

3-Tesla Cerebral Proton Magnetic Resonance Spectroscopy in Healthy Term and Extremely Preterm Infants

Y. Zhou¹, N. A. Parikh², K. Burson², and P. A. Narayana¹

¹Diagnostic & Interventional Imaging, University of Texas Health Science Center at Houston, Houston, Texas, United States, ²Dept. of Pediatrics, University of Texas Health Science Center at Houston, Houston, Texas, United States

Introduction:

Up to 50% of extremely preterm (gestational age [GA] < 28 weeks) or extremely low birth weight (ELBW; birth weight ≤ 1000g) survivors suffer from significant neurodevelopmental impairments (NDI), including cerebral palsy, mental retardation, blindness, and/or deafness. A significant majority of these infants exhibit abnormal brain development or structural brain injury on anatomic MRI prior to NICU discharge. In vivo proton magnetic resonance spectroscopy (¹H-MRS) has been widely recognized as a valuable tool for non-invasive monitoring of brain biochemistry in vivo in animals and humans [1-5]. Assessment of cerebral metabolic development may provide a quantitative biomarker of abnormal development or injury with the potential to improve diagnosis, prognosis and clinical management.

Objective:

To quantify metabolites from three distinct cerebral regions from a single-center cohort of ELBW infants and healthy full-term newborns.

Materials and Methods:

Brain ¹H-MRS was performed on 65 ELBW infants (mean GA: 26.0 ± 1.5 weeks) at 38 weeks post-menstrual age (PMA) or prior to NICU discharge (PMA at MRI: 38.6 ± 1.9 weeks). ELBW infants were recruited from the Children's Memorial Hermann Hospital NICU. A comparison group of 12 healthy term newborns (mean GA: 38.0 ± 0.7 weeks) were recruited from the well-baby nursery and imaged within a week of birth (PMA at MRI: 39.0 ± 0.9 weeks). Infants with major congenital anomalies were excluded. All MRS scans were performed on a 3T Philips MRI scanner. Proton MRS data were acquired using a single voxel point-resolved spectroscopy sequence (PRESS) from a region of 18x10x10mm³ that was located predominantly in the subventricular zone (SVZ), hippocampus (HC) and parietal cortical (PC) areas. The acquisition parameters were TR=2000 ms, TE=37 ms, spectral width=2000 Hz, 1024 data points, and 128 averages. The total MRS acquisition time for each region was about 5 min. To guarantee high quality MRS data and data acquisition at the precise locations with the same acquisition parameters, the same neonatologist, MRI physicist and technician were involved in all the data collections. Because of subject's stability and scanning time limitation, we could not collect all the three data points on each subject. ¹H-MRS data were analyzed using LCModel [6]. Three datasets were excluded due to severe motion artifacts. All statistically analyzed MRS data exhibited high signal to noise ratios and low standard deviations. N-acetylaspartate (NAA), creatine with phosphocreatine (Cr), choline containing compounds (Cho), and myo-inositol (ml) were quantified and presented as ratios relative to Cr. Student's t-test was performed to investigate differences in NAA, Cho and ml ratios between the groups.

Results:

The average metabolite ratios for term and preterm neonates for NAA, Cho and ml at different regions are shown in the following Figure.

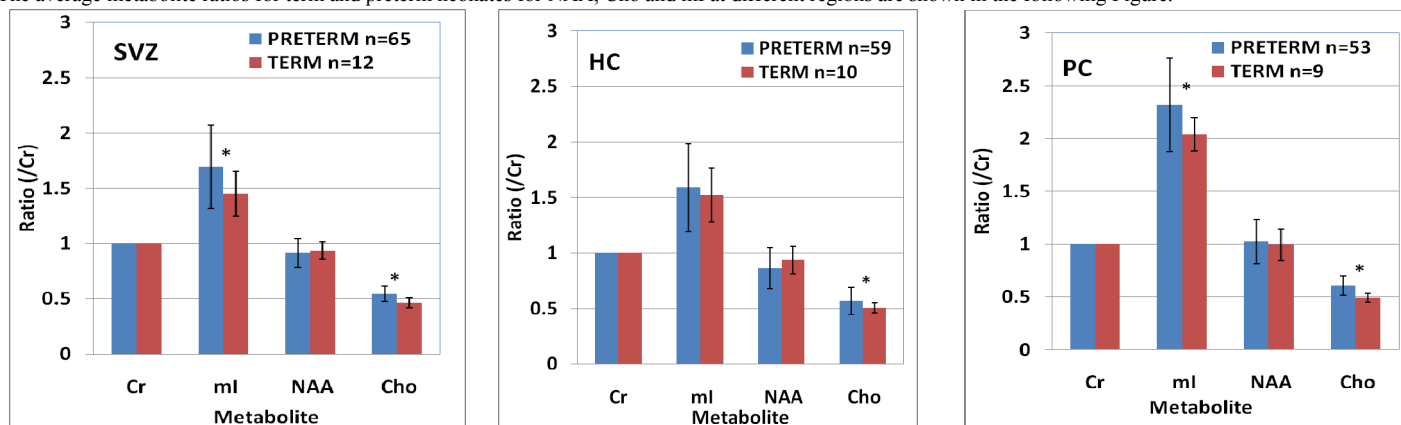


Figure. The average (± SD) metabolite ratios of Cr, ml, NAA, and Cho from the subventricular zone (SVZ), hippocampus (HC), and parietal cortex (PC) regions in preterm and term neonates; * indicates statistically significant group differences.

Data were also analyzed to detect differences in the metabolite ratios between the term and preterm infants in the three regions for different metabolites. The metabolite ratios of NAA/Cr between term and preterm were not statistically different in any of the three regions. However, Cho/Cr was significantly different in all three regions (P<0.006). In addition, statistically significant differences in ml/Cr ratios were observed between term and preterm infants in both cortex and subventricular regions (P<0.005). We also found a significant difference in the concentration of ml/Cr among the three cerebral regions (P<0.005).

Discussion and Conclusion:

We observed significant differences in choline and myo-inositol to creatine ratios between full-term and extremely preterm infants in up to three distinct cerebral regions. Myo-inositol, a glial and osmotic stress marker, also exhibited marked regional variability. Elevated ml/Cr ratios have been reported in preterm infants with documented white matter injury and shown to correlate with severe structural MRI injury and abnormal NDI in term infants with encephalopathy. Choline, reflective of cell membrane turnover and myelination, also appears sensitive to perinatal brain injury/altered development. MRS offers a wealth of data on tissue biochemistry in various brain regions. Our ongoing work, correlating metabolites with neonatal risk factors and NDI, will further determine the value of MRS cerebral metabolites as biomarkers of brain development/injury in extremely preterm infants.

Reference

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