MR Diffusion Tensor Techniques Reveal Regional White Matter Microstructural Alterations in the Prematurely Born Infant

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Introduction: Diffusion weighted imaging (DWI) is an important modality of magnetic resonance imaging (MRI), especially for the diagnosis and characterization of cerebral white matter. In myelinated white matter, for example, water molecular displacements are smaller perpendicular to fibers than parallel to them because motion perpendicular to fibers requires passing through or around layers of myelin membrane, whereas motion parallel to them does not. Thus, water apparent diffusion in mature white matter is more restricted and highly anisotropic in comparison to immature unmyelinated white matter. In this manner, diffusion imaging characterizes cerebral white matter tissue microstructure and its development. It has been clearly demonstrated that ADC values decline while RA values rise during cerebral development in the human infant between 30 weeks and term equivalent [1]. Qualitative MRI abnormalities in the white matter consistent with white matter injury (WMI) in preterm infants at term equivalent have also been shown to be associated with reductions in ADC values implying alterations in cerebral white matter development in preterm infants with WMI [2,3].

Method: Diffusion tensor images (DTI) of the brain were acquired for 132 infants, 20 full term and 112 preterm (gestational age 26 – 32 weeks, mean ± SD, 27.8 ± 2.0 weeks) at term equivalent, using a 1.5 T GE scanner and line scan acquisition protocol (4-6 mm thickness, axial slices, 0.5-1 mm gap, TE=78 ms, TR=2139 ms, FOV=22 cm, matrix=128x128, 2 images at b=5 s/mm^2, 6 images at b=700 s/mm^2). The diffusion gradients for b=700 s/mm^2 were oriented in six non-collinear directions. In addition, conventional T1-weighted and T2-weighted images were also acquired for the qualitative delineation of the presence of white matter injury (WMI). On qualitative review, only 7 preterm infants had significant WMI while 105 did not have significant WMI. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) were calculated from two axial images. Six circular regions of interest (ROI) (area=15 mm^2) were positioned on the superior image which was taken above the lateral ventricles [1] (See Fig. 1). Three regions of interest (ROI) were positioned on the inferior image through the basal ganglia and posterior limb of the internal capsule. (See Fig. 2&3). Student's t-tests were used to compare the ADC, λ_1, λ_2&λ_3, FA and RA values between the full term and the premature infants. A value of p< 0.05 was considered statistically significant.

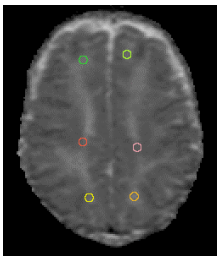

Figure 1: ADC of superior slice with six ROIs

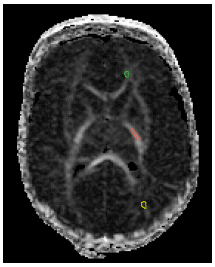

Figure 2: FA of inferior slice with three ROIs

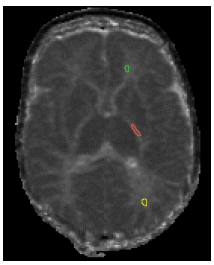

Figure 3: λ_1 of inferior slice with three ROIs

Results: In healthy term infants diffusion imaging demonstrated regional variation with the internal capsule and the central sensorimotor region displaying the most restricted ADC values and the highest anisotropy in the term newborn brain consistent with more advanced white matter maturation in these regions (Table).

Prematurity with cerebral WMI: For premature infants with WMI there was a significant elevation in ADC and reduction in FA in comparison to term infants for most white matter ROIs, particularly when combined. FA was reduced in the sensorimotor region (p< 0.02) and the posterior limb of the internal capsule {PLIC} (p<0.005) regions in preterm infants with WMI compared to term infants.

Prematurity without cerebral WMI: For preterm infants without WMI, *ADC values* were elevated in all superior slice regions and the PLIC (p<0.05 all regions) in comparison to term control infants. The most significantly affected region demonstrating an elevation in ADC values was the frontal region (p<0.001). *FA values* in the premature group were significantly lower than those in the full term (p<0.05) when all superior slice ROIs were combined. Interestingly the FA values for the preterm group without WMI were not significantly different in internal capsule region from those of the full term group.

Superior slice	**Full term infants (n=20) ADC (μm^2/s) &FA (%)**	**Premature infants without WMI (n=105)**	**Premature infants WMI (n=7)**	**Significant differences**
frontal	1.57 ± 0.14 14.5 ± 4.1	1.67 ± 0.17 13.6 ± 4.5	1.68 ± 0.12 14.2 ± 4.6	ADC: Prem WMI vs Term ADC: Prem no WMI vs Term
Sensorimotor	1.4 ± 0.19 22.3 ± 8.9	1.49 ± 0.22 20.2 ± 7.5	1.57 ± 0.30 17.2 ± 4.3	ADC & FA: Prem WMI vs Term ADC: Prem no WMI vs Term
Occipital	1.58 ± 0.14 16.9 ± 4.3	1.67 ± 0.18 15.6 ± 4.5	1.65 ± 0.16 14.2 ± 4.9	 ADC: Prem no WMI vs Term
6 ROIs combined	1.52 ± 0.16 17.9 ± 5.8	1.61 ± 0.19 16.5 ± 5.5	1.63 ± 0.20 15.2 ± 4.6	ADC & FA: Prem WMI vs Term ADC & FA: Prem no WMI vs Term
Inferior slice	**n=8**	**n=51**	**n=6**	
frontal	1.66 ± 0.15 16.6 ± 5.3	1.74 ± 0.17 12.9 ± 3.3	1.72 ± 0.15 14.8 ± 8.7	 FA: Prem no WMI vs Term
LS PLIC	1.07 ± 0.01 48.6 ± 2.5	1.10 ± 0.04 46.8 ± 5.0	1.12 ± 0.03 38.1 ± 6.4	ADC & FA: Prem WMI vs Term ADC: Prem no WMI vs Term FA: Prem no WMI vs Prem WMI
LS Occipital	1.63 ± 0.13 19.5 ± 6.1	1.73 ± 0.17 14.9 ± 3.2	1.80 ± 0.12 12.1 ± 7.1	ADC: Prem WMI vs Term FA: Prem no WMI vs Term

Discussion: In the present study, we demonstrate that diffusion MR techniques correlate with known neurodevelopmental maturation of white matter microstructure revealing the enhanced maturation of the internal capsule > sensorimotor > occipital > frontal regions. White matter injury in preterm infants results in a most marked alteration in the internal capsule and sensorimotor white matter microstructure. Prematurity without WMI also results in significant impact on white matter microstructure affecting the frontal > sensorimotor and occipital regions but apparently sparing the internal capsule. Thus, regional diffusion measures of ADC and anisotropy mirror cerebral development and reflect altering patterns of disturbance in relation to injury or preterm birth per se.

References:

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