Comparing Microstructural and Macrostructural Human Cortical Development: DTI vs. Gyri

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Introduction: Diffusion tensor imaging (DTI) is an emerging method of characterizing human brain development. Unlike conventional T1- and T2-weighted sequences, DTI is sensitive to microstructural changes in the cerebral cortex during development, and depicts the radial diffusivity of the early cortex as increased water diffusion anisotropy [1,2] and as increased λ_1, the radial component of cortical diffusivity [3]. With T1- and T2-weighted MR imaging, the evaluation of cortical maturation has been limited to the assessment of macroscopic gyration and sulcation. However, gyral development does not differ significantly between preterm and term infants and between infants with and without mild brain injury, reinforcing the need for a more sensitive assay of cortical development [4]. In this study, we examined the relationship between the gross morphological changes of the gyri and the microstructural changes in developing cortex by assessing both gyration and DTI parameters in preterm infants. Our hypothesis is that changes in diffusion anisotropy and in λ_1 will correlate with gyration score and with estimated gestational age (EGA). Furthermore, we hypothesize that anisotropy and λ_1 provide information about cortical development independent of cortical gyration, and therefore will not correlate with gyration score once their common relationship with EGA has been accounted for.

Methods: We used an MR-compatible incubator with a high-sensitivity neonatal head-coil to perform MRI at 1.5T in 26 premature newborns born at 24-33 weeks EGA, and imaged at 25-37 weeks EGA, with two serial exams in each of 11 infants, for a total of 37 exams. White matter injury was scored on T1- and T2-weighted images [5]. The protocol included DTI and coronal 3D spoiled gradient-recalled (SPGR) T1-weighted images. The whole-brain axial DTI images were acquired at 1.4 x 1.4 x 3.0 mm voxel resolution using a single-shot EPI sequence with 6 gradient directions, b=0 and 600s/mm^2, TE=99.5ms, TR=7s, and 3 repetitions [2,3]. We identified 4 regions of interest (the left and right pre- and postcentral gyri) on 3 slices just above the roof of the lateral ventricles, and calculated the apparent diffusion constant (ADC), the fractional anisotropy (FA), and the eigenvalues (λ_1, λ_2, λ_3) in all regions. Coronal 3D SPGR images (0.7 x 0.7 x 1.5 mm voxels) were reformatted into an axial orientation at a consistent plane of section across all scans. Our cortical gyration score is based on van der Knaap et al. [6], though instead of assigning a qualitative score of the extent of gyration, we calculated the ratio of gyral depth to gyral width, generating a continuous quantitative variable that increases monotonically with gyral development. The gyration score was calculated for the pre- and postcentral gyri just above the roof of the lateral ventricles. Gyration was not evaluated directly on the DTI images because of EPI warping artifacts, and because they could not be reformatted into a consistent axial orientation across all scans. We determined the correlation coefficients relating EGA, gyration score, ADC, FA, and the eigenvalues, and calculated the Fisher's p value for each relationship. Then, we used a mixed random-effects model to estimate the effects of several of these parameters on gyration score.

Results: On the conventional T1- and T2-weighted exams, there were no focal cortical abnormalities in any of the 37 MR exams. There was no white matter injury in 11 exams, only minimal injury (3 or fewer lesion that are each ≤2mm in size) in 16 exams, moderate injury (more than 3 lesions, or foci that were >2 mm but < 5% of the hemisphere) in 7 exams, and severe injury in 3 exams. Cerebral cortical FA and λ_1 each showed a statistically significant inverse correlation with EGA (FA: r=-0.572; λ_1: r=-0.525; p<0.0001), as did ADC to a lesser extent (r=-0.18, p=0.028). Gyration score also correlated positively with EGA, (r=0.834, p<0.0001). The minor eigenvalues λ_2 and λ_3 were not significantly correlated with EGA (λ_2: r=0.088; λ_3: r=0.053; p>0.2). Cortical gyration also correlated with cortical FA and λ_1 (FA: r=-0.435; λ_1: r=-.406; p<0.0001), but not ADC, λ_2 or λ_3(ADC: r=-0.142, p=0.085; λ_2: r=-0.084, p=0.313; or λ_3: r=0.028, p=0.737). However, in a mixed random-effects model accounting for EGA, white matter injury score, and repeated measures for the serial DTI scans, neither FA nor λ_1 showed any statistically significant residual correlation with the gyration ratio (p>0.05).

Discussion: This study compares the relationship between cortical gyration, a traditional measure of brain maturation, and microstructural changes in the developing cortex as assessed by DTI. We confirm that FA and λ_1 are strongly correlated with EGA [1,2,3], as is cortical gyration [6]. However, we also show that FA and λ_1 are not significantly correlated with gyration score beyond their common association with EGA, suggesting that the microstructural changes reflected in these DTI parameters may provide unique information that is not revealed by the macrostructural changes of cortical gyration. Further research is ongoing to discover whether DTI may be superior to conventional MR imaging for detecting and characterizing abnormal cortical maturation and cortical injury in premature newborns.

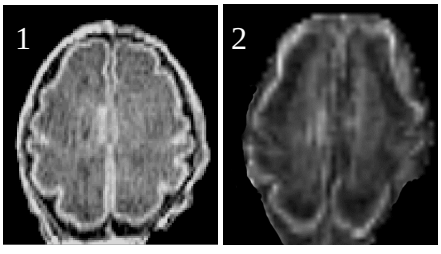

Figure 1: 3D SPGR reformatted into axial plane; 28 week EGA infant.

Figure 2: Axial FA image from same infant; axial level corresponds to the slice scored on the reformatted SPGR image.

References:

1. McKinstry RC et al. (2002). *Cereb Cortex* 12:1237-43.
2. Mukherjee P et al. (2003). *Proc ISMRM*. Toronto, 2094.
3. Mukherjee P et al. (2003). *Proc ISMRM*. Toronto, 540.
4. Slagle et al. (1989). *Pediatr Res* 26:598-602.
5. Miller SP et al. (2002). *J Magn Reson Imaging* 16: 621-32.
6. van der Knaap MS et al. (1996). *Radiology* 200:389-96.