Longitudinal changes in infant brain metabolites at age 6 and 13 months using 3D high-speed MR spectroscopic imaging at 3 Tesla

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INTRODUCTION Brain development between 6 and 12 months is critical for imprinting language function and social reciprocity. Therefore, it is a crucial period for understanding abnormalities of brain development in infants who at a later age develop symptoms of Autism Spectrum Disorder (ASD). As part of a multi-site brain imaging consortium-Infant Brain Imaging Study (IBIS http://www.ibisnetwork.org/), we are studying infants at high risk due to an affected older sibling or at low risk with no family history of ASD. For this study, at our site, we employed a novel 3-D Proton Echo Planar Spectroscopic Imaging (3D PEPSI) chemical imaging method, using high spatial resolution (0.3cc), short echo-time (11msec) and short measurement time (4.5 mins) for metabolite data acquisition. The intent of this communication is to present preliminary findings from longitudinal measurement of brain metabolite changes between 6 and 12 months in a subset of infants studied to date.

MATERIALS AND METHODS 8 infants (7males, 1female) were longitudinally studied during natural sleep at age 6.8($\pm$0.2) months and 13.1($\pm$0.3) months on a 3T clinical scanner equipped with 12 channel head coil. A T1 MP- RAGE sequence was used for 3-D PEPSI volume localization- a 6cm slab from the ACC to above the ventricles. 3-D PEPSI scans (TR:2s, TE:11/136 ms; FOV=220x220x80 mm3; 32 x 32 x 8 matrix, elliptical sampling, scan time 4.5 min), and a water reference scan (TR:630msec, TE:11ms; FOV=220x220x80 mm3; 32 x 32 x 8 matrix, scan time 1.5 min) were acquired using manual positioning of 8 outer volume suppression slices [1] as shown in **Figure 1**. PEPSI spectroscopic imaging data were analyzed using custom software that employs LCModel for spectra fitting [2,3]. Metabolite quantification was performed with correction for T1-weighting and NMR visibility of water [1] Low quality spectra were filtered out based on Cramer-Rao lower bound > 20% for NAA, Cho, Cre, and full width half maximum >0.1ppm. Approximately 150 voxels from a central slice were used for metabolite quantification. Spectra from each voxel were averaged and a composite FID fitted to obtain estimated metabolite values [2]. Metabolite ratios are presented, as partial volume correction has yet to be calculated.
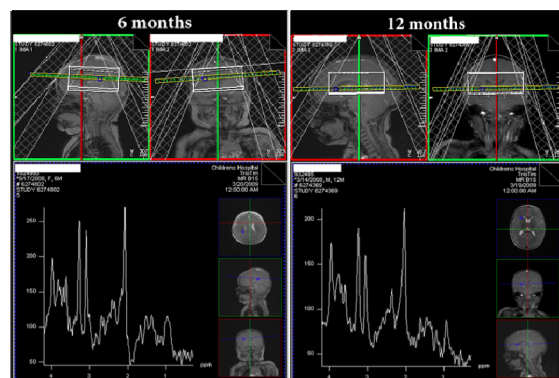

Fig.1 A spectra showing the 3D PEPSI volume, individual voxel Placement and outer volume sat band positioning for a 6mo LR Infant and a returning 12mo HR infant.

RESULTS AND DISCUSSION Preliminary results, averaged across subjects, as shown in Table1, correspond to previous reports using single-voxel MRS [4,5]. Figures 2 and 3 show individual and group averaged changes in metabolite concentrations. Briefly, NAA increased significantly (p<.02; paired t-test) for all subjects during this 6 month interval whereas Choline, myo-Inositol, Glutamate/Glutamine demonstrated heterogeneous patterns of changes across individual subjects. Patterns of chemical changes will be evaluated in the context of other brain developmental measures. Additionally, these results reflect initial analysis of a larger 3-D PEPSI dataset acquired for each infant (8 contiguous slices).

CONCLUSION These preliminary findings demonstrate the feasibility of a rapid 3D MR spectroscopic imaging protocol to evaluate metabolite changes during brain development in infants. The technique is well tolerated with approximately 80% success rate in the sleeping infants studied to date. Absolute quantification utilizing the water scans and partial volume correction, and ROI based analysis in reference to a brain atlas are in progress.

	6mo	12mo
NAA/Cre	1.28±0.03	1.38±0.03
Cho/Cre	0.31±0.01	0.31±0.01
Ims/Cre	0.65±0.04	0.64±0.03
GluGln/Cre	1.38±0.04	1.40±0.03

Table1 Mean metabolite ratios (±SE) from 8 infants longitudinally scanned at 6 and 12 mo.

REFERENCE
1. Posse S, et al: Magn Reson Med 2007; 58:236-244
2. Neva MC, et al:. Psychiatry Res 2010; 182: 40-47.
3. S Provencher: NMR in Biomedicine 2001; 14: 260-264
4. Kreis R, et al: Magn Reson Med 1993; 30:424-437.
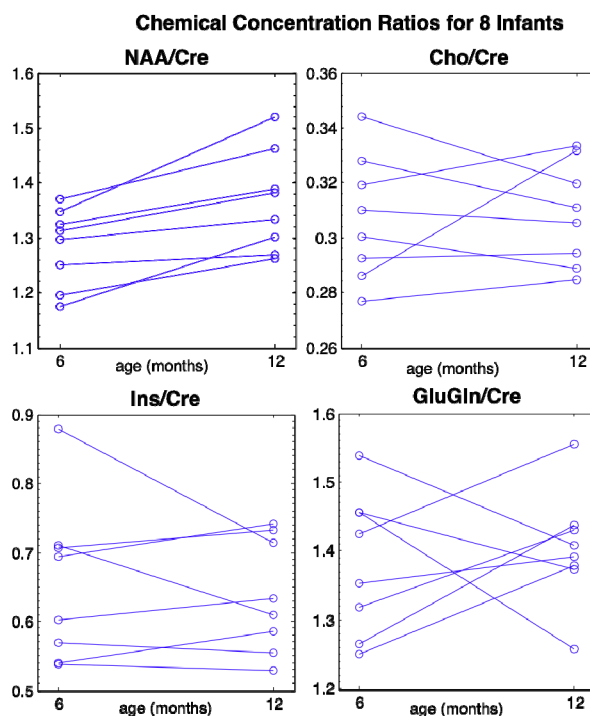5. Huppi PS, et al Pediatr Res 1991;30:574-578

Fig.2 Individual subject longitudinal metabolite ratio changes