Strategies for reliable quantification of intracerebral GABA by 1H-MRS

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Introduction:

Gamma-aminobutyric-acid(GABA) is an important inhibitatory neurotransmitter in human brain with anticonvulsive character. Because of an increased interest in GABA metabolism we tested the reliability of special editing sequences which allow non-invasive intracerebral measurements of this neurotransmitter in healthy adults.

Methods and Materials:

We determined the reproducibility of GABA quantification obtained with a J-coupling based editing sequence on a 3T scanner (Siemens Tim Trio, Erlangen, Germany) with a Tx/Rx-1H-Head-coil by placing single-voxel spectroscopy(SVS) ROIs in left/right occipital lobe of subjects localized on T2-weighted images avoiding the ventricles. A Point Resolved Spectroscopy (PRESS) sequence incorporating a MEGA suppression scheme[1] (TR/TE 1500/68 ms, TA~6min, 1200 Hz acquisition bandwidth, 128 averages, vector size 1024) was optimized for the detection of the $^4CH_2$ resonance (triplet) of GABA. Every second acquisition a frequency selective, refocusing Gauss pulse with minimal bandwidth (40Hz) is irradiated to the $^3CH_2$ resonance at 1.9 ppm, affecting the weakly J-coupled triplet peak at 3.02 ppm. In between the same pulse is applied symmetrically to the other side of the water peak. Subsequently time domain subtraction is applied(Fig.1). In addition unsuppressed water was measured using 16 averages as quantitation reference.

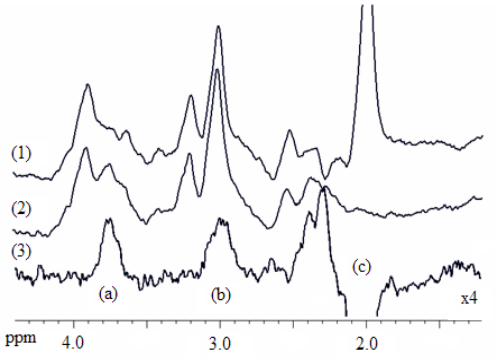

Fig. 1: (1) unsuppressed spectrum; (2) spectrum with MEGA-suppression at 1.9 ppm; (3) edited spectrum as subtraction of spectrum (2)-(1); (a) Glx+Gln, (b) GABA, (c) NAA

Intra- and inter-subject reproducibility was evaluated. 9 volunteers were measured in total, 2 proband repeatedly on 4 days (5male, 6female). Side differences between left/right hemisphere were investigated. GABA/Cr and GABA/H2O-ratios were compared. 4 voxels were measured per session. Furthermore a detailed comparison of 2 different post-processing routines for the evaluation was accomplished. Integration of signals(GABA/Cr/H2O) was done using MestreC compared to time-domain line-fitting-routine(AMARES-jMRUI).
Mean value, standard deviation(SD) and coefficient of variation(CV) were calculated among groups. Segmentation was performed using T2 images to determine liquor contamination in each voxel using MINC-tools (McConnell Brain Imaging Center, Montreal, Canada). Lowered GABA+/H2O ratios compared to GABA+/Cr were correlated with liquor contamination using Pearson Correlation - SPSS 15.0 (Chicago, Illinois, USA).

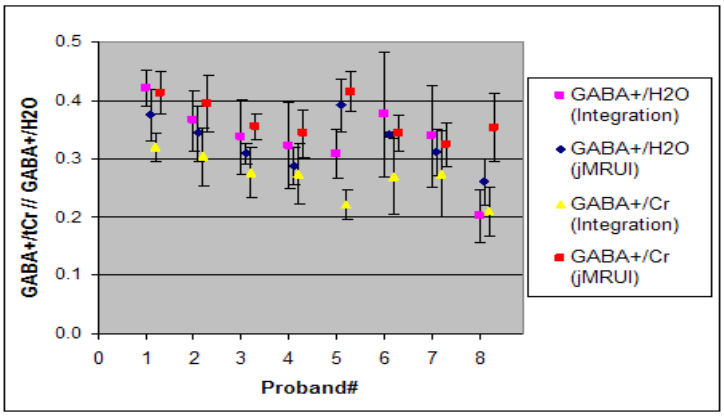

Fig. 2: Intra-subject reproducibility in 9 volunteers showing smallest variations for GABA+/Cr ratios using AMARES line fitting(scaling factor - water 2400) (mean and standard deviation)

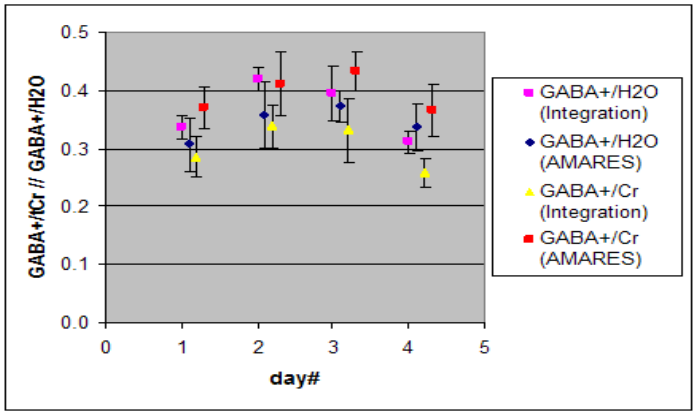

Fig. 3: Inter-subject reproducibility in one patient measured on 4 consecutive days (using 4 different quantification methods)

Results:

Using data from all subjects lower CVs can be observed for line-fitting compared to integration. GABA/Cr ratio performs better than GABA/H2O or GABA alone (GABA/Cr: 13.6% and 21.55%; GABA/H2O: 14.8% and 21.68%; GABA: 20.62% and 26.42%). Single subject 4-day measurements showed slightly better intra- than inter-subject reproducibility (GABA/Cr 12.23%)(Fig.2,3). No left/right-difference could be found (GABA/Cr: 0.372±0.058 and 0.366±0.042) as well as no gender difference (male/female: 0.366±0.05/0.393±0.046). Small intra subject fluctuations of the GABA level could possible add to uncertainties of quantification(Fig.3). Outliers of GABA+/H2O correlated with high CSF contamination (Pearson: r=-0.47; p<0.01).

Discussion and Conclusion:

With a CV of ~13% for GABA/Cr, the technique turns out to be a precise and promising tool which easily detects changes of up to +300% found during antiepileptic drug intake.[2] Due to minor liquor contamination GABA/Cr-ratios are slightly more reliable than GABA/H2O and GABA alone. Automated line-fitting performed better than integration.

References:

[1] Mescher M, et al NMR in Biomed 1998; 11(6):266-272
[2] Mueller SG, et al Epilepsia 2001; 42(1):29-40