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The specificity of GluCEST imaging at low temperatures

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Purpose/Introduction

The dependence of the CEST effect between amine protons of glutamate and protons of bulk water on glutamate concentration and pH, and its high specificity has been shown for 37°C.[1] Therefore, GluCEST is a promising tool for observing neurological disturbances and intracellular pH in the brain. However, this technique might be also of interest for other applications, e.g., studying the physiological response of aquatic ectothermic animals to the climate change. Therefore, the aim of this study was to investigate the temperature dependent specificity of the GluCEST effect and the main drivers for potential contributions.

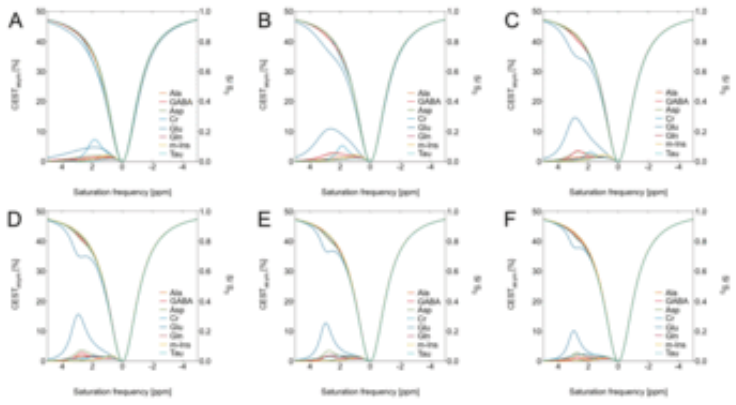
Subjects and Methods

For phantom I, solutions of eight brain metabolites (Tab.1) were prepared in PBS (7.0pH, 10mM). Phantom II consisted of three solutions: glutamate (10mM), all eight metabolites and PBS. The observed temperature range was 1-32°C. All NMR measurements were performed on a 7T animal scanner (Biospec 70/20/USR, Bruker-Biospin) equipped with a gradient system BGA-12S2 and a quadrature birdcage coil (72mmø). CEST images were obtained by pre-saturated FISP imaging. Pre-saturation was accomplished by a train of 12 rectangular pulses (tp=1s, B_1=2.94µT or B_1=5.87µT). The CEST asymmetry was calculated as $CEST_{asym}=(M_{sat}(-\Delta\omega)-M_{sat}(\Delta\omega))/M_{sat}(-\Delta\omega)$. Exchange rates k_{sw} were determined by numerically fitting the Bloch-McConnel equations to the experimental data. Simulations were performed by numerically solving the Bloch-McConnel equations with the determined exchange rates and concentrations expected *in vivo*.

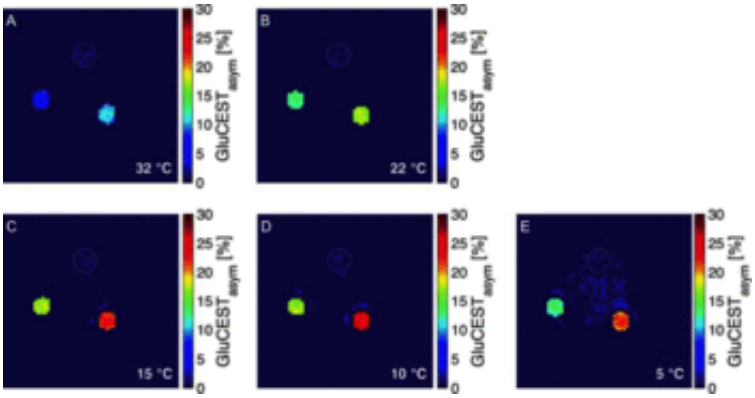
Metabolites	Concentration [mM]	Δδ of the exchangeable protons [ppm]
Ala	1	2.8
GABA	2	2.75
Asp	2	2.8
Cr	6	1.9
Glu	10	3
Gln	2	2.8
m-Ins	10	0.6
Tau	2	2.8

Results

The simulated z-spectra and their asymmetries significantly changed as a function of temperature (Fig.1). While the CEST effects of creatine and myo-inositol decrease with lower temperature, the CEST effects of aspartate and taurine increase.



Nevertheless, the percentage contribution of glutamate to the CEST effect is in the range of 65-80% depending on temperature (Fig.2). However, note that the asymmetry curves also depend on B_1 and pH. The buffer PBS showed no own CEST effect at any temperature.



Discussion/Conclusion

For 7.0pH and the B_1 field used, the CEST effect at 3ppm is dominated by glutamate at all temperatures observed (1-32°C), despite various contributions from other metabolites. Thus, the results fit well with the postulated glutamate contribution to the CEST effect (at 3ppm) at 37°C of around ~70-75%.[1] In summary, GluCEST can also be used at lower temperature, particularly to study the physiological response of aquatic ectothermic animals.

References

1. Cai, K. *et al. NatMed,* **18**,302-306(2012).

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