Application of DTI in human fetal brain development study

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Introduction

DT-MRI has been proved to be an effective technique for the study of normal and injured developing human brain [1,2,3]. Its application in the newborn and pediatric brains remains an area of active investigation. This study focuses on the DTI application to the brain development before birth. High resolution DTI data was acquired for fixed fetal brains from 13 to 21 gestational weeks. High contrasts from diffusion tensor can delineate most neural structures of developing fetal brains. Primary eigenvector of the tensor have been demonstrated as a good probe of revealing microstructures in the developing brain. To quantify the correlation of the primary eigenvector orientation and cortical surface morphology, the angles between the normal vectors of cortical surface and primary eigenvector of diffusion tensor were measured to reveal the growth pattern of cortical surface. DTI not only provides the high contrast for structure identification and 3D reconstruction, but also helps understanding of cortical surface folding.

Method

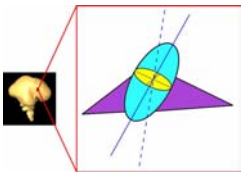

Fig. 1 Demonstration of angle measurement.

Data acquisition: For DT imaging, a set of DWIs were acquired in 7 linearly independent directions with 3D multiple spin echo diffusion tensor sequence. For 13, 14, 15, 16 gestational week fetal brains, 11.7 T Bruker system was used. Diffusion weighed imaging (DWI) parameters were: TE=35ms, TR=0.8s, FOV=37mm/28mm/28mm, imaging matrix=128×80×80 (zero filled to data matrix=128×128×128 with voxel size = 0.219×0.219×0.219mm after rotation and zero padding). For 17, 18, 19, 20 gestational week fetal brains, 4.7 T Bruker system was used. DWI parameters were: TE=32.5ms, TR=0.8s, FOV=54mm/53mm/37mm, imaging matrix=128×72×72 (zero filled to data matrix=128×128×128 with voxel size = 0.289×0.289×0.289mm after rotation and zero padding). Co-registered T_1-weighted images were also acquired for both scanner systems. ***Angle measurement:*** As shown in fig. 1, the triangular meshes of the surface were rendered by using software (Amira; TGS). For each triangular mesh (purple triangle), the normal vector (dashed blue line) was calculated. With the primary eigenvector (solid blue line) of the tensor (cyan ellipsoid) located at the same voxel of this triangular mesh, the angles between the two vectors can be calculated.

Results

Fig. 2 shows comparison of contrasts of a postmortem fetal brain at 19 weeks of age. The images are coronal images at the paracentral lobule. Four of them (aDWI: averaged diffusion-weighted image, FA: fractional anisotropy map, Color: color-coded orientation map, and ADC: averaged diffusion constant map) are derived from DTI. Fig. 2e and 2f show conventional T_2 and T_1-weighted images. The relaxation-based images (Fig. 2e and 2f) excel in delineating overall brain shape, several cortical layers, and ganglionic eminence (GE), a transient structure for basal ganglion. White matter tracts are well delineated in the FA and color-coded maps that have DTI based contrasts. Relaxation and DTI based contrasts, thus, seem to provide complementary information.

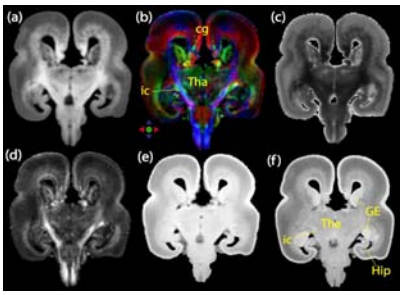

Fig. 2 Different image contrasts of 19 week fetal brain. (a) Average diffusion weighted image, (b) color-coded orientation map, (c) ADC map, (d) FA map, (e) T2 weighted image, (f) T1 weighted image. Abbreviations are; cg: cingulum, ic: internal capsule, GE: ganglionic eminence, Hip: hippocampus, Tha: thalamus.

