In Vivo Characterization of Developing Rabbit Brain with Diffusion Tensor MRI and Tractography

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Introduction

The brain is extraordinarily complex, and yet its origin is a simple tubular structure. Characterizing its anatomy at different stages of brain development not only aids in understanding this highly ordered process but also provides clues to detecting abnormalities caused by genetic or environmental factors. Diffusion tensor imaging (DTI), a non-invasive method of magnetic resonance imaging (MRI), is sensitive to structural ordering in brain tissue particularly in the white matter tracts. Diffusion anisotropy changes with demyelinating diseases and also with neural development [1, 2]. In the animal studies, however, only ex vivo brains have been studied [3]. Therefore, the goal of this study was to study developmental changes in regional diffusion anisotropy and white matter fiber tract maturation of in vivo rabbit brains. In this study, DTI data of in vivo rabbit brains (4 weeks to 24 weeks) were acquired and analyzed. Normalized trace apparent diffusion coefficient (ADC), generalized fractional anisotropy (GFA), R2 mapping and fiber tracts were generated and compared across the ages. Our results showed that color maps of diffusion indices, R2 mapping, and 3D tractography revealed that important white matter tracts, such as the olfactory tract, corpus callosum and hippocampus, become apparent during mature period. Regional DTI tractography of the white matter tracts showed refinement in regional tract architecture with maturation. The white matter anisotropy and R2 values increased with age, and the diffusion coefficient decreased with age.

Materials and Methods

All images of the whole brain were acquired from five healthy New Zealand rabbits with ages from 4 to 24 weeks using 1.5T MRI scanner (Siemens SONATA, Germany). During MRI experiments, each rabbit was anesthetized with 2-3 % isoflurance mixed with 300 ml/min air using a standard mask (inner diameter = 40 mm, outer diameter = 93 mm), and animal temperature was maintained at ~35.5°C using heat pad. Rabbits were immobilized and double loop array coils were used.

Whole brain T2W images were acquired using turbo spin echo (TSE) sequence with the following parameters: in plane resolution= 0.391 × 0.781 mm^2, thickness= 1.5 mm, slice number= 30, repetition time/ echo time (TR/TE)= 3790 ms/ 114 ms, number of excitation (NEX)= 20, and the scan time was about 7 min. For DTI acquisition, whole brain was obtained with two slab scans. For each slab, diffusion weighted images (DWI) were acquired using 2D echo planar imaging (EPI) sequence with the following parameters: in plane resolution= 0.781× 0.781 mm^2, thickness= 2 mm, slice number= 12, TR/TE= 2900 ms/ 133 ms, NEX= 9. The diffusion-encoding scheme constituted 12 diffusion-encoding directions with multiple q sampling. Diffusion attenuated images were obtained with diffusion sensitivity (b values) changing from 0 to 2000 s/mm^2, and scan time was about 42 min for each slab. To improve detection sensitivity over the full extent of T2 changes during rabbit brain maturation, image data for R2 mapping were acquired. To obtain R2 mapping, single-slice (covering corpus callosum and hippocampus) multi-echo spin echo sequence with the same spatial resolution was performed to acquire 32 sets of images corresponding to 32 different TEs, ranging from 15 to 480 ms, to sample along the decay of transverse magnetization. With NEX= 4, the scan time was about 8 min.

DTI maps and tractography analyses were performed using DSI Studio (National Taiwan University, Taiwan). For tractography, three regions of interest (ROI), olfactory bulbs, corpus callosum and hippocampus, were selected for further analysis. Generalized fractional anisotropy (GFA), normalized trace apparent diffusion coefficient (ADC) and R2 values of these tracts were then calculated. The changes of these diffusion indices across the ages were also compared and discussed.

Results and Discussions

Our results showed that color maps of diffusion indices, R2 mapping (Fig. 1), and 3D tractography (Fig. 2) revealed that important white matter tracts, such as the olfactory tract, corpus callosum and hippocampus, become apparent during mature period (24 weeks). Regional DTI tractography of the white matter tracts showed refinement in regional tract architecture with maturation. There was some minor interanimal tract variability, but there was remarkable similarity between the tracts in all animals. In Fig. 3, the white matter anisotropy and R2 values increased with age, and the diffusion coefficient decreased with age. The changes of diffusion indices implied the more restrictive diffusion during mature period. The increases in R2 values reflected the increases of lipids due to the myelination process with maturation.

Fig. 1

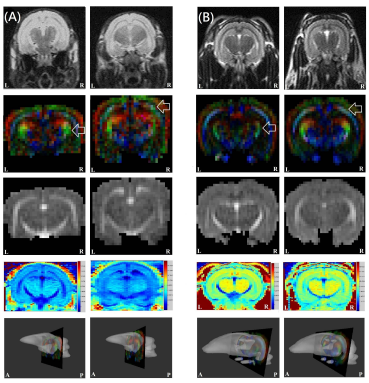

Fig. 2

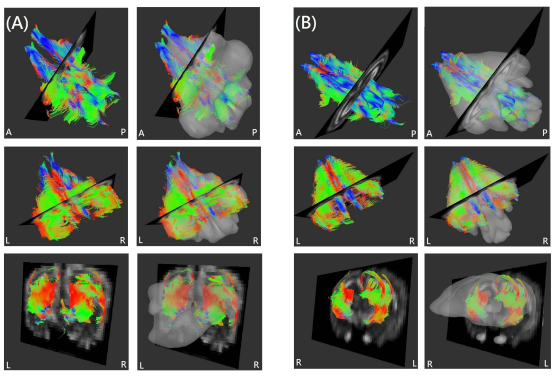

Fig. 3

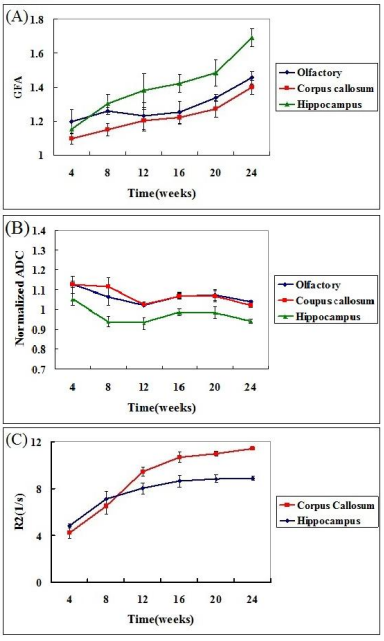

Fig. 1 T2W images, color FA, ACD, R2 mapping and 3D whole brain images of hippocampus (arrow in the left column) and corpus callosum (arrow in the right column) in rabbit brains of 4 weeks old (A) and 24weeks old (B).

Fig. 2 Whole brain DTI tractography of 4 week-old (A) and 24 week-old (B) rabbit. Three white matter tracts from top row to bottom row were olfactory tracts, corpus callosum and hippocampus, respectively.

Fig. 3 The changes of GFA (A), normalized ADC (B) and R2 value (C) of white matter tracts in the normal rabbits from 4 to 24 weeks.

Conclusions

The developing brain DTI database presented can be used for education, as an anatomical research reference, and for data registration. In vivo DTI tractography is also a potentially powerful tool for neuroscience investigations and may also reveal effects, such as fiber tract pruning during development, which may be important targets for in vivo human studies.

References

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