Distinguishing primary from non-primary visual cortical areas by DTI at early stages of brain development

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Introduction In the immature cerebral cortex, radial organization of pyramidal neurons and glia gives rise to anisotropic water diffusion [1]. As the cortex matures, anatomical differentiation causes diffusion anisotropy to decrease with time. In previous studies of post-mortem non-human primate brain, we have observed regional patterns in the loss of cortical diffusion anisotropy with development [2]. In primary cortical areas, anisotropy is diminished at earlier stages of development than in non-primary cortices. To address the generality of this finding, we have analyzed changes in cortical diffusion anisotropy within ferrets (a non-primate species). The confirmatory findings we present here suggest that regional patterns in cortical diffusion anisotropy are general across species and can be used to detect histological differences between primary and non-primary cortical areas.

Methods Six female ferrets ranging in age from P6 to P31 (corresponding to the last half of primate gestation) were perfused intracardially with 4% phosphate-buffered paraformaldehyde. Single-turn solenoidal MRI coils matched in size to each brain were fabricated and used to acquire diffusion tensor imaging (DTI) data using published procedures [3]. Image resolution ranged from 0.25 to 0.35 mm-sided cubic voxels, and scaled with size of the RF coil. Diffusion anisotropy was measured using a 25 direction sampling scheme [4], and a *b* value of 2.7 $\mu m^2/ms$.

Surface models of the right hemisphere for each brain were constructed using Caret software (http://brainmap.wustl.edu/caret). Each surface model was registered to an adult surface atlas using a multiresolution morphing algorithm implemented in Caret. Boundaries of primary, parietal, and temporal visual areas [5] were delineated on the adult atlas (inset, Figure 2A), and projected to the P6-P31 surface models using the surface registration information (indicated by borders on Figure 1 surface models).

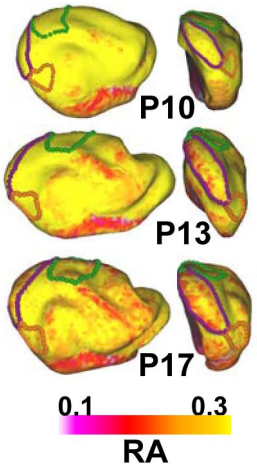

Figure 1

Results Figure 1 shows lateral and posterior views of cortical surface models for P10, P13, and P17 ferret brains. The surface color encodes cortical relative anisotropy (RA). Boundaries of primary, non-primary parietal, and non-primary temporal visual cortices are outlined in purple, green, and orange, respectively. Reduced anisotropy within the primary visual cortex relative to other areas is evident. Mean RA values for the three cortical areas are plotted versus age in Figure 2A. For each age, mean RA is lowest in primary visual cortex, intermediate in parietal, and highest in temporal visual cortex. Distributions of cortical RA within the three areas are summarized in the Figure 2 box plots. Significant differences in mean RA values between primary and both non-primary cortical areas are observed at each of the three ages ($p < 0.0001$, two-tailed t-tests for each of the six comparisons).

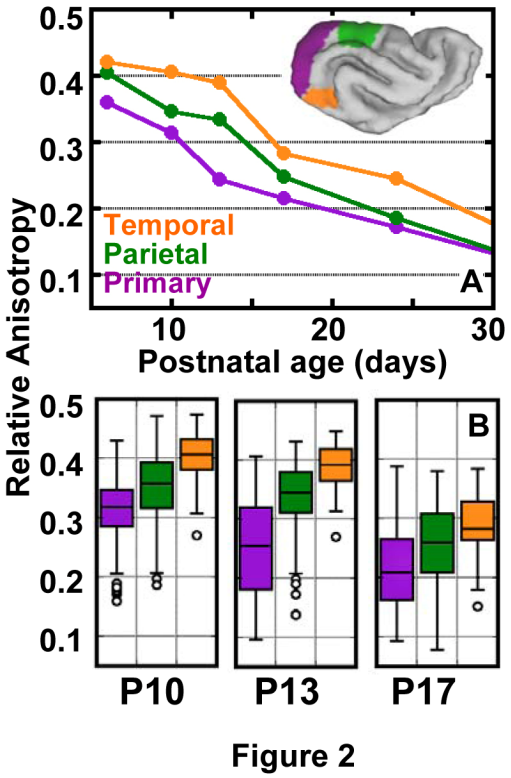

Figure 2

Discussion We detect differences in cortical diffusion anisotropy between primary and non-primary visual cortices in the developing ferret brain. The observations reported here buttress previous findings within prenatal non-human primate tissue [2]. In the adult cerebral cortex, histological structure varies among different functional cortical areas [6]. Our comparative approach provides evidence that, within developing brain, DTI can detect differences in histological structure and/or developmental tempo between primary and non-primary cerebral cortex.

References **1.** McKinstry, R.C., et al., Cereb Cortex, 2002. 12 p. 1237-1243. **2.** Kroenke, C.D., et al., J. Neurosci., 2007. In Press. **3.** Kroenke, C.D., et al., NeuroImage, 2005. 25 p. 1205-1213. **4.** Batchelor, P.G., et al., Magn Reson Med, 2003. 49 p. 1143-51. **5.** Bizley, J.K., et al., Cereb. Cortex, 2007. 17 p. 2172-2189. **6.** Zilles, K., in *The human nervous system*, G. Paxinos and J.K. Mai, Editors. 2004, Elsevier Academic Press: San Diego, CA. p. 997-1055.