MEASURING CHANGES IN BRAIN METABOLITE LEVELS USING LIVE-ANIMAL MAGNETIC RESONANCE SPECTROSCOPY AND OFFLINE LC-MS METABOLOMICS IN A BINGE-ETHANOL MURINE MODEL

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Alcoholism and acute alcohol binge are significant public health concerns. Liquid chromatography-mass spectrometry (LC-MS) based metabolomics is a robust and sensitive technique for determining and quantifying transient or permanent biochemical changes within the central nervous system (CNS). However, access to human tissue and CNS biofluid for such analyses is limited in a clinical context. *In-vivo* magnetic resonance spectroscopy (MRS) is an attractive alternative for clinical measurement but currently the technique is limited to a small to a number of well-characterized, highly abundant analytes. We therefore seek to correlate LC-MS and MRS measurements to better understand and leverage the strengths of each.

Following live animal MRS measurement, metabolites in hippocampal brain punch homogenates were quantified by LC-MS, and a Spearman's correlation coefficient was calculated. We found that the measurements for glutamine and glutamate,, were significantly correlated. Other established neurochemicals, including NAA and aspartate, showed non-significant correlations. NAAG showed little correlation between the two measurements. Additional experiments are ongoing to resolve these discrepancies, and determine how to achieve better agreement between the two methods. In addition,, we used Elements (Proteome Software) to determine differentially expressed metabolites between ethanol exposed and control mice.. An initial pass shows more than 1000 peak-picked features identified in the two conditions, with approximately 200 analytes identified in the metabolite database (human) based on accurate mass. Differentially expressed candidates can be validated further using tandem mass spectrometry and, where possible, the use of authentic standards. Metabolites that change after binge ethanol exposure are reported along with an overview of comparing MRS with LC-MS datasets.

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