Detection of Glutamate at 3T with a Chemical Shift Selective Filter

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Introduction

Glutamate (Glu) is one of the major excitatory neurotransmitters in the central nervous system and thus is of great interest in several psychiatric disorders. Unequivocal detection of Glu is difficult due to strong coupling effects and similarities of the resonances to glutamine (Gln). Here, we apply a chemical shift selective filter (CSSF) [1, 2] to the *in vivo* detection of Glu. This type of filter is an acquisition based technique with the major advantage that only the chemical shifts of multiplets need to be resolved and not the detailed structure of the multiplets themselves. The target of the filter is the Glu multiplet at 2.35 ppm, which is separated by 0.09 ppm from the nearest Gln resonance at 2.44 ppm. For this resolution, a shim better than 12 Hz on 3T is required.

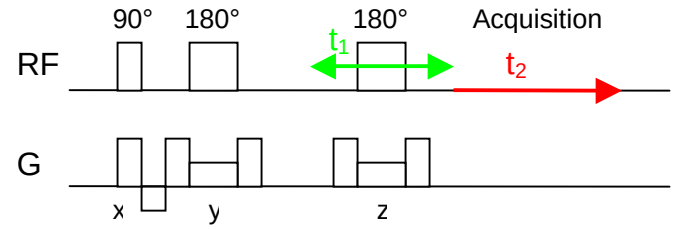

Fig. 1: Sketch of the basic acquisition, which is similar to PRESS. The normal acquisition is commonly referred to as t_2-domain. Instead of averaging the signal many times over the same echo time a second dimension (t_1) is acquired through shifting the second 180° pulse. The acquisition starts directly after the crusher gradient of the second 180° pulse and is shifted subsequently to a constant start of the acquisition.

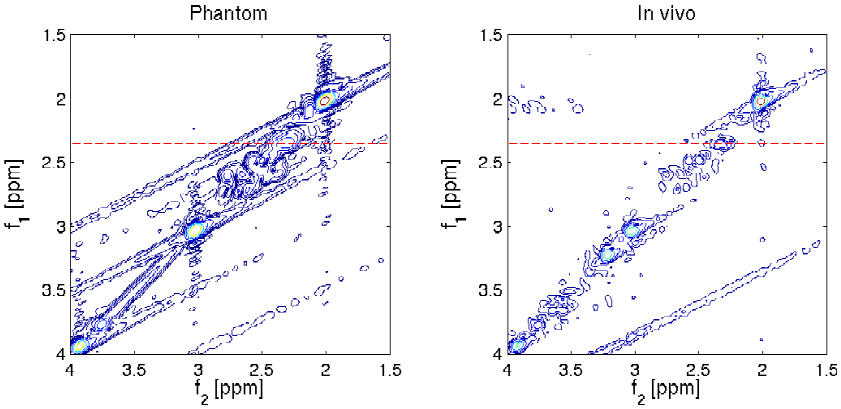

Fig. 2: CT-PRESS spectra acquired in a phantom (left; 18 mM Glu, 9 mM Gln, 24 mM NAA, 3 mM GABA, 4 mM GSH, 16 mM Cre) and *in vivo* (right). The CSSF spectrum of Glu is the cross section along the red dashed line (f_1 = 2.35 ppm). The side lobes are more pronounced because the magnitude is plotted. One dimension of the side lobes is tilted due to a maximum acquisition of the echo.

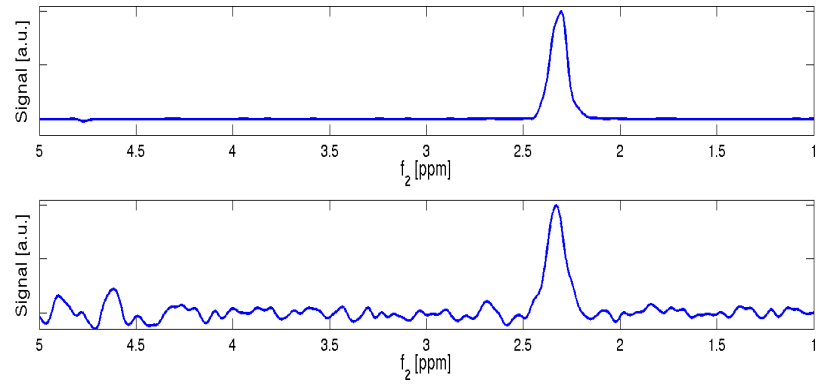

Fig. 3: CSSF spectra of Glu in phantom (top; 100 mM Glu) and *in vivo* (bottom). Note the excellent suppression of other metabolites and water. Here, the real part of the phase corrected spectrum is shown.

Theory and Methods

CSSF is related to a 2D NMR experiment and requires the acquisition of spectra at different echo times (T_E). Spatial localisation for CSSF is achieved with point resolved spectroscopy (PRESS), which is modified to acquire different T_E's (t_1-domain) by shifting the last 180° pulse as shown in Fig. 1. The acquisition (t_2-domain) starts right after the crusher gradients of the last pulse. A so-called constant time (CT-PRESS) experiment [3, 4] is obtained by shifting the different spectra in the t_1-domain to the same effective time. The 2D Fourier transform yields a 2D spectrum (see Fig. 2) with the resonances aligned along the diagonal and its multiplets split in the f_2 direction. The CSSF spectrum (Fig. 3) is the cross section (f_1 = 2.35 ppm in case of Glu) through the 2D spectrum.

The data were acquired on a Philips 3.0 T Intera whole body scanner equipped with a transmit/receive head coil. The bandwidth in the t_2-domain was 2 kHz with 2048 samples and T_R = 2 s. In the t_1-domain 100 echo times were acquired from 31 to 229 ms with ΔT_E = 2 ms. Each echo time was averaged four times leading to a total experimental duration of 13 minutes. Post-processing was performed in MATLAB. For better line shapes and suppression of truncation artefacts, a Lorenz-to-Gauss transform was applied (t_2-domain: exp = -5 Hz, gauss = 20 Hz; t_1-domain: exp = -1 Hz, gauss = 20 Hz). The data were reconstructed to an evolution time of 130 ms.

Phantoms were measured to evaluate the performance of CSSF, both with a mixture of Glu/Gln/NAA/GABA/GSH/Cre in *in vivo* concentration ratios and purely with 100 mM concentrations. The suppression quality of Gln and GABA was determined experimentally by integration. For *in vivo* validation five healthy volunteers with written informed consent were measured in the prefrontal cortex.

Results

Typical line widths achieved with second order shimming were 7 Hz *in vivo* and 4 Hz in phantoms. Contamination was 1.4% and 34.7% for Gln and GABA, respectively. The [Glu]/[Cre] ratio was 0.493 ± 0.023.

Discussion and Conclusion

CSSF is a robust and straight forward method which is as easy to apply as a routine PRESS sequence. The averaging required for sufficient sensitivity in PRESS can advantageously be used to gain additional information by resolving an additional spectral dimension. The theory of CSSF holds strictly only for weakly coupled spin systems but proved to work as well for the strongly coupled glutamate. The suppression of neighbouring metabolites is good, except for GABA, which has a much lower concentration than Glu and can be safely neglected.

References

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The authors like to thank Prof. Albert Thomas and Drs. Ralph Hurd and Jeffrey Tsao for fruitful discussions.