The regional pattern of diffusion anisotropy in the preterm primate cerebral cortex

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Introduction In the immature cerebral cortex, radial organization of pyramidal cell bodies and axonal/dendritic processes give rise to significant water diffusion anisotropy [1]. In humans, this occurs during the second half of gestational development. Changes in cortical diffusion anisotropy are of potential clinical relevance as deviations from normal could indicate altered development or injury [2]. We have measured diffusion anisotropy in post mortem prenatal baboon brain to provide a model of anisotropy changes during primate gestation. Previous studies have reported regional patterns in preterm cortical diffusion anisotropy [3]. We hypothesize two potential sources of regional variations (Figure 1): global cortical maturation gradients, and area specificity of diffusion anisotropy. Cortical surface analyses [4] presented here provide evidence that both mechanisms likely influence the regional pattern of cortical diffusion anisotropy.

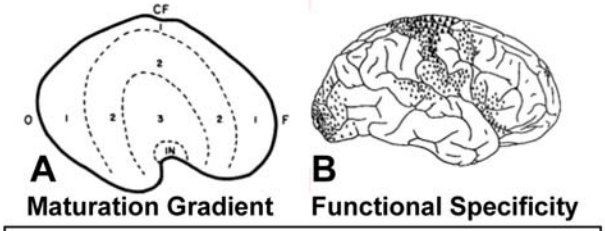

Figure 1. Two potential factors that influence regional heterogeneity in cortical diffusion anisotropy. (A) is from [6] and (B) is from [7].

Methods Relative anisotropy (RA) measurements were performed in three E125 baboon brains using previously described procedures [5]. Embryonic day 125 is roughly equivalent to 31 weeks human gestation. Relative anisotropy values were mapped onto cortical surface models constructed using Caret software (http://brainmap.wustl.edu/caret), and the three surfaces were registered onto an atlas surface. Geodesic distances along the individual surfaces were also calculated using Caret.

Results Figure 2 shows RA maps for individual surfaces and the mean RA value mapped onto an atlas surface. Regional heterogeneity can be observed with lowest RA along the precentral gyrus and highest anisotropy in the inferior temporal lobe. Figure 3 is a plot of RA as a function of geodesic distance from the insula along the individual surfaces. Data points are color-coded according to location in either sensory/motor (green), V1 (yellow), or primary auditory (blue) cortex. Remaining cortical areas are shown in red. In support of the Figure 1A mechanism, F-statistic calculations indicate a significant dependence of anisotropy on distance from the insula (the dotted line is to guide the eye in Figure 3). Statistical analyses of a potential RA dependence on cortical region (Figure 1B) are currently underway.

Discussion Two potential mechanisms for generating regional variability in cortical diffusion anisotropy are investigated. In the first case, diffusion anisotropy is modulated by gradients in maturation, with areas surrounding the insula being more mature than distal areas (Figure 1a). The second possibility is that anisotropy differences arise from functionally different areas possessing differing characteristic cellular morphology (Figure 1b). Our measurements provide support that both mechanisms contribute to regional variation in anisotropy, with the former providing a stronger influence than the latter.

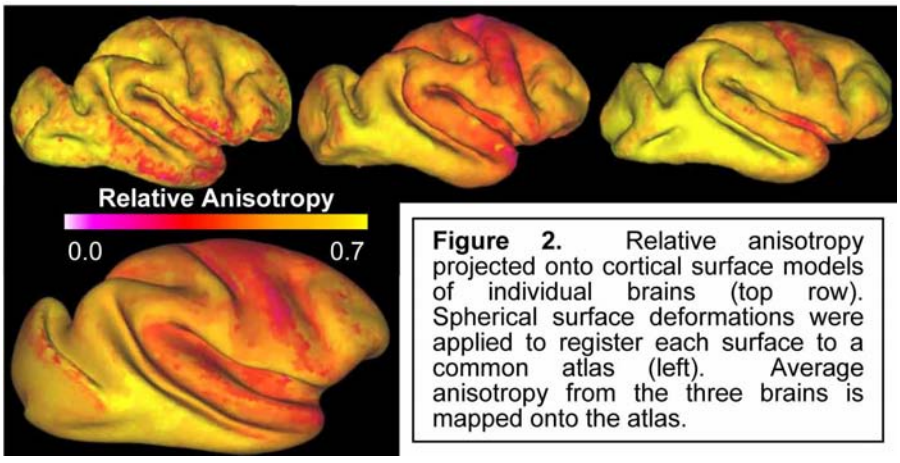

Figure 2. Relative anisotropy projected onto cortical surface models of individual brains (top row). Spherical surface deformations were applied to register each surface to a common atlas (left). Average anisotropy from the three brains is mapped onto the atlas.

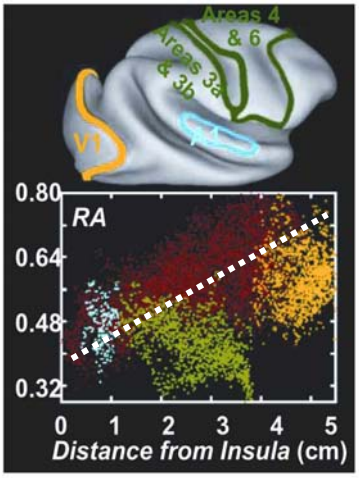

Figure 3. Diffusion anisotropy is plotted versus geodesic distance from the insula along the Figure 2 surfaces. Data are color coded according to the borders in the upper panel. Distance from the insula appears to be the primary determinant of regional variation in anisotropy, however differences between projectional and association areas are also apparent.

References **1.** Neil, Shiran, McKinstry, Schefft, Snyder, Almli, Akbudak, Aaronovitz, Miller, Lee, and Conturo, Radiology, 1998. 209: p. 57-66. **2.** Mukherjee, and McKinstry, Neuroimag Clin N Am, 2006. 16: p. 19-43. **3.** delpolyi, Mukherjee, Gill, Henry, Partridge, Veeraraghavan, Jin, Ying, Miller, Ferriero, Vigneron, and Barkovich, NeuroImage, 2005. 27: p. 579-586. **4.** Van Essen, NeuroImage, 2004. 23: p. S97-S107. **5.** Kroenke, Bretthorst, Inder, and Neil, NeuroImage, 2005. 25: p. 1205-1213. **6.** Poliakov, Comp. Neur., 1961. 117: p. 197-212. **7.** Sidman, and Rakic, in *Histology and histopathology of the nervous system*, 1982, p. 3-145.