Two-Dimensional Zero-Quantum Coherence $^1$H NMR Spectroscopy of Glutamate and Glutamine

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Introduction:

In vivo detection of the important neurometabolites glutamate (Glu) and glutamine (Gln) by means of NMR spectroscopy remains a challenge, not only due to their high metabolic turnover, but also to complex scalar-coupled multiplets and strong signal overlap in the $^1$H spectrum. In order to more precisely differentiate the two, we make use of zero-quantum coherences (ZQC) in a stimulated-echo acquisition mode (STEAM) sequence. This is based on the method of volume-localized editing by means of ZQC in a STEAM sequence as introduced by Sotak and Freeman [1]. By varying the mixing-time interval (TM) between the second and third RF pulses of the STEAM sequence, phase modulation of scalar-coupled spins can be observed. The frequency of this modulation is equal to the difference of the chemical shifts of the coupled spins. Addition of a second axis along which the frequency of the ZQC evolution is plotted, allowed detection of lactate in human brain tumor in vivo at $B_0 = 1.5$ T in a measurement time of 31 min. [2].

For Glu with its $\alpha$-CH peak at $\delta = 3.74$ ppm and $\beta$-CH peak at $\delta = 2.03$ ppm, the frequency of the ZQC modulation is 212 Hz for the outer $\alpha$-CH triplet peaks at $B_0 = 3$T. For Gln at the same $B_0$, this value is 203 Hz due to Gln’s $\alpha$-CH peak at $\delta = 3.75$ ppm and $\beta$-CH peak at $\delta = 2.13$ ppm. [3].

Materials and Methods:

Glutamate and glutamine model solutions (40 mmol/L each) were examined via localized two-dimensional (2D) ZQC $^1$H NMR spectroscopy on a whole-body MR tomograph (3 T, Magnetom Trio; Siemens Medical Solutions, Erlangen, Germany). Series of water-suppressed $^1$H NMR spectra were obtained from a 2x2x2 cm$^3$ voxel with TR = 2000 ms. Series of sixteen spectra were recorded from the Siemens Medical Solutions, Erlangen, Germany). Series of water-suppressed $^1$H NMR spectra were allowed detection of lactate in human brain tumor in vivo at $B_0 = 1.5$ T in a measurement time of 31 min. [2].

Results:

In vivo detection of the important neurometabolites glutamate (Glu) and glutamine (Gln) by means of NMR spectroscopy remains a challenge, not only due to their high metabolic turnover, but also to complex scalar-coupled multiplets and strong signal overlap in the $^1$H spectrum. In order to more precisely differentiate the two, we make use of zero-quantum coherences (ZQC) in a stimulated-echo acquisition mode (STEAM) sequence. This is based on the method of volume-localized editing by means of ZQC in a STEAM sequence as introduced by Sotak and Freeman [1]. By varying the mixing-time interval (TM) between the second and third RF pulses of the STEAM sequence, phase modulation of scalar-coupled spins can be observed. The frequency of this modulation is equal to the difference of the chemical shifts of the coupled spins. Addition of a second axis along which the frequency of the ZQC evolution is plotted, allowed detection of lactate in human brain tumor in vivo at $B_0 = 1.5$ T in a measurement time of 31 min. [2].

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Dicussion:

We have proven that both Glu and Gln can be well identified in individual solutions due to their ZQC modulation frequency, as can Glu in solution with other metabolites. In spite of this, initial attempts to resolve a model solution containing both Glu and Gln prove more challenging due to the high resolution that is necessary along the ZQC frequency axis. We conclude, that were it possible to increase the number of TM increments without increasing the measurement time, Glu and Gln could be unequivocally differentiated.

References: