Diffusion-weighted MRI analysis of the effects of prematurity and white matter injury on cerebral cortical development

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Background and aims:

Preterm infants often develop complex cognitive and behavioral problems that may stem from early disorders of cerebral cortical gray matter development. Preterm infants have been found to have reduced volumes of cortical gray matter when imaged at term equivalent or during adolescence. Diffusion tensor imaging offers another means by which to assess disruptions in cortical gray matter maturation during the newborn period. This project aims to (1) assess the effect of premature birth on cerebral cortical gray matter microstructural development through measurement of apparent diffusion coefficient (ADC) and relative anisotropy (RA) values for frontal and parieto-occipital (PO) cortex and (2) study the effects of perinatal white matter injury (WMI) on cerebral cortical development.

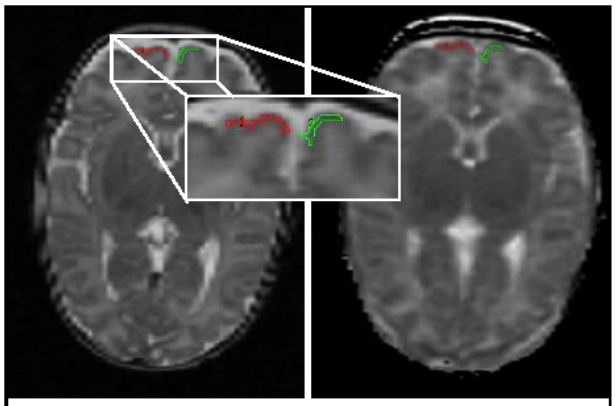

Figure 1: Frontal gray matter regions of interest (ROI) on aligned T2-weighted image (left) and ADC map (right).

Methods:

MRI scans were undertaken on 78 premature infants (birthweight <1250 grams) and 12 term-born control infants at the Royal Women's and Children's Hospitals, Melbourne. All MR images were obtained at term equivalent on a 1.5T GE scanner utilizing a 1.5 mm SPGR 3D sequence and coronal T2 sequences for primary acquisition. Diffusion tensor images were acquired using a line scan protocol (5-6 mm axial slices, 0.5-1 mm gap, TE=78 ms, TR=2139 ms, FOV=22 cm, matrix=256x256, b=5 and 700 s/mm^2) with diffusion gradients oriented in six non-collinear directions. Registration between the diffusion data and the T2 image series was done to optimize region of interest placement. Quantitative measures of ADC and RA were calculated from an axial image after manual outlining of regions of interest in the frontal and PO cortex (Fig. 1).

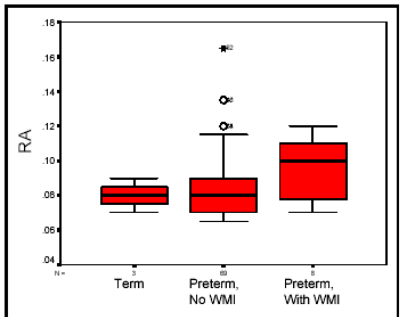

Figure 2: Frontal gray matter RA values for term infants, preterm infants with no WMI, and preterm infants with WMI. Preterm infants with WMI had higher RA

Results:

Premature infants demonstrated significantly lower ADC values in PO gray matter in comparison to term born infants (mean +/-sd: preterm 1.27 +/- 0.13; term 1.17 +/- 0.10; p=0.01). In frontal cortex, there was a similar trend towards lower ADC values in premature infants compared to term infants, though this did not reach statistical significance (preterm 1.29 +/- 0.08; term 1.24 +/- 0.07; p=0.11). Term infants had lower ADC values in PO cortex, as compared with frontal; in contrast, premature infants had similar ADC values for both frontal and PO cortex. There was a trend toward lower gestation at delivery being associated with an increase in ADC at term equivalent (PO ADC versus gestational age at birth; r= -0.19, p=0.09). The ADC and the RA values demonstrated high correlations between frontal and PO regions in all infants. White matter injury was associated with a higher PO ADC (no WMI, n=70, 1.23 +/- 0.11; WMI, n=8, 1.36 +/- 0.22; p=0.01; Fig. 2). Frontal RA was also significantly higher in the premature infants with WMI (no WMI, n=70, 0.083 +/- 0.019; WMI, n=8, 0.096 +/- 0.019; p=0.01).

Conclusions:

This study demonstrates alterations cortical gray matter diffusion indices in premature infants at term equivalent. Significantly lower ADC values are found in PO gray matter for these infants. Trends towards lower ADC values are found in frontal cortex as well. Cerebral cortical development normally occurs in a rostral-caudal fashion, with maturation of PO cortex occurring before frontal cortex. The premature infants had similar values for both frontal and PO cortex, suggesting impaired maturation when compared to the term infants, for whom PO cortex had lower ADC values than frontal cortex. However, in the absence of WMI, RA values were not significantly different for preterm versus term infants, despite the differences in ADC. This suggests that the differences in ADC may be related to loss of cell and/or synaptic density, which correlates to previous work demonstrating cortical volume loss in premature infants, rather than differences in cellular organization. For both frontal and PO cortex, RA is significantly decreased in those infants with discrete white matter injury. This indicates an association between white matter injury and alterations in gray matter maturation. RA and ADC may be useful as tools in the future to further identify those infants who may be at risk for later developmental challenges.