BLISS: Determining neurometabolite concentration using H-MRS in patients with bipolar disorder

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INTRODUCTION

Bipolar disorder (BD) is highly debilitating, but can be treated effectively with lithium.

Not all patients respond to lithium, and it can have serious side effects.

Being able to predict response would be of great help to both patients and prescribers.

Current methods for predicting response are surprisingly poor, with modest power and a reliance on clinical features such as family history of response.

The Bipolar Lithium Imaging and Spectroscopy Study (BLISS) aims to find imaging markers of response, to allow improved prediction.

IMPROVING PREDICTION

Levels of N-acetylaspartate (NAA) and myo-inositol (mI) are altered in the brain in BD.

These brain metabolites are also likely therapeutic targets of lithium, so they may act as markers of response.

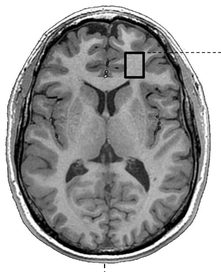
To use them as predictive tools, however, they must be able to be reliably measured.

Proton magnetic resonance spectroscopy (H-MRS) can be used for this, but in order to obtain valid results a standardised acquisition and analysis protocol is needed.

RESEARCH AIMS

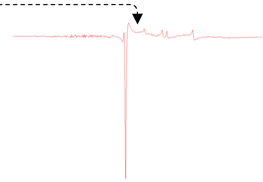
- Codify proton magnetic resonance spectroscopy data analysis procedures for BLISS.
- Use this procedure in the investigation of changes in brain levels of N-acetylaspartate and myo-inositol in bipolar disorder.

PROCEDURE



Initial scan: single 8ml voxel H-MRS acquisition yields spectroscopic data from the right fornix.

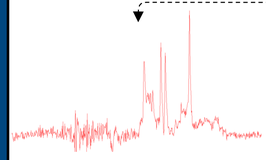
Fourier transformation gives a spectrum – the area under each peak reflects the concentration of specific neurometabolites in that brain region.



Fourier transformed spectrum

Pre-processing: water and lipids are major components of the brain and these dominate the spectrum.

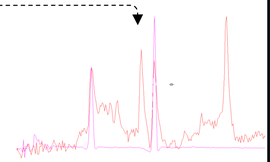
This peak must be removed before the neurometabolites can be measured, after which the remaining signal is brought into phase.



Pre-processed spectrum

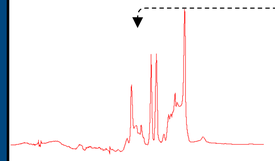
Identification of peaks: the pre-processed signal is examined to determine the identity of each peak.

Some chemicals contribute to multiple peaks, these contributions must be added together to get the total concentration.



Known concentration comparison

Quantification through comparison: the absolute concentration of each metabolite is extrapolated by comparison to the amplitude of spectra produced by known concentration samples.



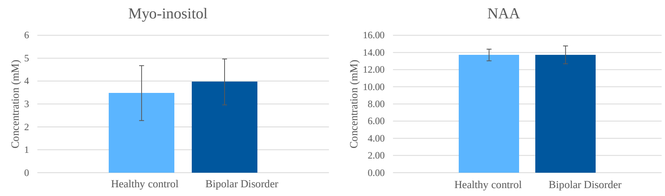
Output spectrum after processing

Final output: the software provides a numerical quantification of metabolite concentration. This can be compared across samples to quantitatively observe neurometabolite changes.

STUDY

Methods: 5 patients with bipolar disorder and 5 healthy controls (all lithium naïve) were scanned in a 3T magnetic resonance scanner at the Newcastle University Magnetic Research Centre.

The procedure described to the left was then followed to obtain neurometabolite concentration values.



Results: NAA was found to be unchanged, and myo-inositol increased. This increase did not achieve statistical significance, however.

Discussion: Failure to reach significance in mI changes could be a false negative due to a small sample size reducing statistical power.

Voxel placement likely caused the lack of change in NAA, as this change in BD has been linked to grey matter.

Further work should be done with multiple voxels of differing brain matter content and more participants.

With the inclusion of a lithium treated patient group and comparison of clinical variables, this procedure can be used to find correlations between metabolite changes and clinical response in lithium treatment.

Conclusion: Original aim of codifying data analysis procedure for BLISS was met, but study of neurometabolite changes in bipolar disorder requires scan data from more participants to be fully explored.