

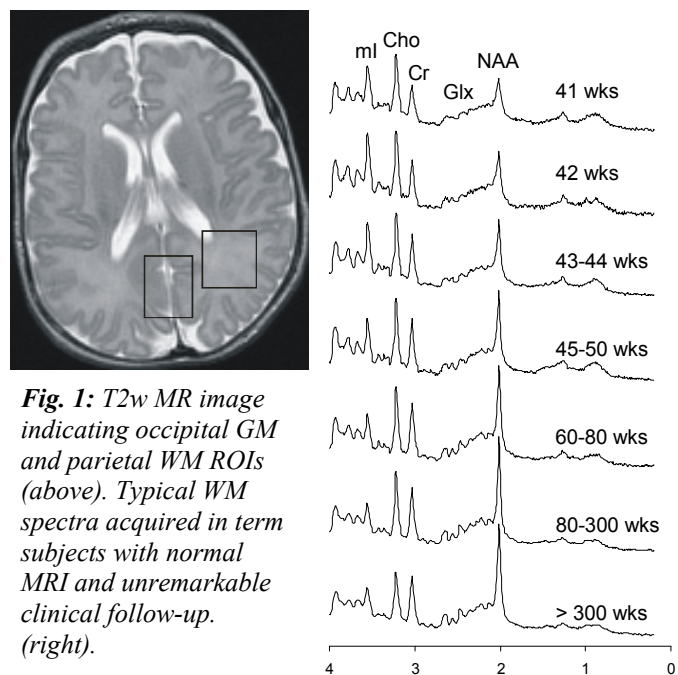
## Differences in Biochemical Maturation in Term and Preterm Newborns

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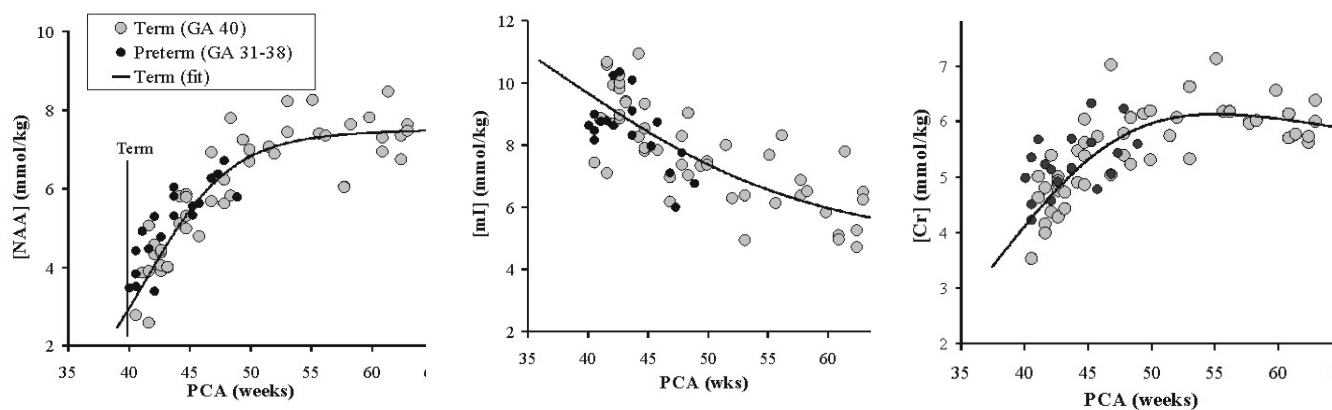
**Purpose:** To compare age-dependent changes of metabolites in white and grey matter of premature neonates without brain injury with normal biochemical maturation in age-matched term neonates.

**Methods:** Control data for "term" metabolic maturation of the human brain were generated from 223 spectra of parietal white matter (WM) occipital grey matter (GM) obtained from 159 subjects (age < 5 yrs). 35 spectra (19 WM, 16 GM) from 29 prematurely born subjects born at gestational age (GA) 31 - 38 weeks were analyzed. All control subjects were born term (GA=40 weeks). MRI (including diffusion imaging) was reported normal, and clinical follow-up (where available) was unremarkable for all subjects. There was an increased incidence of sepsis in the preterm group compared to the term group. Otherwise, clinical indications for brain MR studies were equivalent and included suspicions of encephalitis, metabolic disorders, seizures (retrospectively classified as febrile seizures), hypoxic-ischemic episodes, and others. Single-voxel PRESS (TR/TE = 1500ms/35ms) spectra were acquired (Fig. 1). Spectra were processed with LCModel software (Stephen Provencher Inc., Oakville, Ontario, Canada, LCModel Version 6.1-4F) and absolute metabolite concentrations were determined. Control concentrations as function of post-conceptional age (PCA) were obtained by fitting functions to the metabolite concentrations measured in term subjects (not explained in detail).

**Results:** In WM, NAA increased rapidly within the first few months of life whereas myo-inositol (mI) decreased (Fig. 2). For 15 of 19 prematurely born subjects, NAA levels were higher (preceding) than in term born babies at equivalent age. Myo-inositol (mI) levels in 14 of 19 premature born subjects were lower (also preceding) than those observed in term subjects at equivalent age. Consistent observations were made also for creatine (13 of 19 preceding). The measurement of these metabolites is independent (no significant covariation) and the combined distribution (42 preceding vs. 15 lagging) is significantly asymmetric ( $p < 0.01$ ). In contrast, there was no significant asymmetry observed for GM.



**Fig. 1:** T2w MR image indicating occipital GM and parietal WM ROIs (above). Typical WM spectra acquired in term subjects with normal MRI and unremarkable clinical follow-up. (right).



**Fig. 2:** Shown are metabolite concentrations versus PCA of term (grey symbols) and preterm subjects (black circles) for WM. Overall, the metabolite levels are very comparable. However, the distribution of the preterm data relative to the fitted curves was significantly asymmetric. For example, more NAA measurements in preterm subjects are above the fit curve than below (left).

**Discussion:** There are subtle but significant differences in the biochemical maturation of white matter in premature infants with normal conventional MR imaging when compared to control term infants. The observations suggest accelerated white matter development in premature brain possible from increased sensory-motor stimulation in the extra-uterine environment or possibly a reparative response to subtle brain injury (i.e. possible related to sepsis induced white matter injury). Our preterm cohort also had a older overall mean gestational age which may render them less vulnerable to risk factors for perinatal white matter injury compared to preterm with a gestation age less than 30 weeks. Prior work using DTI in preterm infants have demonstrated accelerated white matter development using a voxel-based morphometry approach (Gimenez et al). Prematurity appears to have relatively less of an impact on biochemical maturation of grey matter compared to the white matter in our cohort.

**Conclusion:** Preterm neonates with normal MR have altered metabolism in the white matter compared to control term infants.

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**References:** Gimenez et al. Neuroimage 41 (2008) 728-734.