Correlation between brain-water T2 relaxometry and 1H MRSI following perinatal transient cerebral hypoxia-ischemia

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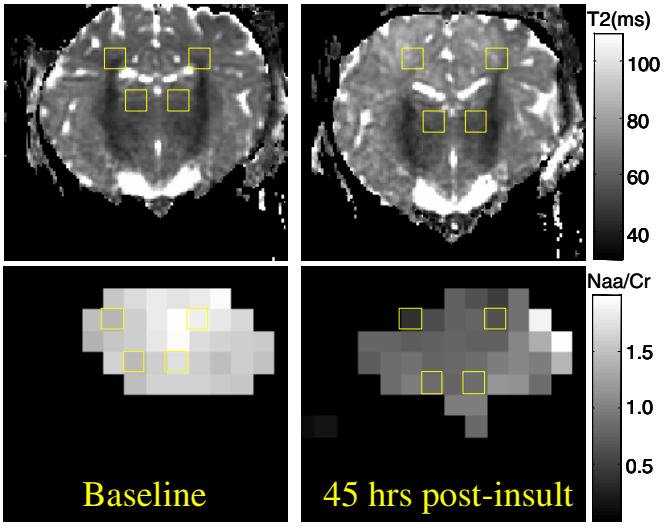
Introduction. Proton (^{1}H) magnetic resonance (MR) spectroscopy (MRS) localised to the deep grey matter (DGM) provides useful prognostic information in neonatal encephalopathy (NE) at a time before conventional MRI is reliable **[1]**. The increase in T2 values within the first 3 days after birth may also provide prognostic information in infants with NE. **[2]**. T2 relaxometry can be performed on any clinical scanner without additional hardware or sequences and is more commonly available than MRS. The aim of this study was to document: (i) the change in brain-water T2 up to 48 hours after transient hypoxia-ischaemia (HI); (ii) the relationship between regional T2 values in 2 regions (DGM and a periventricular region containing mostly white matter (WM)) and metabolite ratios from the same regions obtained using 1H MRS imaging (MRSI) in a validated piglet model of transient HI.

Methods. Six Large-White piglets aged <24 hr were studied before, during and after transient HI for 20-46 hr (mean 35.5 hr). The HI insult was perfomed inside the MR spectrometer by reversibly occluding both carotid arteries and reducing the fractional inspired oxygen to 12% for 29 ± 6 min **[3]**. Quantitative MR data were acquired in a 7 Tesla Bruker Biospec spectrometer with a 6.5 cm x 5.5 cm elliptical surface coil positioned over the intact scalp. MRI and MRSI data were acquired continuously; the acquisition protocol was repeated at ~ 4 hourly intervals. Eleven axial imaging slices were used with the central slice intersecting the thalami and the lateral ventricles. Single-shot spin-echo EPI (echo times (TE) 66 and 110 ms, repetition time (TR) 3 s, bandwidth 200 kHz, field of view (FOV) 5 cm x 4 cm, 128 x 128 matrix, slice thickness (ST) 2 mm and 30 averages per TE) was used to obtain images from which quantitative T2 maps were calculated assuming mono-exponentially signal decay with TE. Spin-echo ^{1}H MRSI data were obtained from a single slice (ST 4 mm, FOV 6 cm x 6 cm, matrix 16 x 16, TE 135 and 270 ms, TR 2 s and a single average). After removal of the water signal using a finite impulse response filter **[4]**, magnitude spectra were reconstructed for each MRSI voxel. To facilitate spectrum analysis the major peaks, i.e. choline (Cho), creatine (Cr), N-acetylaspartate (Naa) and lactate (Lac), were integrated over narrow, non-overlapping, chemical-shift ranges. The background noise was also measured. Cr signal-to-noise ratio maps were used to identify and remove extracerebral voxels. Metabolite ratios, corrected for the number of equivalent nuclei, were calculated after the mean background level had been subtracted from each peak integral. TE 135 ms spectra were used for Naa/Cr, Naa/Cho and Cho/Cr; for Lac ratios TE 270 ms spectra were used to reduce contamination by the large lipid peak at ~1.3 ppm. Two WM and two DGM MRSI voxels were selected for serial comparison with brain T2 values (see figure); the average brain-water T2 for each MRSI voxel was computed following removal of cerebro-spinal-fluid pixels (identified on the basis of their T2). Metabolite ratios for each acquisition cycle and each animal were plotted against the corresponding T2 values and linear regressions calculated. If the residuals to the regression line were normally distributed with constant variance, the regression was considered valid and the correlation tested using the Pearson product moment. If the linear regression was invalid, Spearman rank order was used.

Results. Before HI, the WM and DGM brain-water T2s were 57 ± 2 and 54 ± 4 ms respectively. By the end of the experiments both WM and DGM T2s had significantly increased to 73 ± 6 and 71 ± 8 ms respectively (t-tests: P< 0.001). The metabolite ratio and T2 linear-regression slopes (when valid), correlation coefficients (CC), and P-values are presented in the table. There were significant correlations (positive for Lac/Cr, Lac/Cho and Lac/Naa; negative for Naa/Cr and Naa/Cho, Cho/Cr) for all metabolite ratios in both the WM and DGM, except DGM Cho/Cr. The T2 increase (top) and Naa/Cr decrease (bottom) by 45 hr post-insult in a representative animal can be seen in the figure.

		Naa/Cr	Naa/Cho	Cho/Cr	Lac/Cr	Lac/Cho	Lac/Naa
WM	**Slope**	-0.0552	-0.0940				
	CC	-0.76	-0.43	-0.26	0.77	0.619	0.71
	P	<0.0001	<0.0001	0.02	<0.0001	<0.0001	<0.0001
DGM	**Slope**	-0.0266	-0.0529	-0.00136			
	CC	-0.69	-0.65	-0.10	0.80	0.80	0.80
	P	<0.0001	<0.0001	NS	<0.0001	<0.0001	<0.0001



Discussion. This study confirms the increase in brain-water T2 following transient HI observed in NE infants. Significant correlations between brain-water T2 and metabolite ratios (except DGM Cho/Cr) were observed across all experimental subjects and time-points studied. Brain-water T2 relaxometry may be a useful early prognostic alternative to localised ^{1}H MRS at a time when conventional MRI is unreliable. As well as providing information about the severity of the injury, T2 maps may also provide early information about the pattern of injury, enabling specific neuroprotective strategies such as selective head or whole body hypothermia to be targeted to particular patterns of injury.

References. [1] Hanrahan JD *et al.*, Dev Med Child Neurol, 1999; 41: 76-82. **[2]** Thornton JS *et al,*. Proc ISMRM 2005, p635 **[3]** Iwata O *et al.*, Ann Neurol, 2005; 58(1):75-87. **[4]** Sundin T *et al.* J Magn Reson, 1999; 139(2):189-204.