Fig. 3 and 4 show the 3D reconstruction of the half hemisphere without (upper row) and with (lower row) color encoded by angle measurement from the lateral and middle views of the half brains at the age of 13, 15, 17 and 19 gestational weeks. From fig. 3, except the brain at 13 week, blue color is dominant at most areas of the hemispheres, indicating that the primary eigenvector at the surface almost perpendicular to the local triangular mesh plane. The colors other than blue indicate the tangential rather than radial microstructures at the surface, implying the tension at the surface for the sulcal formation and cortical folding [4]. The red/yellow areas in 13 week brain display a C-shaped structure, which matches with the growth pattern of the human brain in the literature [5]. The 3D reconstruction in the upper row can reveal some of the sulcal formations. For example, white arrows in fig 3 and red arrows in fig 4 clearly demonstrate the formation of the sylvian fissure and calcarine sulcus, respectively. Formation of central and parieto-occipital sulci, however, can not be characterized only by 3D reconstruction. For the angle maps in the lower rows of figs. 3 and 4, there are consistent non-blue colors in all the sulcal formations because of the non-radial microstructures around the emerging sulci. These microstructures exerting the driving force of cortical folding are usually not perpendicular to the surface [4]. Figs. 3 and 4 also indicate that the order of the sulcal formation is that sylvian fissure and calcarine sulcus appear first, then central sulcus forms, at last the parieto-occipital sulcus emerges.

Discussion

For researches of brain development, there is accumulated knowledge based on histology, but there are a surprisingly small number of resources that systematically describe human brain development. One of the excellent resources is atlases by Altman et al, which were published only recently [6,7]. Although MRI-based anatomy studies can not provide anatomic information as detailed as those by histology, it excels in characterizing 3D architectures of developing brains. Especially, the study of cortical folding is hard to be accomplished by histology. Employment of MRI-based techniques, together with histology, could enhance our understanding about dynamics of human brain development. Data acquisition and analysis of more fetal brains is under way.

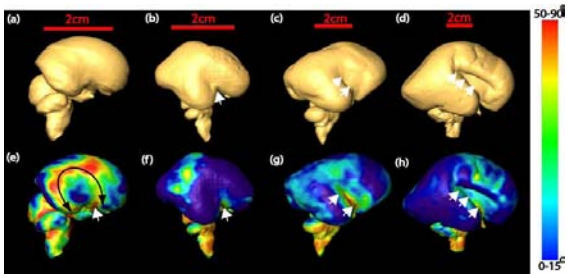

Fig. 3 Lateral view of half hemisphere of 13 (a,e), 15 (b,f), 17 (c,g) and 19 (d,h) week fetal brain. White arrows indicate Sylvian fissure.

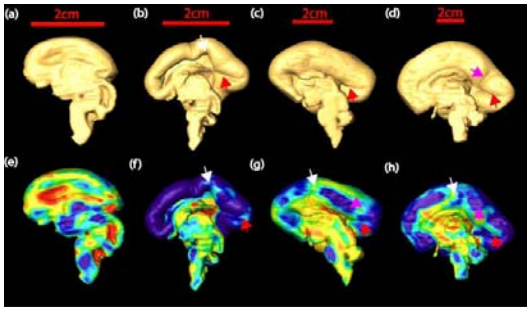

Fig. 4 Medial view of half hemisphere of 13 (a,e), 15 (b,f), 17 (c,g) and 19 (d,h) week fetal brain. Red, white and purple arrows indicate calcarine, central and parieto-occipital sulcus, respectively.

References: [1] Partridge, SC. (2004) NeuroImage 22, 1302. [2] Neil, J. (2002) NMR Biomed. 15, 543. [3] McKinstry, RC. (2002) Cereb Cortex 12, 1237. [4] Van Essen, DC (1997). Nature 385, 313. [5] Nolte, J. (1998) The human brain. Mosby. [6] Bayer, SA. (2004) The human brain during the third trimester. CRC Press. [7] Bayer, SA. (2005) The human brain during the second trimester. CRC Press. **Acknowledgement:** This study is sponsored by NIH grant R01 AG20012.