In vivo assement of neurite density in the preterm brain using diffusion magnetic resonance imaging

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Background

Preterm birth is a leading cause of perinatal mortality and morbidity, and creates significant personal, social and health care costs. The most severe long-term morbidities are neurological and behavioral and these disabling deficits are related to abnormal brain development.[1,2] However, the search for suitable treatments for these infants is limited by a lack of detailed knowledge of the underlying pathobiology and by the insensitivity of imaging tools to assess quantitatively neonatal grey and white matter (WM) microstructure. Powerful new diffusion MRI (dMRI) methods are now available, which are able to model neurite morphology *in vivo*, for example neurite orientation dispersion and density imaging (NODDI).[3] The aims of this study were to assess neurite density index (NDI) in WM and thalamus in the preterm brain at term equivalent age.

Methods

We studied 44 preterm infants, median (range) gestational age (GA) at birth 30 (24^{+2}–32^{+5}) and post-menstrual age (PMA) at scan 42^{+1} (38^{+3}–47^{+1}) weeks, who had no evidence of abnormality on conventional MRI. dMRI was acquired in 2 shells; b value 750 s/mm^2, 32 directions and b value 2500 s/mm^2, 64 directions using a Philips 3T system sited on the neonatal intensive care unit. We explored the relationship between increasing maturation and dMRI measures in WM using tract based spatial statistics (TBSS).[4] In order to explore the relationship between NDI, traditional dMRI measures (fractional anisotropy, FA and mean diffusivity, MD) and increasing age at scan in the thalamus in a subgroup of infants (n=23), we segmented T2 weighted images, performed b0-T2 registration and propagated thalamic labels to dMRI maps.

Results

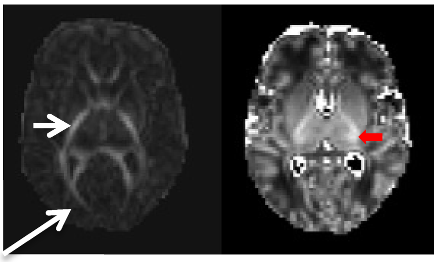

Figure 1. Left, FA and Right, NDI images at the level of the basal ganglia in a preterm infant imaged at term equivalent age. These imaging data provide complimentary information. In the myelinated posterior limb of the internal capsule (short arrow) which comprises of tightly packed coherently organised fibres, FA and NDI values are high. However, in the optic radiation (long arrow), which is unmyelinated at this age, FA values are high and NDI values are low. The central grey matter and cortex show a pattern of relatively high NDI compared to unmyelinated WM but exhibit low FA. The ventrolateral nuclei (red arrow) can be clearly seen as having a higher NDI than surrounding thalamic tissue.

FA and NDI increased with maturation between 38 and 47 weeks PMA throughout the WM on TBSS analysis, however correlations with NDI were more extensive (Figure 2). In thalamus, NDI increased significantly ($p = 0.001$) and MD decreased ($p = 0.01$) with increasing PMA at scan. There was a non-significant trend for FA values to increase with PMA ($p = 0.09$).

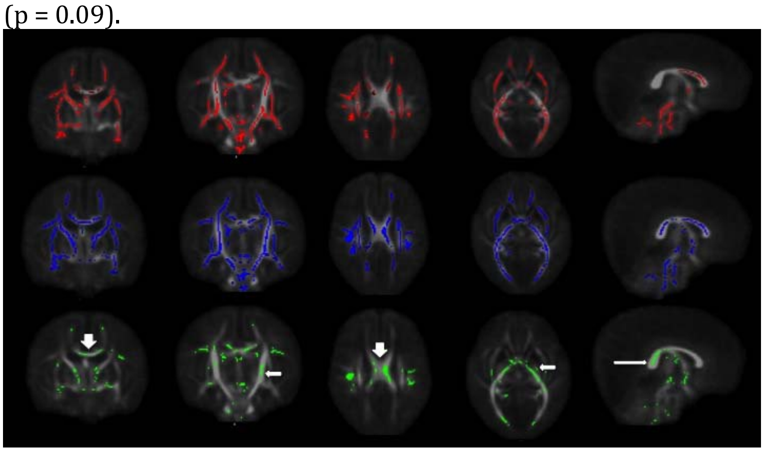

Figure 2. Increases in FA (red) and NDI (blue) with increasing age at scan (TFCE corrected $p < 0.05$). Regions where correlations were observed between age at scan and NDI but not FA are shown in green and include body of corpus callosum (thick arrow), posterior limb of the internal capsule (short arrow), splenium (long arrow), parts of the centrum semiovale and optic radiation.

Discussion

These data show that acquiring multishell dMRI data in a cohort of preterm infants is feasible. The ability of the NODDI model to distinguish neurite density from orientation distribution reveals microstructural changes more readily than anisotropy measures. Increases in NDI with maturation probably reflect reductions in the extra-neurite space associated with myelination and pre-myelination events.

Conclusions

NODDI derived measures appear to be more sensitive than FA to microstructural changes associated with maturation and may, therefore, have a role to play in assessing cerebral dysmaturation in the developing brain.

References

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