Using Diffusion Anisotropy to Monitor Development of Primate Cerebral Cortex

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Abstract Immediately following its formation, the cerebral cortex is highly organized on the cellular scale, with neuronal and glial structures oriented perpendicular to the cortical surface. Upon maturation, cortical microstructure becomes more heterogeneous. Herein, the spatial and temporal dependencies of diffusion anisotropy upon normal cortical development are explored within post mortem developing baboon cortex. Midway through gestation, an intra-cortical gradient in relative anisotropy (RA) is observed, with RA highest in superficial layers. Substantial reductions in this gradient accompany cortical maturation, and at term the gradient is absent.

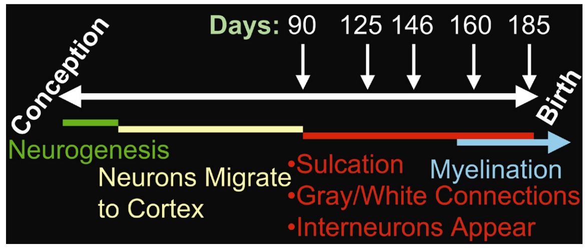


Figure 1. The baboon gestational period

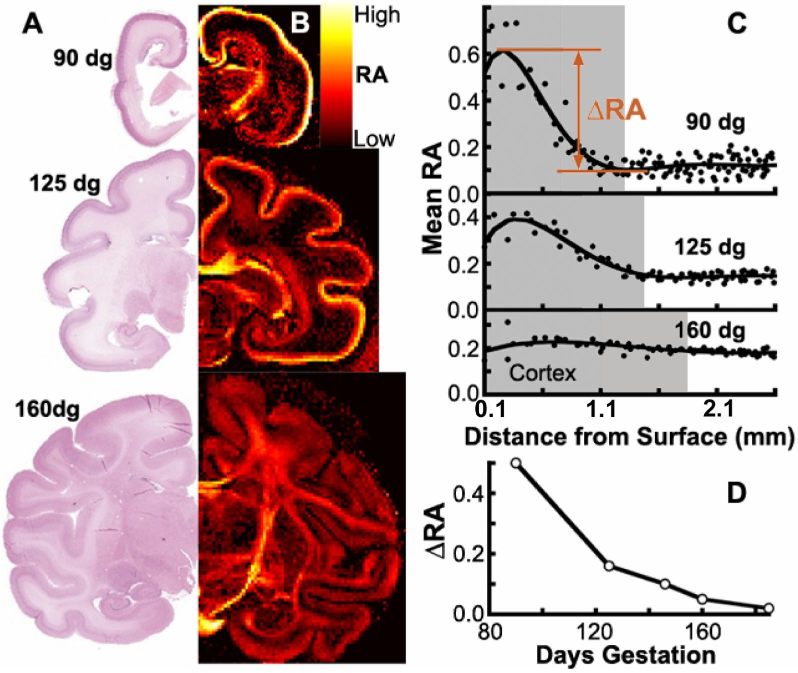
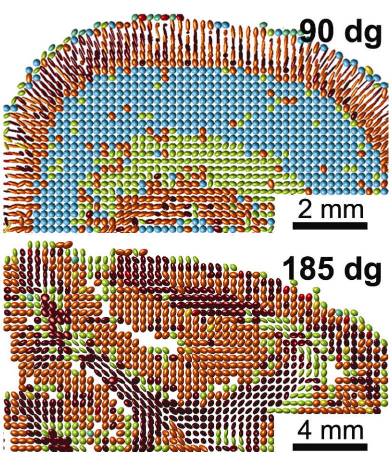


Figure 2. (A) H&E stain (B) RA maps versus gestational age. (C) Variation in RA throughout cortex, with larger RA in superficial layers. (D) The intra-cortical RA gradient decreases during gestation.

Introduction In the developing human cerebral cortex, radially-oriented neural processes and glial fibers give rise to anisotropy in MRI-measured water diffusion (1). This effect is most pronounced early in development. To investigate whether diffusion anisotropy can provide cortical layer specificity, and to delineate changes in RA throughout development in normal primate brain, diffusion anisotropy was measured in a series of post-mortem baboon (*Papio sp*) brains of varying gestational ages. The RA measurements were then compared to histological analyses of the same brains.

Methods Immersion-fixed brains from baboons delivered by cesarean section at (n=2 for all brains) 90, 125, 146, 160, and 185 days gestation (Figure 1, arrows); were obtained from the Southwest Foundation (San Antonio, TX). Forty five diffusion-weighted 2D spin-echo images were acquired with a 4.7 T imaging system, utilizing *b*-values of varying strength (0 to 13 ms/μm^2) and direction. In-plane resolution ranged from (200 to 400 μm)^2, and the slice thickness was 1.5× the in-plane voxel width. A Bayesian probability theory based algorithm (2) was used to estimate RA. Subsequent to MRI, brains were embedded in paraffin, sectioned, and stained with haematoxylin and eosin (H&E).



Results Figures 2A and 2B show H&E images and RA maps, respectively, as coronal views 40% of the brain length posterior to the anterior pole. The cerebral cortex width was estimated from H&E images, and mean RA values were calculated from all pixels, and plotted versus the distance from the cortical surface in Figure 2C. Solid lines are arbitrary polynomials fitted to the data. The peak-to-peak difference in RA, ΔRA, is plotted versus gestational age in Figure 2D. Figure 3 illustrates the consistently radial orientation of cortical diffusion anisotropy.

Discussion In newly-formed cerebral cortex, an RA gradient exists with superficial layers possessing higher anisotropy than deeper layers. This gradient decreases substantially between 50% and 75% of the baboon gestational period. Therefore, diffusion anisotropy provides a means for assessing cortical structure, and staging its early development.

Acknowledgement This research was supported by NIH grants NS37357, NS43010, HL52636 BPD Resource Center, and P51RR13986 for facility support.

References 1. Neil J.J., et al., *Radiology* 209: 57-66, 1998 2. Bretthorst G.L., et al. 24th International MaxEnt Workshop, 2004, *In Press*.

Figure 3. Displacement isosurfaces, color coded according to symmetry in diffusion anisotropy (2). Within the cortex, diffusion anisotropy exhibits mostly prolate symmetry (orange ellipsoids) and is radially oriented.