IN VIVO DTI STUDY OF DEVELOPMENTAL RAT BRAIN

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Introduction

Diffusion tensor imaging (DTI) is capable of assessing tissue ultrastructural changes in vivo. Recently DTI was applied to study fixed and intact mouse brains at different development stage[1-3]. The goal of this study is to employ DTI to quantitatively characterize the developmental normal rat brains in vivo from neonatal day 8 (D8) up to day 80 (D80).

Method

Sample sizes: Normal Sprague-Dawley rats were used. The sample sizes were N=11 for D8 and D14, and N=6 for D21, D37, D60 and D80, respectively. Inconsistency in N was due to the fact that the rats were scanned in batches and some rats had not reached the later time points.

DTI study: All experiments were performed using a 7T Bruker scanner. The rats were anesthetized with isoflurane gas and in prone position inside a mouse brain coil (for D8 and D14) or a rat brain coil (for D21, D37, D60 and D80). DTI images were acquired with a respiration-gated spin-echo 4-shot EPI sequence. An encoding scheme of 30 gradient directions that were homogenously distributed on the unit sphere was used to acquire DT images. The imaging parameters were: TR/TE = 3000ms/32ms, Δ = 20ms, δ = 4ms, FOV = 32mm (for D8 and D14), 40mm (for D21, D37, D60, D80), thickness = 0.5mm (for D8 and D14), 0.7mm (for D21, D37, D60, D80), acquisition matrix = 128 x 128 (zero filled to 256 x 256), image resolution = 250 x 250 μm^2 (for D8 and D14), 313 x 313 μm^2 (for D21, D37, D60, D80), acquisition time = ~8 min.

Post-processing and analysis: Fractional anisotropy (FA), axial diffusivity ($\lambda_{//}$), radial diffusivity ($\lambda_{\perp}$) and apparent diffusion coefficient (ADC) trace maps were generated by DTIStudio v2.4 (JHU, Baltimore, mri.kennedykrieger.org). Regions of interest (ROIs) were manually drawn in ImageJ (Wayne Rasband, NIH, USA) on the consecutive slices that covered one cerebral cortex region (CX) and three dominant white matter regions, corpus callosum (cc), anterior commissure (ac) and cerebral peduncle (cp). ROI was first defined in FA map because its relatively clear white/gray matter boundary, and placed on the identical sites on the trace, $\lambda_{//}$, $\lambda_{\perp}$ maps. T-test was performed to determine the change in values between consecutive time points.

Results

Corpus callosum (cc): FA was found to increase significantly in D8 (p=0.001), D21 (p=0.003) and D37 (p<0.001). $\lambda_{//}$ changed significantly in the first 4 time points (p<0.001 in D8, D14 and D37, p=0.039 in D21). In the first 2 time points the signal dropped and after that it raised to a value close to that in D8. $\lambda_{\perp}$ dropped significantly from D37 onwards (p<0.001 in D37, p=0.044 in D60).

Anterior commissure (ac): FA in ac only increased significantly in D21 (p<0.001) and D37 (p<0.001) and then came to a plateau in D60 to D80. The trend was similar to FA change in cc. $\lambda_{//}$ increased significantly in D8 (p=0.003) and D37 (p<0.001). $\lambda_{\perp}$ slightly increased without significance at the first 2 time points and decreased at D21 and D37 significantly (both p<0.001).

Cerebral peduncle (cp): FA increased at D14 and D21 significantly (both p<0.001). Trend in $\lambda_{//}$ also showed significant change in D14 and D21 (both p<0.001). $\lambda_{\perp}$ was not changed significantly until D14. Then it dropped in D14 (p=0.004), D21 (p=0.002) and D37 (p=0.025). The changes in cp were found earlier than in ac and cc in FA, $\lambda_{//}$ and $\lambda_{\perp}$.

