CAN METABOLITE LEVELS QUANTIFIED WITH 1H-MRS IN THE HIPPOCAMPUS PREDICT RECURRENCE OF MOOD EPISODES IN FIRST EPISODE MANIA PATIENTS? A 5-YEAR FOLLOW-UP STUDY.

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INTRODUCTION:
- First episode mania (FEM) marks the onset of BD.
- Studies suggest that recurrence rates are common and occur in 58% of patients within 1 year and 74% of patients within 4 years of FEM despite clinical care.
- While numerous clinical factors have been reported to be associated with recurrence, none lend themselves to accurate prediction of recurrence.
- Studies using proton Magnetic Resonance Spectroscopy (1H-MRS) have found differences in markers of neuron oligodendrocyte coupling – N-acetyl aspartate (NAA), as well as the excitatory neurotransmitter, Glutamate (Glu).

OBJECTIVE:
- To examine if the baseline metabolite levels, NAA & Glu measured using 1H-MRS predict recurrences over 5 years follow-up of patients with FEM.

METHODOLOGY:
- FEM (DSM-IV criteria) patients, with/without psychotic symptoms, with/without comorbidities within 3 months of FEM were recruited from Vancouver Hospital Health Sciences Center (VHHSC) and affiliated sites from 2009-2015.
- Patients were excluded based on the standard criteria for exclusion for Magnetic Resonance Imaging (MRI) and a previous manic episode diagnosed retrospectively.
- Age and sex matched healthy controls with no history of psychiatric disorder and no family history of any major psychiatric disorder in the first- or second-degree relatives were recruited.
- It was a naturalistic follow-up study for 5 years and treatment was given as per clinical need.
- The baseline assessment included a structured clinical interview using the Mini International Neuropsychiatric Interview (MINI) to confirm the diagnosis of FEM/BD by an academic research psychiatrist.
- The clinical rating scales were Positive and Negative Syndrome Scale (PANSS), Young Mania Rating Scale (YMRS) and Hamilton Depression Rating Scale (HAM-D).

Baseline MR Data Collection:
- 3T Philips Achieva (Best, The Netherlands).

MRI:
- T1 & T2 weighted images were obtained first.

MRS localized with PRESS:
- 30*15*15 mm3 hippocampus in right and left hemisphere.
- TE / TR = 35/2000 ms.
- Chemical shift selective (CHESS) pulses were used to suppress the water signal, and water-unsuppressed signals were also obtained for eddy current correction and to reference metabolite signals.
- In total, 128 water-suppressed and 16 non-water-suppressed transients were acquired from each voxel.

MRS Data Processing:
- FSL-FAST segmentation of the 3DT1 images into grey matter, white matter, and cerebrospinal fluid with the single voxel location mapped to the segmentation maps. Figure 1 gives the Voxel location.
- The metabolite basis set for the FSL-MRS fitting routine was simulated with actual radiofrequency pulse shapes.
- Residual water peak removal and phase correction was done as a part of processing.
- Metabolite concentrations with absolute errors higher than 30% of median were considered poorly fit and rejected. Figure 2 gives one of the best spectroscopy fits.

RESULTS:
- We had collected baseline MRS for 65 patients and 35 controls. But, there were 17 patients and 17 controls with baseline MRS with better fit and had completed 5 years of follow-up.
- There were no recurrences in 3 (17.6%) patients. 9 (52.9%) patients had depressive episode, 4 (23.5%) had manic and 1 (5.9%) had hypomanic episode as the first recurrence after FEM.
- Baseline NAA was significantly higher in the patients and controls (Figure 4, patients mean rank = 20.71; controls mean rank = 14.29, p = 0.04).
- However, Glu levels at baseline were trending towards significance and were lower in the patients than controls (Fig 3, patients mean rank = 13.82; controls mean rank = 20.38, p = 0.056).
- Cox regression analysis done to see if NAA/Glu predict the time to first recurrence of any mood episode was not significant (NAA mean – 17.09, Hazard ratio – 0.88 [95% C.I – 0.77,1.09] p = 0.34; Glu mean -17.5, Hazard ratio – 2.0 [95% C.I – 0.79, 1.03] p = 0.15).

DISCUSSION & CONCLUSION:
- The levels of NAA were significantly higher in patients with BD when compared to controls which shows there are changes in NAA in patients with BD.
- However, early in the course of illness, NAA/Glu levels don’t predict the time to first recurrence.
- Limitations: Poor quality of the MRS data leading to lesser sample size.

REFERENCE/BIBLIOGRAPHY:

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