Detection of Glutamate in the Human Brain at 3 Tesla Using Optimized CT-PRESS

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Abstract
A CT-PRESS sequence was implemented on a 3 T MR scanner and optimized for the detection of the C4 resonance of glutamate. The sequence was tested on phantoms containing solutions of various brain metabolites and healthy human volunteers. 121 encoding steps in t_1 were sufficient to separate the glutamate resonance while the highest signal–to–noise ratio was achieved at an average echo time of 131 ms. Other resonances detected *in vivo* were N–acetyl aspartate, total creatine, choline containing compounds and *myo*-inositol. However, glutamine resonances could not be resolved due to severe signal overlap from glutamate and N–acetyl aspartate.

Introduction
As one of the major excitatory neurotransmitters in the central nervous system, glutamate (Glu) is of tremendous interest in a variety of neurological and psychological diseases. But even at a field strength of 3 T its detection via 1D ^{1}H NMR spectroscopy is often hampered by spectral overlap, especially from resonances from glutamine (Gln) and N–acetyl aspartate (NAA), and line splitting due to J–coupling. Constant Time PRESS (CT–PRESS) [1] has been introduced as a method to detect coupled resonances with effective homonuclear decoupling and high signal–to–noise ratio (SNR). Therefore, the aim of this work was the implementation and optimization of a CT–PRESS sequence on a 3 T MR scanner for the separate detection of Glu.

Materials and Method
All measurements were performed on a GE 3 T MR scanner equipped with self-shielded gradients (35 mT/m, 200 mT/m/ms). A standard GE head coil was used in measurements on phantoms containing metabolite solutions. For *in vivo* experiments on healthy volunteers both RF excitation and signal reception were carried out by a quadrature, dome-shaped bird-cage coil [2] to increase the SNR.

The implemented CT–PRESS sequence consists of a PRESS module (TE = 25 ms, SW_2 = 2500 Hz, 2K complex data points) and an additional refocusing pulse for constant time chemical shift encoding. The pulse was shifted in increments of 0.8 ms corresponding to a spectral width in f_1 of 625 Hz. For each t_1 step the data acquisition started after the spoiler gradient following the last RF pulse. Due to RF power restrictions all refocusing pulses had flip angles of 167°. Water presaturation was accomplished by three CHESS pulses and TR was 2 s. Measurements were performed with 191 t_1 steps and a TE for the central encoding step (t_c) of 187 ms. To find optimized values for the nominal spectral resolution in f_1 and t_c, different subsets with respect to t_1 were evaluated. The experiments were supplemented by numerical simulations of the pulse sequence using the full density matrix [3].

Data postprocessing comprised a t_1 dependent shift in t_2 considering the different start of data acquisition, zero-filling and multiplication with sine–bell functions. After 2D–FFT of the data subsets CT–PRESS spectra were calculated as a projection onto f_1 with an integration interval of ±13 Hz around the spectral diagonal.

Results and Discussion
Both experimental and simulated data showed that 121 t_1 steps are sufficient to separate the C4 resonance of Glu (2.35 ppm) from signals from both Gln and NAA. The highest SNR was achieved at a t_c of 131 ms (minimum t_c for the implemented sequence). CT–PRESS spectra obtained from phantoms containing solutions of Glu (50 mM), Gln (50 mM), NAA (49 mM) and a mixture of these (each 50 mM) are shown in Fig. 1. All the resonances appear as single lines as the line splitting is suppressed in f_1. Note the NAA peak at 2.58 ppm which is a consequence of effective homonuclear decoupling. For strongly coupled spins this technique leads to an additional signal at the mean chemical shift of the coupled resonances [4]. The intensities of all 3 peaks depend on t_c. For Gln the additional resonance would be observed at 2.29 ppm. However, the spectrum shows that it can be neglected at a field strength of 3 T and the chosen t_c. While CT-PRESS experiments at 4.7 T have shown the feasibility of separating the Gln C3 resonance [5], at 3 T it was not possible to distinguish this resonance from NAA.

For the *in vivo* application of the method a 2×2.5×2.5 cm^3 voxel was selected in the occipital lobe of the brain of a healthy volunteer. The CT–PRESS spectrum in Fig. 2 shows that the Glu C4 resonance can be separated clearly. Additionally, signals from total creatine (tCr), choline containing compounds (Cho) and *myo*-inositol (mI) could be detected.

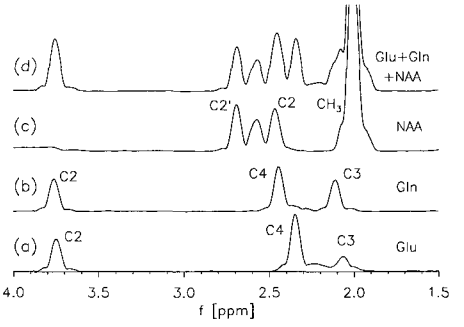

Fig.1: CT–PRESS spectra from solutions of (a) Glu, (b) Gln, (c) NAA and (d) Glu + Gln + NAA (2×2×2 cm^3, t_c = 131 ms, T_{meas} = 4 min).

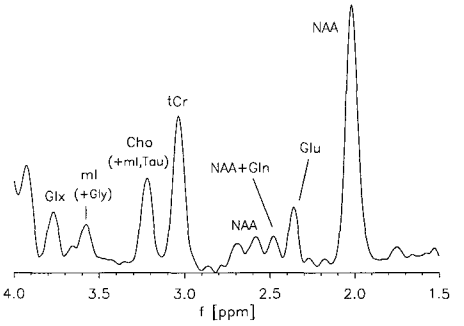

Fig.2: CT–PRESS spectrum from a voxel of a healthy human brain (2×2.5×2.5 cm^3, t_c = 131 ms, T_{meas} = 4 min).

Conclusion
Good separation of the Glu C4 resonance is feasible at 3 T using optimized CT-PRESS. However, it was not possible to resolve signals from Gln. In contrast to methods based on spectral editing this sequence has the advantage of additionally detecting singlet resonances. Although more accurate knowledge of relaxation times is necessary for absolute quantitation, this method is a valuable tool for the relative quantitation of Glu in various pathologies. A spectroscopic imaging variant of this method with an acceptable total measurement time is possible by using spectral undersampling in f_1 and time–varying gradients during data acquisition.

References
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