 T, for a noise standard deviation (arbitrarily) equal to 1, the CRBs on the GABA amplitude of a simulated signal containing GABA and eleven metabolites with concentrations corresponding to a normal adult human brain were found to be 0.15 (0.53 in the presence of an additional background) and 0.071 for the signal simulated with a PRESS-DQ Filtered sequence, leading to an expected quantitation-precision gain of 2 to 7 *in vivo*.

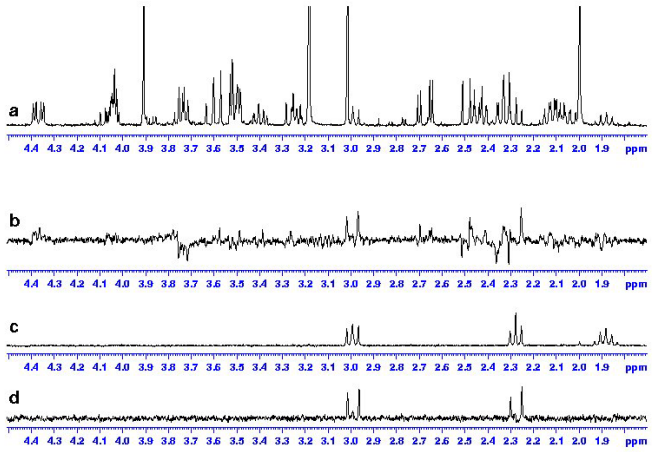

Fig.1. Spectra of metabolite phantom solutions obtained at 7 Tesla with a PRESS-DQF and a one pulse sequence respectively. a) Zoom-in of normal spectrum of the solution containing GABA and eleven metabolites with concentrations corresponding to a normal adult human brain. b) Edited double-quantum spectrum of this solution; note that mainly GABA is edited. c) Normal spectrum of GABA. d) Double quantum spectrum of GABA.

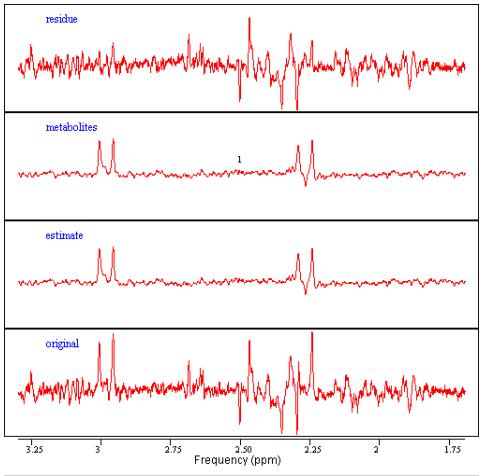

Fig.2. Edited double-quantum spectra of a solution containing GABA and eleven metabolites, see Fig.1b, quantitated by QUEST.
From bottom to top, raw edited DQ-spectrum, estimated spectrum, individual DQ spectrum of GABA and the residue.
The DQ signal of Fig.1d was used in the QUEST metabolite basis set.
http://www.mrui.uab.es/mrui/mruiHomePage.html

Conclusion

- We successfully edited the GABA signal from a solution containing GABA and eleven metabolites with concentrations corresponding to a normal adult human brain using a PRESS-DQ Filtered sequence.
- We demonstrated that QUEST is well-suited to accommodating sequence-dependence of the edited signals.
- GABA in edited PRESS DQ Filtered *in vitro* signals of metabolites was automatically and reliably quantitated with QUEST.
- We showed that at 1.5 T the editing sequence leads to an expected precision-gain of GABA-quantitation of at least 2 to 7.

Acknowledgements

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References

[1] Pearl P.L. and Gibson K.M.,, Current Opinion in Neurology, 17, 107–113, 2004.
[2] McLean M.A., Busza A.L., Wald L.L., Simister R.J., Barker G.J., and Williams S.R., Magn. Reson. Med., 48, pp. 233-241, 2002.
[3] Ratiney H., Sdika M., Coenradie Y., Cavassila S., van Ormondt D., and Graveron-Demilly D., NMR in Biomedicine, 18, 2005, in press.