Diffusion Spectrum Imaging (DSI) Tractography of Neonatal Cat Brains

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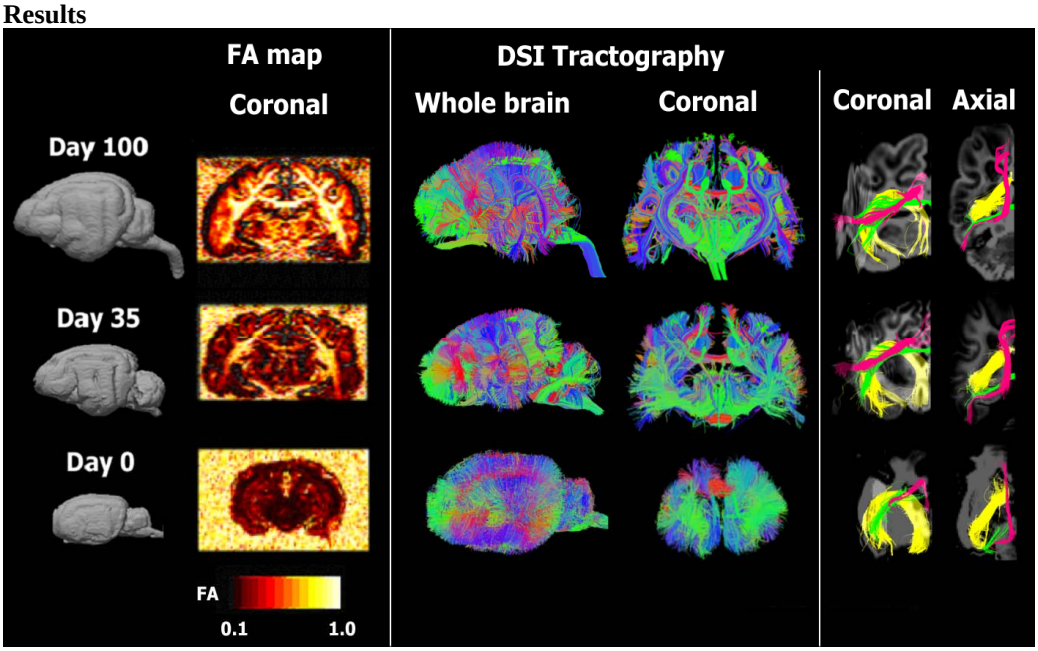
Abstract

Neonatal brains are very watery because they are less myelinated. In the diffusion imaging, these properties result in higher water diffusivity in all directions and lower directional bias of diffusion. However, directional bias does exist, although to a lesser extent than in myelinated brains, due to the presence of unmyelinated axons. In neonatal brains, it is therefore difficult to detect accurate fibers under the standard methods of diffusion tractography. There have been several studies on diffustion anisotropy (e.g. Zhang et al., 2007) and tractography (e.g. Savannah et al., 2005; Counsell et al., 2007) of newborn brains. No one to date, however, successfully depicted high-resolution white matter structural organization in detail, because it is one of the big challenges in diffusion tractography to find a way to detect and follow less myelinated (low anisotropy) fibers accurately. Diffusion spectrum imaging (DSI) can resolve multiple distinct fiber orientations by obtaining hundreds of measurements in different directions (Wedeen et al., 2005) even in areas with low anisotropy, but it has not been previously applied to the newborn brain yet. In this study, we demonstrate for the first time that DSI can successfully depict detailed 3D white matter structures in neonatal brains, which promises future applications of the technique to pediatric disorders in humans.

Methods

- Two adults (day 100 and 60), two middle-aged kittens (day 35) and two neonates (day4 and day0).
- Cats are perfused and fixed with 4% formalin with 1mM Gd-DTPA for at least 7 days to significantly reduce the T1 relaxation time, with minimal reduction of T2 relaxation time (D'Arceuil et al., 2007).
- During the scans, brains are soaked into fomblin (Magnevist) to reduce the susceptibility artifact.
- 4.7T and 9.4T Bruker Biospec system.
- 3D diffusion weighted spin-echo echo-plannar imaging.
- TR/TE = 1000/50 ms, spatial resolutions are 300~400 microns.
- 515 diffusion weighted measurements.
- Maximum b value = 40,000 cm^2 /sec.
- Total acquisition time: 18 h.
- Tracts are calculated by TrackVis.

Results



Left column: 3D view of gyral structures and Coronal sections of FA maps of cats.

Compared to the adult brain, the neonatal brain showed less fractional anisotropy (FA) in the white matter.

Middle column: Diffusion tractography of the entire brains of cats.

High-resolution (~300 um) tracts were detected by DSI even in the white matter with low FA values. Colors represent the orientation vector between the end-points of each fiber.

Right column: Major tracts of the cat brain (Day100, 35: at 4.7T, Day0: at 9.4T) .

To validate the technique in the neonatal brain, and also to see structural changes in the white matter tracts during developmental stages, we identified three tracts (the fornix: yellow, cingulum bundle: pink, and hippocampal commisure: green).

Conclusions and Discussions

We found dramatic structural changes of major white matter tracts during postnatal development. Particularly, the cingulum bundle increased its length and complexity a lot in the first month of the postnatal development. The cingulum bundle was much shorter in the neonatal brain, although the fornix and hippocampal commisure were already well developed. Also, the angle between the cingulum bundle and fornix in the axial plane was drastically changed during developmental stages.

We successfully identified neonatal white matter organization in cats at 4.7T and 9.4T, by the diffusion tractography using DSI. Although tracts were detected even in the areas with very low FA values in neonates at 4.7T, 9.4T was much effective in obtaining higher FA values and depicting more tracts.

The ability to detect alterations in white matter organization in developing brains is crucial to the early detection of a malformation of cortical gyral development. Furthermore, the study of developing brains from the earliest postnatal stages and/or even prenatal periods will be necessary for early detection and to better understand the abnormalities. We believe that our approach here is fundamental to understand the normal and abnormal formation of cortical gyri related to underlying the white matter structures.