Development of Major White Matter Tracts in Fetal Brains revealed by DTI

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Introduction

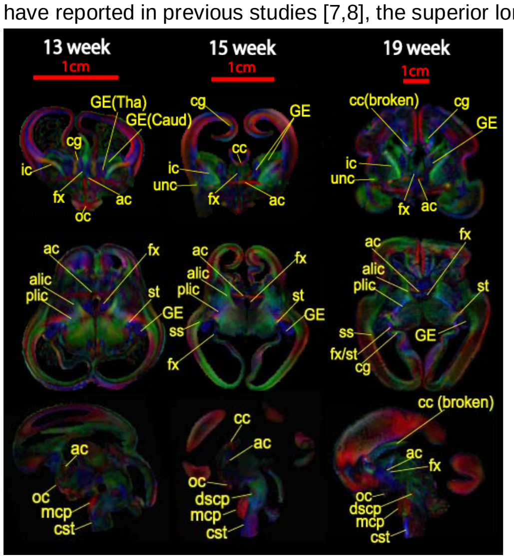
The human fetal brain development is characterized with dramatic structural changes. Specifically during the second trimester, some important white matter tracts begin to form and the existing tracts undergo significantly morphological changes. DT-MRI has been proved to be an effective technique for the study of normal and injured developing human brain [e.g. 1,2,3]. DTI colormap and tractography are capable of revealing the white matter changes. In this study, DTI data of postmortem human fetal brains from 13 to 22 gestational weeks were acquired. There are three samples at each time points. The reproducibly identified tracts were annotated in the two-dimensional colormaps and coherent tracts were traced with DTI tractography. Tracts in brain stem and limbic tracts are among those developing early and before second trimester. During second trimester, some commissural and association tracts, specifically corpus callosum (cc), uncinate (unc), inferior fronto-occipital (ifo) and inferior longitudinal fascicule (ilf), begin to form.

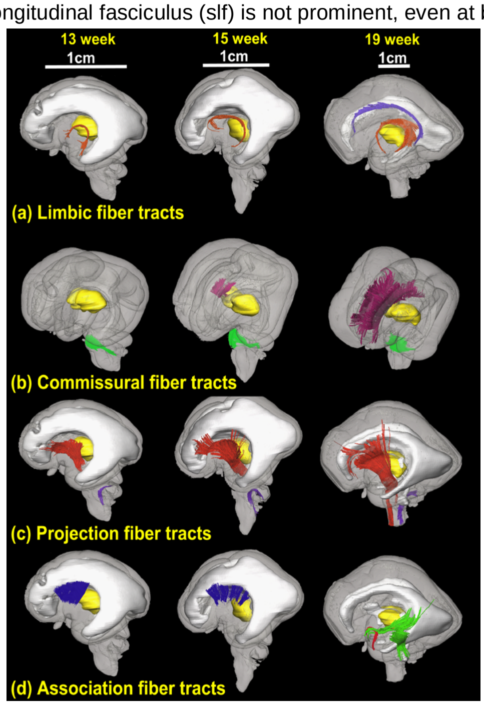
Methods

Data acquisition: 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 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 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 (zero filled to data matrix=128×128×128 with voxel size = 0.289×0.289×0.289mm after rotation and zero padding). ***Annotation and fiber tracking:*** Histological atlases [4,5] were used for annotation of colormaps. A line propagation method [6] was used for tractography.

Results

The DTI derived images provide unique contrasts of white matter fiber bundles. Fig. 1 shows the 2D DTI colormap of second-trimester brains. For comprehensive illustration of the brains, 2D slices in three orientations, i.e., axial, coronal and sagittal, are displayed. The upper and middle rows show coronal and axial slices at anterior commissure (ac) level and lower row shows mid-sagittal slices. Various white matter structures that can be seen in these images are assigned and annotated. Furthermore, the DTI-based tractography reveals information of global morphology of individual tracts during development. Three-dimensionally reconstructed white matter tracts of fetal brains at 13, 15 and 19 weeks are shown in Fig. 2. Tracts in brain stem and limbic tracts are among those developing early and before second trimester. During second trimester, some commissural and association tracts, specifically cc, unc, ifo and ilf, begin to form. ***Tracts in the brain stem:*** At 13 weeks, the corticospinal tract (cst) can already be identified at this stage. During 15 – 21 weeks, the cst increases its size relative to the pons. From Fig. 2, middle (Fig. 2b) and inferior (Fig. 2c) cerebellar peduncles (mcp and icp) exist with good shapes from 13 weeks. ***Limbic tracts:*** Limbic tracts include stria terminalis (st), fornix (fx) and the cingulum (cg) bundle. Among these tracts, the st and the fx, which are relatively small tracts in adult brains, can be clearly appreciated as major tracts at 13 weeks (Fig. 1). Meanwhile, the cg becomes traceable at 19 weeks. ***Commissural tracts:*** The midsagittal plane of Fig. 1 demonstrates the development of the commissural tracts. In a 13-week fetal brain, the cc cannot be identified, while the mcp, optic chiasm (oc) and ac are observed. The cc appears at 15 weeks; however, the midsagittal cc of the fetal brain is extremely fragile and often severed (e.g., 19-week brains). In these cases, such fiber tracts had to be identified in para-sagittal or axial slices. ***Projection tracts:*** The internal capsule (ic) is recognizable early at 13 weeks. It is a good landmark to delineate the ganglionic eminence (GE) and caudate nucleus from the putamen and globus pallidus. Throughout development, the ic seems to extend from its core to the more anterior and posterior areas (Fig. 2c). ***Association tracts:*** The sagittal striatum (ss) and the external capsule (ec) contain major association fibers. The ec, unc and ilf appear at 15 weeks. The ec can be traced in early second trimester brains at 13 or 15 weeks (Fig. 2d). For 19 week brains, ifo, ilf and unc can be traced, shown as Fig. 2d. Unlike the cc or ic, these association fibers do not undergo significant development during the second trimester. As we have reported in previous studies [7,8], the superior longitudinal fasciculus (slf) is not prominent, even at birth.





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. Although DT-MRI-based anatomy studies can not provide anatomic information as detailed as those by histology, it excels in characterizing structural changes of white matter with colormaps and 3D reconstructed tracts. Employment of DT-MRI-based techniques, together with histology, could enhance our understanding about dynamics of human brain development.

Fig. 1 (left): Annotations on 2D DTI colormaps in coronal (upper), axial (middle) and midsagittal (lower) slices. Please see the text for abbreviation. Fig. 2 (right): 3D depiction of developmental white matter tracts. (a) fornix and stria terminalis. Purple fibers in 19 week brain indicate the cingulum bundle. (b) pink and green fibers are the corpus callosum and the middle cerebellar peduncle. (c) red and purple fibers are the cerebral peduncle and the inferior cerebellar peduncle. (d) blue fibers in 13 and 15 week brains are the external capsule; green and red fibers in a 19 week brain are inferior longitudinal/inferior fronto-occipital fasciculus and uncinate fasciculus. For anatomical guidance, thalamus (yellow structure in a,b,c,d) and ventricle (gray structure in a,c,d) are also shown.

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