Early neonatal brain development: Correlation between DTI and MRS

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INTRODUCTION: Cellular-level changes in the developing brain, such as changes related to myelination, can be indirectly tracked using non-invasive MR techniques including diffusion tensor imaging (DTI) and magnetic resonance spectroscopy (MRS). While DTI measures the motion of water molecules reflecting cellular microstructure, MRS measures brain metabolite concentrations. Each technique represents independent measures related to brain development, and combining the two techniques can provide complementary information regarding brain changes. Previous work that combined the two techniques evaluated various disease states1-3, but no studies have combined these two modalities to examine the rapidly developing neonatal brain. Therefore, we aim to evaluate the relationships between MRS and DTI measures during normal early brain development.

METHODS: Thirty healthy, full-term infants (birth age: 39.2 ± 1.5 weeks post-conception) were scanned 1-3 times between the ages of 4 days (first visit) and 3 months (third visit; post-conceptional age: 42.6 ± 3.6 weeks). Mothers who reported prenatal drug use, other than nicotine or light alcohol use (<3 drinks/month), were excluded. Localized 1H MRS was performed using a 3 Tesla Siemens Trio MR scanner in five brain regions: medial frontal gray matter (FGM), right frontal white matter (FWM), right basal ganglia (BG), medial thalamus (TLM), and left corticospinal tract (CST). In each region, the concentrations of total Creatine (tCr), Myo-Inositol (MI), N-Acetyl-Aspartate (NA), and Glutamine+Glutamate (GLX) were measured using a standard PRESS acquisition sequence (TR/TE=3000/30ms, 48 averages) with absolute quantitation4. Additionally, all infants were imaged using a 12 direction echo-planar DTI sequence (128x128 resolution, 3mm slices, $b=(0,1000)$/mm²). Infants were scanned during unsedated sleep. The mean values of fractional anisotropy (FA) and average diffusion coefficient (ADC) across the MRS voxels were calculated using a custom Matlab program that registered MRS voxel coordinates into the DTI image space.

RESULTS: Diffusion and metabolite measures independently showed expected developmental changes. FA values increased and ADC values decreased with age in all regions except in the CST and TLM. These measures also showed developmental changes when correlated. The NA increase in FWM was closely associated with an increase in FA but a decrease in ADC (Figure 1, left). Similarly increases in both NA and GLX in the CST were associated with decreased ADC (Figure 1, middle, right). Decreased MI in the CST was associated with increased FA and decreased ADC and increasing tCr and decreasing CHO in FGM were associated with decreasing ADC.

DISCUSSION: Correlating DTI and MRS measurements provides some specific information about the developing brain that cannot necessarily be inferred from either measure alone. Consistent with ongoing early brain development, age-related increases in FA and decreased ADC in the frontal WM reflect more coherent fiber organization occurring while the increased NA indicate axonal growth. Similar results were also seen in the rapidly developing corticospinal tract with the addition of decreased MI which suggests myelination or reductions in radia glia. Changes in tCr and CHO in the frontal gray matter combined with a decrease in ADC suggest cellular pruning. Future analyses will further explore these relationships to determine what drives brain development.

Figure 1: Percent ADC and metabolite represent the percent change with post-conceptional age relative to the highest ADC value or lowest metabolite value of a first-visit subject. ADC decreases with age and indendently with NA in the FWM (left) as well as in the CST (middle). Similarly, CST ADC decreases with age and as GLX increases (right).

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