New Insights into Rabbit Brain Development with Generalized Q-Sampling MRI

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Introduction

Characterizing complex anatomy at different stages of brain development not only aids in understanding this highly ordered process but also provides clues to detect abnormalities caused by genetic or environmental factors. Diffusion MRI allows for the in vivo delineation of white matter tracts in the brain in a manner that is individualized to the particular neuroanatomy of each subject. Diffusion anisotropy and diffusivity change in some brain regions with demyelinating disease and also with neural development [1-3]. Previously we used diffusion tensor imaging (DTI) to detect the changes of white matter tracts of rabbit during brain development [4]. However, DTI suffers from resolving the complicated neural structure, i.e. fiber crossing, which is observed frequently during mature period. Therefore the goal of this study was to characterize the changes of quantitative diffusion indices in the developing rabbit brains using generalized q-sampling imaging (GQI) [5]. GQI is a q-space reconstruction method that can reconstruct orientation density functions (ODFs) from a variety of diffusion datasets, including multiple-shell dataset used in the study. GQI can provide directional and quantitative information about the crossing fibers, and the tractography generated from GQI is also similar to those generated from q-ball imaging (QBI) and diffusion spectrum imaging (DSI). In this study, multiple-shell diffusion data of in vivo rabbit brains (4 weeks to 40 weeks) were acquired and GQI were used to analyze. Normalized quantitative anisotropy (NQA), generalized fractional anisotropy (GFA), and isotropic value of the ODF (ISO) in three major white/gray matter tracts, i.e. hippocampus, corpus callosum, and olfactory tract, were calculated and compared across the ages. In our results, the tracts showed refinement in regional tract architecture with maturation, and the diffusion indices revealed the white/gray matter tracts change during mature period.

Materials and Methods

Whole brain images were acquired from five healthy New Zealand rabbits with ages from 4 to 40 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, and animal temperature was maintained at ~37°C using heat pad. Rabbits were immobilized and double loop array coils were used. For GQI 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= 0.78 × 0.78 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 2,000 s/mm^2, and scan time was about 42 min for each slab. Tractography and diffusion indices of the tracts were analyzed using DSI studio (National Taiwan University, Taiwan) after denoising [6]. For tractography, three tracts, hippocampus, corpus callosum, and olfactory tract, were selected for further analysis. Normalized quantitative anisotropy (NQA), generalized fractional anisotropy (GFA), and isotropic value of the ODF (ISO) in the tracts were then calculated. The indices in the cortex were used for normalization. The changes of these diffusion indices across the ages were also compared and discussed.

Results and Discussions

In our results (Fig. 1), tractography of the major white/gray matter tracts, such as hippocampus, corpus callosum, and olfactory tract, 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. Fig. 2 showed the GFA, ISO and NQA mapping of rabbit brains with ages from 4 to 40 weeks. In Fig. 3, it was observed that the GFA and NQA of hippocampus and corpus callosum increased with age. The ISO of corpus callosum decreased with ages, and there is no significant change in the ISO of hippocampus with age. The changes of GFA and NQA implied a more restrictive diffusion as the myelination of neural fiber greatly take place during the maturation period.

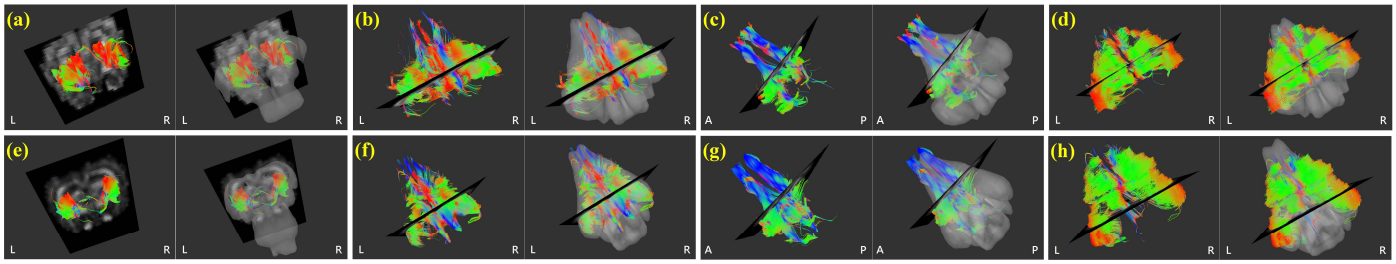

Fig. 1 DTI tractography of (a) hippocampus, (b) corpus callosum, (c) olfactory tract, and (d) cortex of 4 week-old rabbit. (e-h) The same tracts of 40 week-old rabbit.

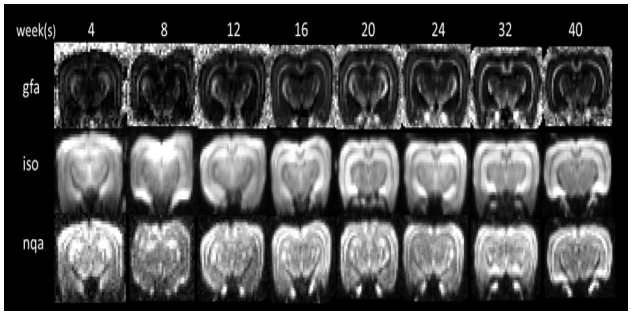

Fig. 2 The GFA, ISO and NQA mapping of rabbit brains with ages from 4 to 40 weeks.

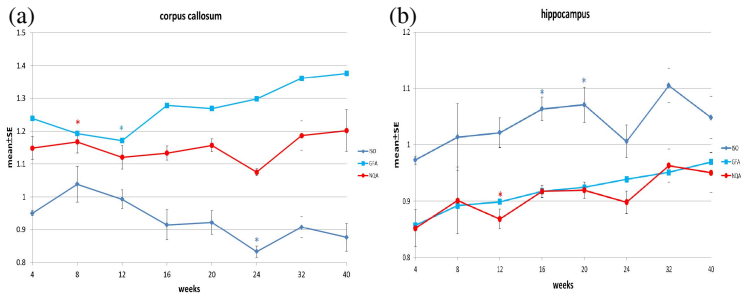

Fig. 3 The changes of GFA, ISO and NQA in the (a) corpus callosum and (b) hippocampus of the rabbits with ages from 4 to 40 weeks. (*: $p<0.05$)

Conclusions

Our results showed that both tractography and GQI diffusion indices revealed the major white/gray matter tracts change during mature period. In vivo GQI tractography is a potential tool for neuroscience investigations and can reveal effects, such as fiber tract pruning during development, which may be important targets for in vivo human studies.

References

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