Brain-water ADC and 31P MRS imaging metabolite ratios and intracellular pH in a piglet model of transient hypoxia-ischemia

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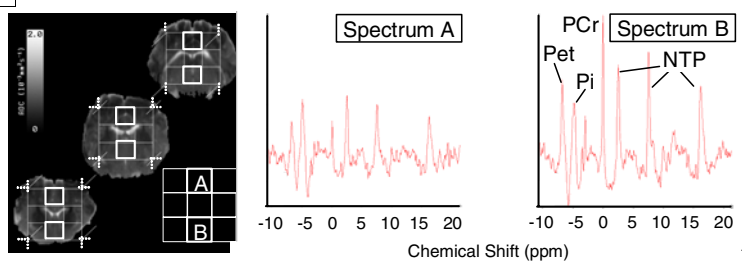
Introduction: Following transient cerebral hypoxia-ischemia (HI) in the newborn piglet the apparent diffusion coefficient (ADC) of brain-water (averaged over the cerebral cortex and subcortical white matter, down to the lateral ventricles) correlates with the evolving failure of cerebral energy metabolism as assessed by surface-coil phosphorus (^{31}P) magnetic resonance spectroscopy (MRS) **[1]**. Finer spatial discrimination of ^{31}P data can be achieved using MRS imaging (MRSI). The aim of this study was to compare ^{31}P MRSI measurables with spatially and temporally related brain-water ADC following transient HI.

Methods: Six Large-White piglets aged < 24 hr were studied before and after transient cerebral HI; the duration of each experiment after HI was 45, 33, 46, 30, 40 and 20 hr respectively. A transient HI insult was performed inside the magnetic resonance (MR) spectrometer by reversibly occluding the carotid arteries and reducing fractional inspired oxygen to 12% for up to 30 min. Whole-brain ^{31}P MRS showed decreased phosphocreatine (PCr) and nucleotide triphosphate (NTP) during HI followed by their renormalisation on reperfusion and then secondary progressive declines during the remainder of each experiment. MR data were acquired in a 7 Tesla Bruker Biospec spectrometer using 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. For ADC acquisition, eleven axial imaging slices were used with the central slice intersecting the thalami and lateral ventricles. Single-shot spin-echo diffusion-weighted EPI (TE 76 ms; acquisition bandwidth 200 kHz; b 0 and 1155 sec mm^{-2}, 6 diffusion encoding directions) was used to measure the diffusion tensor **[2]**. Maps of trace ADC were reconstructed. ^{31}P MRSI data were obtained from a single axial central slice (slice dimensions 3 cm x 8 cm x 8 cm, matrix 8 x 8 (from which only the central 3 x 3 are shown on adjacent ADC imaging slices in the figure), 40 averages, repetition time 2 sec). A single slice-selective pulse was used followed by phase encoding and collection of the FID. Extracerebral voxels were rejected on the basis of low FID signal to noise ratio. The remaining spectra were analysed using AMARES **[3]** as implemented in the jMRUI package **[4]**. Each spectrum analysis was quality checked and reprocessed if necessary. The following metabolite ratios were calculated: PCr/inorganic phosphate (Pi), Pi/EPP (where EPP is the exchangeable phosphate pool PCr + Pi + (γ + α + β)-NTP) and NTP/EPP. For the comparison of MRSI and ADC results, ADC maps from imaging slices that intersected the larger MRSI slice were first thresholded to remove cerebro-spinal-fluid signal and then the average ADC for each MRSI voxel was computed. A subcortical (SC) and a deep grey matter (DGM) MRSI voxel (A and B respectively in the figure) were selected for analysis. Metabolite ratios and from each acquisition cycle in each piglet were plotted against the corresponding ADC values for the SC and DGM voxels separately. Linear regressions were calculated. If the regression residuals were normally distributed with constant variance, the regression was considered valid and the correlation was tested using the Pearson product moment. Linear regression was invalid, Spearman rank order was used.

Results: Representative spectra from the SC and DGM voxels during the secondary decline in ADC are shown in the figure (spectrum A and B respectively). Before HI, mean SC ADC was 1.15 $\pm$ 0.03 mm^{2}sec^{-1} and DGM ADC 1.09 $\pm$ 0.04 mm^{2}sec^{-1}. By the end of each experiment mean overall SC ADC was lower (0.71 $\pm$ 0.16 mm^{2}sec^{-1}) than DGM ADC (0.92 $\pm$ 0.12 mm^{2}sec^{-1}) (t test; P < 0.05). Linear-regression slopes, correlation coefficients (CC), and probabilities (P) are given in the table. If the linear regression was valid, the slope (a in metabolite ratio = a.ADC + b) is presented.

Discussion: In this study, ADC reduction following HI was anatomically heterogeneous, with SC ADC falling more than DGM ADC. The degree of impairment of cerebral energy metabolism measured using 31P MRSI was also regionally heterogeneous. There were significant correlations between ^{31}P measurables (particularly PCr/Pi and Pi/EPP) and ADC in both the SC and the DGM. We have demonstrated the utility of ADC as a surrogate measure of cerebral energetics with higher spatial resolution than previously achieved.

Parameter		PCr/Pi	Pi/EPP	NTP/EPP
SC	Slope			0.234
	CC	0.680	-0.574	0.365
	P	<0.001	<0.001	<0.02
DGM	Slope		0.702	0.379
	CC	0.475	-0.481	0.35
	P	<0.01	<0.001	=0.02



References

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