Diffusion tensor imaging of the developing rabbit brain

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Introduction

We have developed an animal model of fetal hypoxic-ischemic injury (H-I) that results in a spectrum of deficits, including motor deficits mimicking human cerebral palsy postnatally (1). In this rabbit model, white matter development is similar to that of humans with myelination occurring predominantly after birth. Diffusion anisotropy indices, measured by DTI, have been shown to be sensitive to white matter properties at very early stages of brain development, starting from an embryonic stage even before myelination has occurred (2). The objective of this study was to develop normative data on diffusion indices for major white matter tracts in rabbits, which has not been previously reported. Myelination in corpus callosum (CC) and internal capsule (IC) follow different timetables in the rabbit.

Methods

Animals: Rabbit pups at postnatal age P1 (n=9), P5 (n=8) and P11 (n=7) were anesthetized with Ketamine/Xylazine mixture and placed on a cradle. Body temperature was maintained using water warming pad.

MR Imaging and data processing: Images were performed on a 4.7 T Bruker scanner using custom made 20 mm circular surface coil. The coil was used for both transmission and reception. 8 coronal slices were positioned using the most inferior points of cortical lobes, end of olfactory bulbs and superior colliculus as landmarks. DTI acquisition consisted of 7 non-collinear diffusion weighted spin echo images, TR/TE 2000/35 ms, with b value 780 mm/s^2 and one image with b=50 mm/s^2, matrix size was 128x64. Slice thickness /inplane resolution was 1/0.156 mm for P1, 1.2/0.179 mm for P5 and 1.5/0.195 mm for P11 animals. Diffusion tensor was calculated using multivariate regression and parametric maps of diffusion indexes were calculated for apparent diffusion coefficient (ADC) and fractional anisotropy (FA). Series of 8 spin echo images with different echo time from 20 to 160 ms were used to calculate T2 map in the same slice positions.

Directionally encoded FA maps were used to identify major fiber tracts and selected regions of interest (ROI). Multiple ROIs were selected for each animal, including major projections and comissures, basal ganglia, hippocampus and cerebral cortex (Fig. 1).

Results

FA in the white matter increased significantly with age in white matter tracts, such as IC and CC ($p<0.05$, ANOVA) (Fig.2) and decreased with age in gray matter structures, such as hippocampus and cerebral cortex ($p<0.05$, ANOVA). T2 values significantly decreased with age in white and gray matter structures. The largest FA increase in IC was observed between day 5 and 11, which mirrored the myelination increase in the rabbit IC. However, the largest FA increase in CC was observed between day 1 and day 6, prior to myelination.

Discussion

This is the first study investigating white matter development by DTI in rabbit fetuses. The FA changes reflect both pre-myelination (CC) as well as myelination changes (IC) in the rabbit white matter. We speculate that multiple processes that affect white matter tract development may affect DTI changes in the rabbit.

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References

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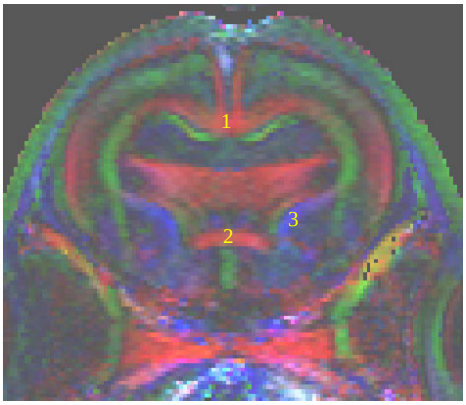

Fig 1. Directionally encoded FA maps for a P1 rabbit pup. Color gives direction of the primary eigenvector with red =left/right, green=up/down, blue=in/out of image plane. 1-corpus callosum (CC), 2 – anterior comissure (AC), 3 –internal capsule (IC).

Fig 2