BRAINO 2.0. A new phantom for NMR & MRS development

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Introduction

In order to test the quantification of existing of existing MR techniques, and develop new ones, high quality phantoms are required. For this work we are focusing on mimicking the composition of low molecular weight metabolites found in rat brains. Traditionally, a solution of metabolites known was developed by GE, however it lacks the complexity seen in the real. To this end an improved formulation, 'Braino 2.0' was previously developed[1]. *In-vivo* spectroscopy shows significantly broader lines due to the slower molecular motions in semi-solid tissues. A further modification in Braino 2.T with the addition of a thickening agent, sodium alginate, was also created to replicate the line widths seen in-vivo. As well as testing potential new NMR sequences, Braino 2.0 can also be used to test techniques, such as polar extraction, used to produce NMR samples. It can be used to identify changes that occur in relative concentrations of metabolites during these processes, as well as to optimize how they are conducted.

Experimental

It is known that pH can alter chemical shifts seen in ^{1}H spectra. During polar extraction methods, which are often used to process brain tissue for solution state NMR experiments, the sample is lyophilized and then reconstituted. Typically this is done either in a buffer or in water, and then pH adjusted. In these experiments, Braino 2 was pH adjusted to between pH 6.5 and 8.0 and the resultant ^{1}H spectra recorded on a Bruker AVIII 500 MHz spectrometer. The spectra were then assigned and analyzed to assess which resonances shifted with changes in pH.

Results and Discussion

Several major brain metabolites were found to shift with changing pH. While these changes are too subtle to see over physiological pH ranges in-vivo, they can lead to changing patterns of overlapping resonances in the 1D spectra. This complicates peak fitting algorithms typically used to quantify the metabolites present. Development of an improved polar extraction protocol using optimized buffers is ongoing. This involves using lyophilized Braino 2 samples, covering a likely range of pH's, and testing a rang of potential buffers that both produce the narrowest range of final pH values, while not impacting the quality of the NMR spectra.

Acknowledgements

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References

[1] Downes, H., *et. al*., ChemPhysChem, DOI:10.1002/cphc.201800917 (2018),

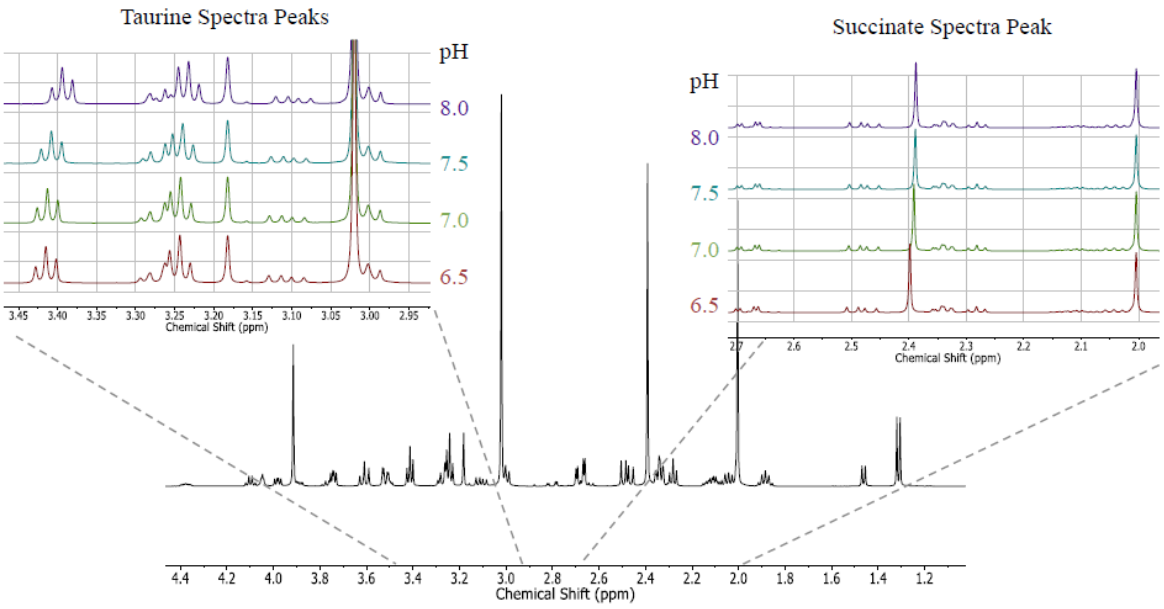

Fig.1 Chemical shift changes in ^{1}H spectra due to variation in pH. Changes in Taurine and Succinate are highlighted. Significant shifts were seen on Acetate, Glutamate, Glutathione, Glycine and Lactate.