

Distinctive temporal changes of FA at different cortical areas of human fetal brain

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Introduction

The fractional anisotropy (FA) from DTI is sensitive to the subtle structural changes in the cortical plate of developmental brains. During brain development, the organized columnar structures in the immature cortex are disrupted by synapse formation and dendrite growth. This process can be revealed with decreased FA in the cortical plate. Several studies using *in vivo* DTI imaging indicated this change in the cortical area of preterm newborn babies [1,2] and rat pups [3]. However, FA mapping all over the entire cortical plate and characterization of the time courses of FA at detailed cortical regions during the human fetal stage have been rarely reported. In this abstract, we aimed to characterize the 4D spatial and temporal FA changes all over the cortical plate and during the second trimester fetal development. The FA distribution is overall inhomogeneous across the cortical plate. Distinctive temporal changes of FA were observed at different functional cortical areas. These unique patterns of FA decrease may serve as biomarkers of development of these functional areas.

Methods

Postmortem sample and data acquisition: Two to three samples at each week from 13 to 22 weeks of gestation (wg) were obtained from a tissue bank.

For diffusion tensor imaging, a set of DWIs were acquired in 7 linearly independent directions with 3D multiple spin echo diffusion tensor sequence. For 13 to 17 gestational week fetal brains, 11.7 T Bruker system was used. Diffusion weighted imaging (DWI) parameters were: TE=35ms, TR=0.8s, FOV=37mm/28mm/28mm, imaging matrix=128×80×80. For fetal brains older than 17 gestational weeks, 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. **Cortical plate sampling and FA measurement:** As shown in Fig. 1, 25 sampling points were evenly placed on the cortical plate of a hemisphere. The spheres centered at the sampling point and with radius of 10 voxels were generated. The averaged FA at the intersectional area of the sphere and cortical plate surface was calculated. Broca's, auditory, somatosensory, visual and cingulate areas were represented by the areas surrounding sample point 7, 10, 13, 17 and 19, as shown in Fig. 1. **Statistical analysis:** The Kruskal-Wallis statistics was used to compare the time courses of FA measurements at different functional cortical areas. Benferroni correction was used for correction of multiple comparisons.

Fig. 1: The sampling points on the cortical surface. The cortical length from the caudal to rostral edge is L. The levels of the vertical dashed lines are represented by the numbers at the bottom denoting proportion of the total cortical length L.

Results

Cortical FA of the fetal brain: From Fig. 2a, the regional high FA for the cortical plate of early second trimester is outstanding, indicated by the yellow arrows. The cortical map in Fig. 2b reveals the 4D spatial and temporal pattern of FA changes. Within each time point, the FA values are generally inhomogeneous across the cortical plate. The FA values across the cortical plate at 13wg and 21wg are less inhomogeneous compared to those at 15wg to 19wg. During the second trimester, the FA of the cortical plate undergoes a dramatic decrease, with the highest value of more than 0.45 at 13wg and 15wg, dropping to around 0.1-0.15 in most cortical areas at 21wg. **Distinct time courses of temporal FA changes:** The distinctive FA decreases across the cortical plate can be qualitatively appreciated from Fig. 2b. With the quantitative measurements, time courses of FA at the five functional cortical areas, Broca's (B1), auditory (A1), somatosensory (S1), visual (V1) and cingulate (C1) cortex, are shown in Fig. 3. Broca's area has the sharpest FA decrease from 13wg and 21wg while cingulate area is featured with quite flat FA time course. The time course of FA of visual cortex is less flat than that of cingulate area, but is milder than those of the other areas. FA changes of somatosensory and auditory areas are closest to the averaged FA change line. With Kruskal-Wallis statistical analysis, Table 1 shows that the FA decrease patterns of all cortical areas except auditory area are statistically different from each other.

Conclusion and discussion

To the best of our knowledge, our study revealed the 4D spatial and temporal pattern of cortical FA changes during second trimester for the first time. Well organized radial structures in the immature cortical plate lead to high FA values [4]. Decrease of FA is likely to be caused by the synapse formation and dendrite growth in the cortical plate which disrupt the organized columnar structures. The unique temporal changes of FA suggest the differentiated cellular and molecular activities which underlie the formation of different functional cortical areas. The FA measurements provide us an effective means to monitor these well organized and important developmental processes of synapse formation and dendrite growth noninvasively. These unique temporal courses of FA changes may serve as references to detect abnormality of FA changes in diseased states during development. FA of fixed tissue is well preserved [5], making it possible to use DTI data of postmortem tissue to reveal the structural changes of developmental cortical plate. Acquisition of high resolution DTI data from more normal fetal brains is underway.

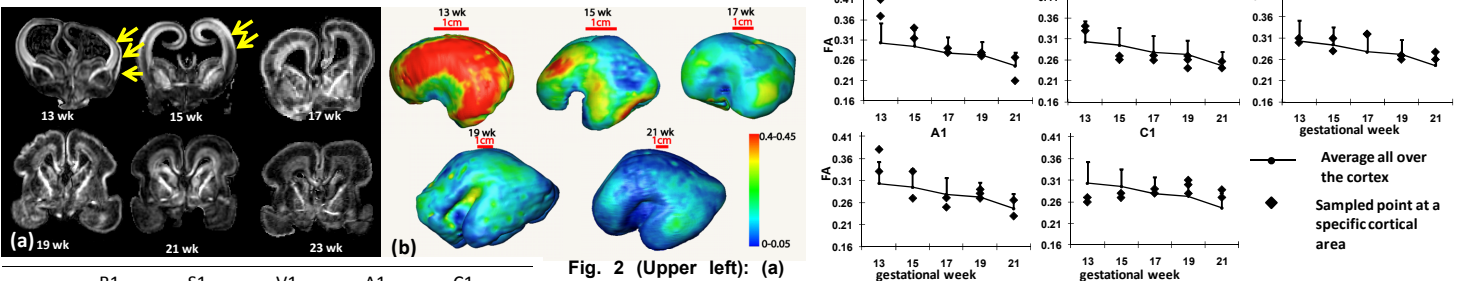


Fig. 2 (Upper left): (a) Coronal slice of the fetal brain FA maps from 13wg to 21wg. The outstanding regions with high cortical FA in early second trimester are indicated by yellow arrows. **(b)** FA mapping of the cortical surfaces of the fetal brains from 13 wg to 21 wg. The color represents FA values as shown in the color bar. **Fig. 3 (Upper right):** Distinctive time course of FA decrease of 5 representative cortical areas. The FA values averaged all over all 25 sampling points are shown as reference curves, with error bars indicating standard deviations.

Table 1 (lower left): p values from statistical comparison between cortical areas. p values smaller than 0.05 are in bold.

References: [1] Maas (2004) Neuroimage 22, 1134. [2] delpolyi (2005) Neuroimage 27, 579. [3] Sizonenko (2007) Cereb Cortex 17, 2609. [4] McKinstry, RC. (2002) Cereb Cortex 12, 1237. [5] Sun (2003) MRM 50, 743. **Acknowledgement:** This study is sponsored by NIH RR014982 and NIH EB009545.