Neuronal injury demonstrated by early quantitative magnetic resonance spectroscopy following acute brain injury.

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Introduction The metabolic processes occurring after acute brain injury are complex and incompletely understood. We have studied patients with acute brain injury from either trauma or SAH, using quantitative MRS. utilising two methods - chemical shift imaging (CSI) and single voxel spectroscopy (SVS). In selected cases DWI was also performed. The aim of this study was to identify neurochemical changes and any associated fluid shift occurring at a molecular level following TBI and SAH, early in the disease process.

Patients Patients were all admitted to neurointensive care and treated according to standard protocols[1,2]. Physiological data was recorded every minute for quantification of secondary insults[3]. Transcranial blood lactate was measured in some patients. Imaging was undertaken as soon as patients were stable enough to transfer to MR. Outcome at 6 months was assessed using the Glasgow outcome score (GOS).

Imaging The initial T2 weighted images identified lesion areas and were used to position the VOI for spectroscopy. The brain slice incorporated part of the lateral and third ventricles, temporal lobes, insular cortex and lentiform nucleus. Large haematomas and areas close to the skull were avoided to minimise lipid contamination. VOIs in the patients were divided into 'T2 normal' areas and 'T2 abnormal' areas (i.e. lesion areas). For the CSI group this involved delineating areas with T2 lesions within the VOI and selecting normal appearing contralateral mirror image areas -'T2 normal'. The SVS group each voxel was deemed to be either T2 normal, or T2 abnormal. Metabolites (N-acetyl aspartate [NAA], creatine, choline and lactate) were quantified for each voxel. In order to combine the data from the two methods (CSI and SVS) the metabolites were expressed as a percentage of the mean of their respective control groups, and the controls expressed as a percentage of their own mean. **CSI** 2D (single slice) PRESS localised SI sequence using 1.5 T MR fitted with a standard circularly polarised head coil. TE=135 ms, TR=1600 ms and 1024 data points sampled with dwell time 1ms. A manual 4 coil shim followed by an optimisation of the CHESS water suppression voltage was done and the two data sets collected with and without water suppression, both with 16×16 phase encodings. Field of view 240 mm, with slice thickness 15 mm. Data processing included shifting the voxel grid in to alignment with the VOI edge, 2D-FFT, zero order phase correction using the water reference scan and 4 Hz line broadening[4]. HLSVD water removal on the time domain data prior to performing time to frequency domain FFT. Spectra were then used to construct metabolite images which were then corrected for B_1 inhomogeneity. **SVS** acquisition protocols were the same as for CSI. Spectra were obtained from two separate 8 cm^3 with similar location to CSI. The water suppressed FID was averaged from 256 separate acquisitions, and the water reference FID was averaged from 8 acquisitions made without CHESS water suppression. **DWI** eight transverse diffusion weighted images were acquired using a navigator corrected spin echo based sequence with the diffusion gradient applied in the phase encoding direction[5]. The slices were positioned to cover the region encompassed by the spectroscopy measurements.

Results 18 patients with TBI and 6 SAH mean age 39 years (S.D. 16.4) and median GCS post resuscitation 6 (S.D. 2.9). Imaging ranged from 1 to 26 days (median 6.5) in 19 ventilated and 5 non-ventilated patients. The 6 month GOS scores ranged from 1 to 5 (median 3.5). Combining the CSI and SVS data sets, there were 26 T2 abnormal VOIs, 19 T2 normal and 16 volunteer control VOIs. NAA was significantly reduced in T2 abnormal areas compared to controls ($p<0.0001$) and in T2 normal areas compared to controls ($p=0.0013$). There was no difference in NAA between T2 normal and T2 abnormal areas ($p=0.23$). Choline was significantly increased compared to the controls in the T2 abnormal ($p<0.03$) and T2 normal ($p=0.03$) areas, with no difference between T2 normal and T2 abnormal areas ($p=0.91$). For creatine there was a significant increase in the T2 abnormal areas compared to controls ($p=0.037$) which was also the case for T2 normal areas compared to controls ($p=0.021$). There was no difference between the T2 abnormal and T2 normal areas ($p=0.93$). We found no relationship between the patients' individual mean metabolite concentrations and age, GOS at 6 months and GCS post resuscitation on admission. There was no difference in mean metabolite concentration when the SAH group were compared to the TBI group. There was no relationship between NAA and age in the controls or patients. Lactate doublet peaks at 1.3 ppm were not visible in any of the spectra, and in the 4 patients where transcranial brain lactate gradients were measured there was no appreciable production of lactate by the brain. There was no relationship between metabolite concentration and secondary insults. 13 patients had DWI, 3 had DWI in 3 planes, the rest unidirectional analysis. Of the 21 areas where the voxels were placed there were only 2 DWI lesions found and these areas were noted to be abnormal on T2 imaging.

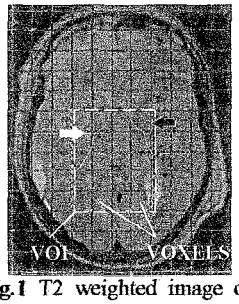

Fig.1 T2 weighted image of a patient with traumatic brain injury. A volume of interest (VOI) is selected and spectra generated for each voxel (fig.2). Areas with T2 lesions ('T2 abnormal') are delineated (solid white arrow), as are contralateral 'T2 normal' areas (black arrow); metabolite concentrations may then be calculated for these areas of particular interest.

Fig.2 Spectra for 4 of the 20 voxels within the volume of interest (fig.1). The three peaks in each spectra from left to right are choline (Cho), creatine (Cre) and N-acetyl aspartate (NAA). *Spectra with depleted NAA.

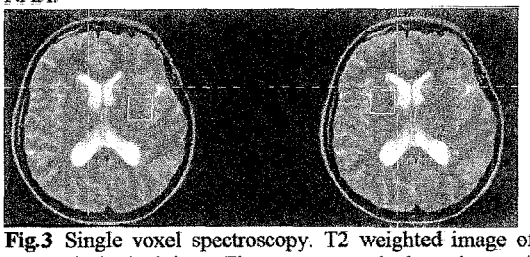

Fig.3 Single voxel spectroscopy. T2 weighted image of a patient with traumatic brain injury. The squares mark the volume of interest (VOI). Left VOI placed over a lesion. Right VOI placed in a contralateral area with no visible lesion. The intersection of the dashed lines represents the isocentre of the magnet of the MR scanner.

Conclusion Early spectroscopic imaging demonstrates occult neuronal injury not visible on T2 imaging. This may help with the clinical management of these patients. NAA is reduced, with increases in choline and creatine. This has implications for earlier non-quantitative studies that used creatine as a fixed standard for metabolite ratios. NAA is not related to age. DWI in acute brain injury added little to spectroscopy and T2 imaging.

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