Quantitative 1H MRS of Hydrocephalic Newborn Infants

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Introduction: Experience with MRS in patients with hydrocephalus is limited. Previous studies of hydrocephalus in infants, children, and adults have failed to show significant metabolite abnormalities (1,2) The goals of this study were (i) to determine absolute brain metabolite concentrations in premature infants and neonates with hydrocephalus and age-matched controls and (i) to conduct an initial survey of potential biochemical abnormalities of the newborn hydrocephalic brain.

Material and Methods: 12 newborns with hydrocephalus were studied on a 1.5T GE clinical scanner. The post-conceptional age (PCA) at birth was 33±6 weeks, while PCA at the time of the study was 40±6 weeks. An MR-compatible incubator (Advanced Imaging Research Inc., OH, USA) with controlled temperature and humidity and integrated head coils tailored to the head size of newborns was employed to ensure safe scanning of this fragile patient population. Single voxel ^{1}H spectra were acquired using a PRESS sequence with TE = 35 ms, a repetition time of TR = 1.5 s, and 128 signal averages. Occipital grey matter was selected because in some cases massive hydrocephalus prevented the selection of white matter regions of interest (ROI) with sufficient tissue enclosed to obtain spectra with good signal-to-noise ratio. Control data were generated from 26 age-matched subjects (PCA 43±4 weeks) imaged for routine clinical indications but found to have normal MRI and unremarkable clinical follow-up. Indications for MRI/MRS in control patients included seizures, hypotonia, and respiratory disorders. Spectra were processed using the LCModel V6.0 software (3) with water as the internal reference for absolute quantitation. Metabolite concentrations were corrected for the partial volume of cerebrospinal fluid (pvCSF) within the ROI. This measurement was based on the differences in the T2 relaxation time of tissue water and CSF (4). Absolute concentrations of N-acetyl-aspartate (NAA), creatine (Cr), choline (Cho), myo-inositol (mI), glutamate (Glu), glutamine (Gln), total Glu + Gln = Glx, and lactate (Lac) were analyzed.

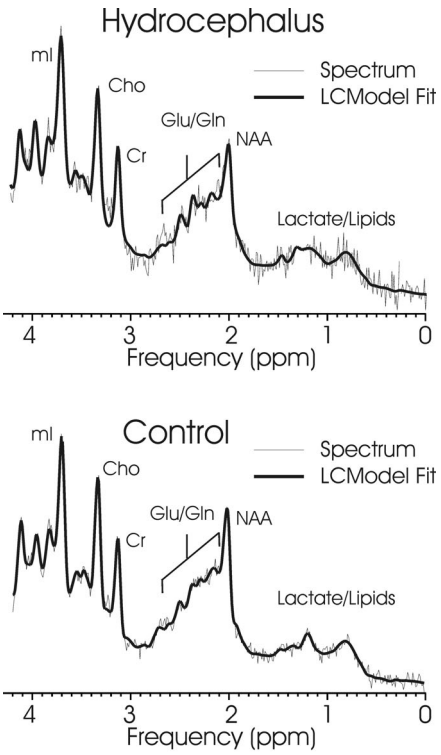

Fig. 1: ^{1}H MRS of a newborn hydrocephalus patient and a control. Post-conceptional age was 42 weeks for both subjects.

Results: Overall, MR spectra of hydrocephalic and control patient were very similar (Fig. 1). When data were pooled, mean Lac (1.4±1.6 vs. 0.4±0.3 mmol/kg, $p<0.005$) and Gln (5.9±2.0 vs. 3.7±1.3, $p<0.0005$) concentrations in hydrocephalic patients were significantly elevated (Fig. 2A). The analysis of NAA, Cr, Cho, mI, and Glu is complicated by significant age-dependent changes during this period of brain maturation. Slope and intercept of linear curves fitted to the hydrocephalus and control data were not significantly different (Fig. 2B+C).

Discussion: Little has been reported regarding hydrocephalus in premature infants and neonates. MRS evaluation of this population is particularly relevant for two reasons. First, the brain matures dramatically during gestation and early infancy and is potentially vulnerable to insults during this timeframe. Secondly, hydrocephalus presents very frequently in this age range, either as a congenital condition or secondary to intraventricular hemorrhage of prematurity. Since the lactate concentration of CSF is higher than that of tissue, the most likely explanation for elevated lactate in hydrocephalus is the systematically larger pvCSF of hydrocephalus ROIs (26%±10% vs. 10%±5%, $p<0.00001$). Glutamine is the dominant amino acid in CSF, however its concentration in CSF is still only ≈ 10% of that in tissue (5) and the larger pvCSF does not explain a ≈ 60% higher mean Gln concentration. The interpretation of elevated glutamine is further complicated by the fact that no true normal control data for this age group are available. Long-term follow-up of hydrocephalus

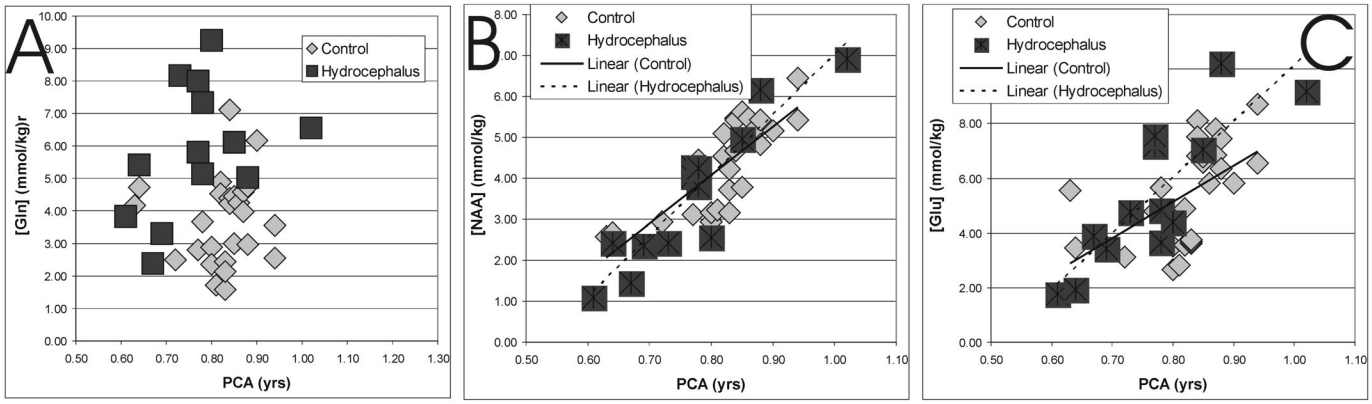

Fig. 2: [Gln], [NAA], and [Glu] of occipital grey matter vs. post-conceptional age (PCA)

patients and controls and correlation with clinical outcome are required to assess the significance of altered glutamine levels.

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