Postnatal Metabolic Abnormalities in the CNS of Neonates with Congenital Heart Disease and Prematurity: A Comparative Study

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Purpose: To test the hypothesis that there are selective regional metabolic differences in the central nervous system (CNS) of both preterm and term neonates with congenital heart disease (CHD) compared to other critically-ill preterm and term neonates without CHD at term-equivalent age. We used short-echo single-voxel MRS technique to evaluate absolute concentrations of n-acetylaspartate (NAA), choline (Cho), creatine (Cr), myo-inositol (mI), glutamate (Glu) and taurine (Tau) across three brain regions.

Materials and Methods: We retrospectively analyzed single-voxel [1]H-MR spectra that were acquired as part of our clinical neonatal imaging protocol utilizing, whenever available, voxels from the medial parietal-occipital gray matter (GM), parietal white matter (WM), and frontal WM. All data were acquired using short echo time PRESS (TE=35 ms; TR=1.5 sec, 128 averages, 3 mm^3 voxel) on a 1.5T GE magnet with a neonatal head coil. Quantitation with LCModel was performed. Metabolite concentrations, measured in term neonates (n=40) with unremarkable MRI and clinical follow-up, were fitted with various functions to obtain "closest-to-normal" reference concentrations as function of age. Z-scores were calculated for neonates in each of our target populations: term CHD (n=32), preterm CHD (n=10), preterm (non-CHD) (n=32) and preterm (syndromic/chromosomal) (n=15) and tested for significant difference from zero using a one-sample Student's t-test.

Results: Plotted in the graphs to the left are mean Z-scores for each metabolite (* $p<.05$).There was no difference in the post-conceptional age at time ofMRI evaluation between the five neonatal groups. The CHD preterm neonates demonstrated an increase in Cho and Tau in the frontal WM region (Figure 1). In contrast the CHD term neonates demonstrated an increase in myo-inositol in all three regions, as well as an increase in Cho in the parietal-occipital GM region and a decrease in Glu in the frontal WM region. The two preterm groups (without CHD) demonstrated other patterns, including, for the non-syndromic preterms, an increase in NAA, Cr, Cho, Tau in the parietal WM and for the syndromic preterms, a marked increase in Cho and Tau in the parietal-occipital GM, compared to term neonates without CHD.

Conclusion/Discussion: Preterm and term neonates with CHD demonstrated distinct patterns of metabolic alteration relative to term neonates without CHD. These patterns were not only distinct from each other, but also from preterm neonates with and without syndromic/chromosomal diagnoses. The preterm CHD group demonstrated elevations in Cho and Tau in the frontal WM. In contrast, the term CHD group demonstrated elevations in mI across multiple brain regions. We hypothesize that the mI (a marker for glial cells and osmolarity) reflects immaturity in these brain regions. Interestingly, the preterm group without syndromic diagnoses demonstrated elevations in NAA, Cr, Cho and Tau, which may reflect an acceleration of normal maturational processes rather than injury per se in this population. These selective metabolic differences among CHD and preterm neonates may help elucidate differential mechanisms of aberrant development which may underlie some of the similar long-term cognitive deficits that are commonly seen in these patients.
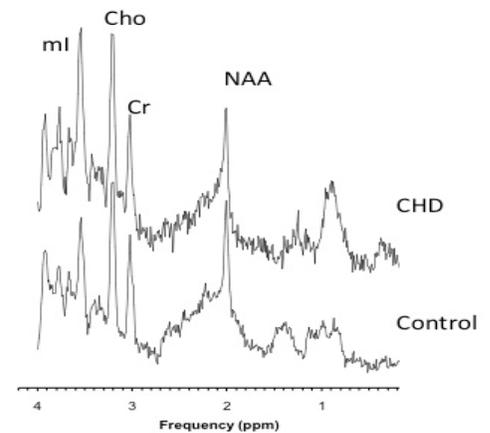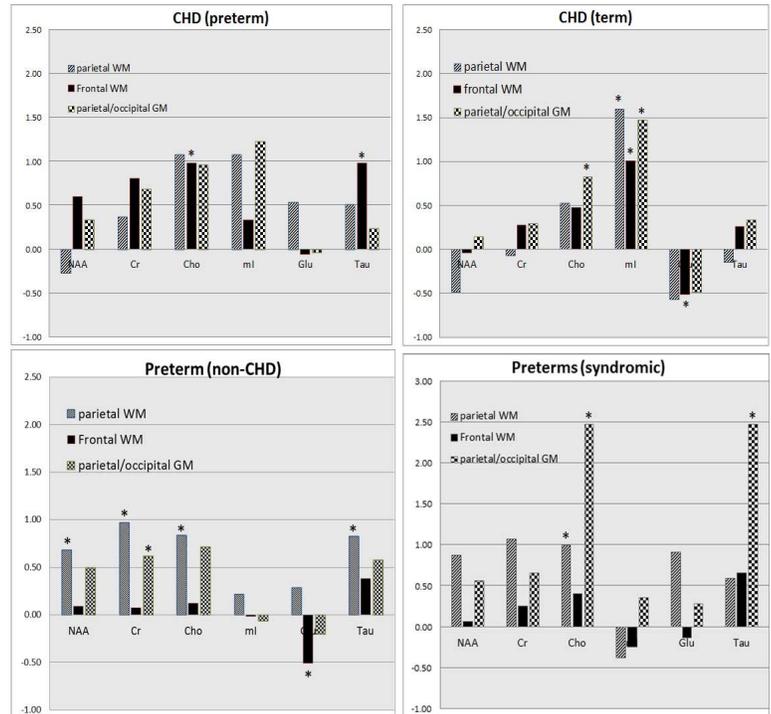
Patient Groups versus Term Neonates

Figure 1 (above): Graph of mean Z-score for each metabolite relative to term neonates without CHD. (* $p<.05$ relative to term neonates without CHD)

Figure 2 (below): Sample spectra obtained from parietal WM from CHD term neonate (top spectra) and term neonate without CHD (bottom spectra) showing peaks for mI. Cho. Cr. and NAA.