Grey and White Matter Differences in 1H-MRS Metabolic Ratios in the Preterm Brain

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Introduction: A major focus of current research involving preterm infants is finding non-invasive techniques that will predict long-term outcome. Magnetic Resonance Spectroscopic Imaging (MRSI) provides a metabolic snapshot of the brain, and therefore has the potential to provide important insight into preterm brain development. In this study, we have combined a short MRSI scan with a fully-automated spectroscopy analysis pipeline and tissue classification to provide estimates of metabolite ratios in white matter and grey matter within a heterogeneous preterm population, data that will eventually serve as a baseline for future study.

Methods: 55 very preterm infants, born at a mean age of 29.1 weeks gestation (±1.7 weeks), were recruited into a multimodal MRI imaging study, and scanned within two weeks of birth on a 1.5T MRI system (Signa EXCITE HD, GE Medical) with a neonatal head coil and MR-compatible incubator (AIR Inc., Cleveland). Spectroscopy data were collected using a 2D MRSI Press sequence (TE=144ms, TR=2000ms), in an axial slab through the basal ganglia with 13.3 x 13.3mm voxels and an average thickness of 18.7mm (±1.44mm). Other scans included T1 SPGR (1 x 1 x 1mm, TR=23ms, TE=4ms), T2 FRFSE (1 x 1 x 1mm, TR=4000, TE=145), and proton density (1 x 1 x 1.5mm, TR=27ms, TE=4ms), all using an axial orientation with a 128 x 128 mm FOV. The spectroscopy data were Fourier transformed, phase corrected, and then processed using LCModel to obtain the concentration of N-Acetylaspartate (NAA) relative to Choline (Cho) and Creatine (Cr) within each voxel, along with an estimate of the signal-to-noise (SNR) and Cramér-Rao lower bound (%SD). The three structural scans were used to segment the brain anatomy into white matter (WM), grey matter (GM) and cerebral spinal fluid (CSF), using an automated multispectral segmentation algorithm based on the trimmed minimum covariance determinant method of Tokha et al [1]. The segmented volume was then aligned to the MRSI data, convolved with the point-spread function of the MRSI scan, and the amounts of GM, WM, and CSF in each MRSI voxel were then summed. Voxels were rejected in the case of SNR < 5 or %SD > 20. For all subjects with at least 4 voxels remaining after this pruning, a linear regression was calculated between metabolite ratios and the proportion of GM in each voxel (corrected for CSF). The parameters estimated by these regressions were used to calculate the corresponding metabolite ratios for pure GM and pure WM. Finally, these two values were compared using a one-way ANOVA for each metabolite ratio, and were regressed against gestational age at scan.

Results: The NAA/Cho analysis included 49 subjects and found mean NAA/Cho values in GM and WM of 1.18 (±0.21) and 0.97 (±0.26), respectively. The NAA/Cr analysis included 46 subjects and found mean NAA/Cr values in GM and WM of 1.07 (±0.13) and 0.79 (±0.23), respectively. A one-way ANOVA of these ratios demonstrated significant differences between pure WM and pure GM for both NAA/Cho and NAA/Cr ($p < 0.05$). Both ratios increased with age in both pure GM and pure WM, but only NAA/Cho in pure GM had a rate of increase that was significantly different from zero ($p < 0.05$, Figures 1 and 2).

Conclusions: These results demonstrate that there are significant differences in the ratios of NAA/Cho and NAA/Cr between GM and WM in the brains of newborn preterm infants, and that, at least in the case of NAA/Cho in pure GM, there is a significant increase with gestational age during the preterm period. These results are in general agreement with the limited literature that is available on this topic [2], though different scan parameters make comparisons difficult. Combined with clinical data collected from these same infants longitudinally, these findings will provide an important baseline for better understanding preterm brain development.

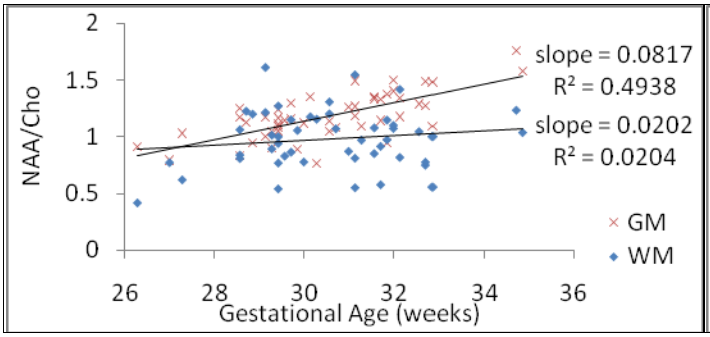

Figure 1: NAA/Cho versus age in pure GM and pure WM

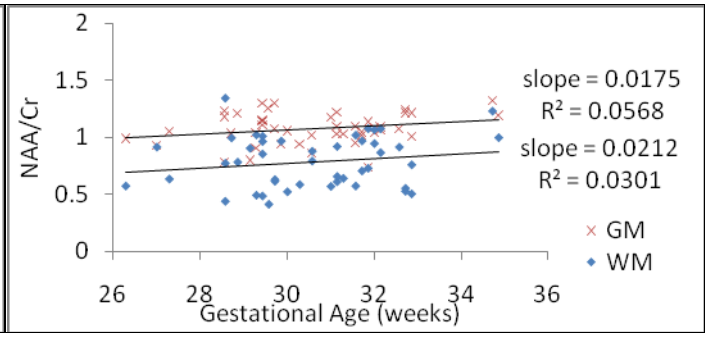

Figure 2: NAA/Cr versus age in pure GM and pure WM

References: [1] Tokha et al. *NeuroImage* 23 (2004), pp. 84-97; [2] Xu and Vigneron. *Sem Perinatology* 34:1 (2010), pp. 20-27