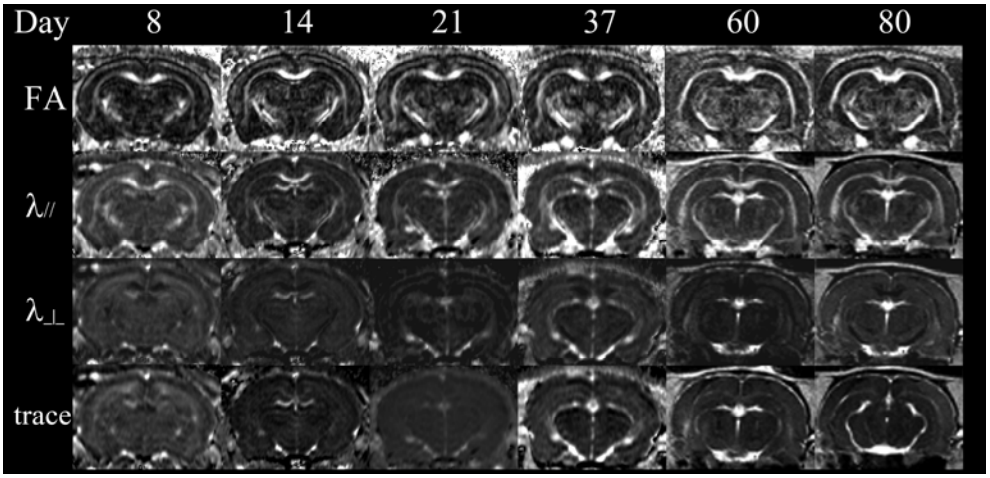

Fig. 1 FA, $\lambda_{//}$, $\lambda_{\perp}$, trace map at different time points.

Cerebral cortex (CX): FA was relatively low compared to the other white matter structures of interest. It increased significantly at D37 only (p<0.001) throughout the period. $\lambda_{//}$ also had a low value and significant changes were detected in D8 (p<0.001) and D60 (p<0.001). $\lambda_{\perp}$, on the other hand, was the highest amongst all the structures of interest. It decreased significantly at D8 (p=0.002) and then D37 (p=0.018) and D60 (p=0.008).

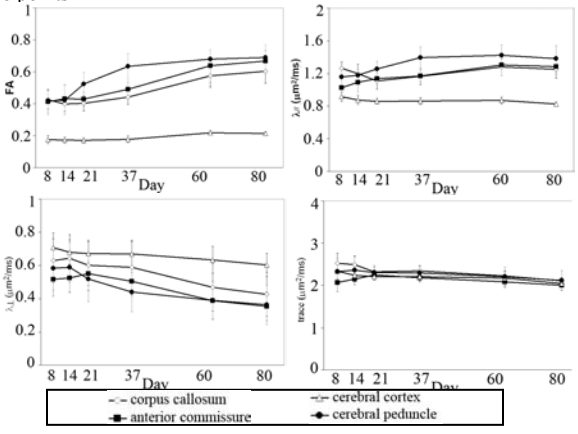

Fig.2 Time courses of measured DTI parameters.

Discussions

The values of DTI parameters of the white matter depends on the density of fibers, degree of myelination, average fiber diameter, and the directional similarity of the fibers[4]. Some suggested that the FA increase was probably due to the myelination of axons[5], but it was found that the development of the brain ultrastructures was a more reasonable explanation[2,6]. The trends observed in this study were similar to those reported in humans[7] and mice[3]. $\lambda_{//}$ increased continuously in ac and cp throughout the period probably due to the myelination of axons which promotes water diffusion in the axial direction and inhibits water diffusion perpendicular to the axon. Some research suggested that trace decreased with age in both white matter and gray matter in other animals, which was related to the decreasing water content and the formation of new barriers to water motility[6]. In both cc and ac, the trend of $\lambda_{//}$ and $\lambda_{\perp}$ showed increase and decrease respectively starting from D21 to D60. This might possibly be due to the myelination of axons which occurred in the period. After D60 the myelination became slower or even no further myelination so the change in value was much less dramatic. Decrease in trace with age was reported in other research[8]. However, although a decreasing trend was shown in the plots, the decrease was significant only after D37 only (p<0.007) in all the structures of interest.

Conclusions

The DTI was employed to document the in vivo changes of FA and diffusivities in normal development rat brains that were associated with ultrastructural changes in maturing white and gray matters. The DTI parameter changes showed similar trends as previous reported in humans[7] and mice[3] though with different time scales. FA and $\lambda_{//}$ increases with time in the developing brain starting at different time point for different brain regions, while $\lambda_{\perp}$ generally decreases with time. Literature reported trace decreases with age[8]. In this study, a general decreasing trend was only observed in the most structures after D37.

References: (1) Harsan LA, et al., JNR 2006;83:392–402 (2) Mori S, et al., Magn. Reson. in Med. 2001;46:18–23 (3) Mori S, et al., Neuron 2006;51:527-539 (4) Prayer D, et al., European Journal of Radiology 2003;45:235-243 (5) Baretti C, et al., Radiology 1999;210:133-142. (6) Neil J, et al., NMR Biomed. 2002;15:543-552 (7) Mukherjee P, et al., ANJR 2002;23:1445-1456 (8) Schmithorst VJ, et al., Radiology 2002; 222:212–218