

## MRS IN EARLY STAGE PSYCHOSIS: DEPENDENCE ON TISSUE FRACTION CORRECTION

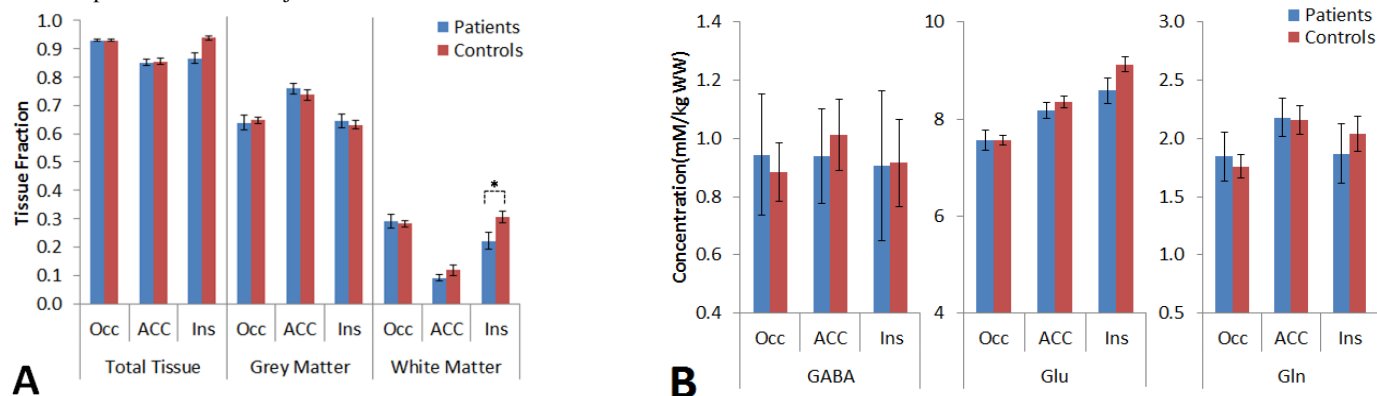
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• **Target audience:** Those interested in MRS in psychosis, or in the impact of tissue correction on MRS data.

• **Purpose:** Psychotic symptoms may be caused by impaired GABAergic regulation of glutamate (Glu) release, resulting in excitotoxicity in the cortex<sup>1</sup>. MRS studies suggest that glutamate concentration is elevated in the early stages of the disorder but is normalised or decreased in chronic or medicated patients<sup>1</sup>. Decreased grey matter and functional abnormalities in the ‘salience network’ (the anterior cingulate cortex (ACC) and insula) have been reported in patients with psychosis and schizophrenia<sup>2</sup>; therefore this study investigated GABA, Glu and glutamine (Gln) in these regions and in a control (occipital) region using 7T MRS, which allows for separation of multiple metabolites within spectra from smaller voxels than in previous studies at lower field strengths.

• **Methods:** 14 medicated patients with early stage psychosis and 20 age and gender-matched controls participated and gave informed written consent. Data were obtained on a 7T Philips Achieva MRI system with volume transmit and a 32 channel receive head coil. MRS voxel dimensions were ACC 20x18x25mm<sup>3</sup>, insula 40x12x18mm<sup>3</sup>, occipital 20x22x20mm<sup>3</sup>. STEAM localisation (TE/TM/TR of 17/17/2000ms) was used and 288 averages were acquired with 8 phase cycles, 4096 samples and bandwidth 4kHz. MOIST water suppression and a parcellated shimming technique<sup>3</sup> were used. Optimised coil combination<sup>4</sup>, phase correction and automatic alignment were applied, data were referenced to water and spectra were fitted from 4-0.2ppm in LCmodel with a CRLB threshold of 30% (spectra not corrected for relaxation effects). A 1mm<sup>3</sup> isotropic MPRAGE (TE/TR=3/7ms, FA=8°) anatomical scan was obtained, bias field corrected in SPM8, brain extracted (BET, FSL4, FMRIB, Oxford) and segmented into grey matter, white matter and CSF partial volume estimates (FAST, FSL4). The fraction of total tissue, grey and white matter was calculated for each voxel position in each subject.



**Figure 1:** Tissue composition (A) and uncorrected metabolite concentrations (B) in occipital (Occ), ACC and insula (Ins). \* is  $p=0.05$ , error bars SEM

• **Results:** The fraction of tissue in the insula was smaller in patients than controls, but unlike previous findings<sup>5</sup> this difference was attributable to decreased white, rather than grey matter (Figure 1A;  $p=0.05$ , no correction for multiple comparisons). MRS data quality was good (FWHM .046, .059 and .055ppm in occipital, ACC and insula, respectively). The concentration of glutamate in the insula showed a trend towards a reduction in patients (Figure 1B;  $p=0.08$ ); however, when correction for the fraction of tissue in the voxel was applied, this difference was abolished ( $p=1.0$ ).

• **Discussion:** Reduced glutamate concentration in the insula of patients with psychosis supports previous MRS studies in medicated patients and gives further evidence for insula abnormalities in psychosis. Reduced tissue volume in patients’ insula was driven by white matter, which has lower concentration of metabolites, particularly glutamate than grey matter<sup>6</sup>. Correcting for total tissue fraction may therefore have obscured group differences in glutamate concentration. Novel methods for accounting for tissue composition may be required. Decreased white matter volume in patients’ insula may reflect impaired connectivity to and/or from this region, but this suggestion requires further research.

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• **References:** [1] Port, Agarwal. JMRI 2011;34(6):1251-61 [2] Palaniyappan, Liddle. JPN 2012;37(1):17-27 [3] Poole, Bowtell. MAGMA 2008;21(1-2):31-40 [4] Hall, Stephenson, Price, Morris. NeuroImage 2013; epub [5] Ellison-Wright, Glahn, Laird, Thelen, Bullmore. AMJ 2008;165(8):1015-23 [6] Srinivasan, Cunningham, Chen, Vigneron, Hurd, Nelson, Pelletier D. NeuroImage 2006;30(4):1171-78.