Evolution of MR DTI Changes in Neonatal Rats after Mild Hypoxic-ischemic Insult

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INTRODUCTION

The mild hypoxic-ischemic (H-I) insult can induce a noncystic periventricular leukomalacia (PVL) in neonates, which is a major cause of later cognitive and behavioral deficits in adolescent children [1]. Diffusion tensor imaging (DTI) has been applied for *in vivo* quantification of myelin loss and regeneration in white matter (WM), delineating normal developmental changes and postinjury modification in gray matter (GM) [2, 3]. However, the assessment of infants and neonatal rat brain with mild H–I insult by multiple DTI parameters has not been performed. In this study, we hypothesized that different DTI parameters would provide sensitive information concerning microstructural evolution of myelin, axon and cortical layers in mild H-I lesion of neonatal rats. Therefore, apparent diffusion coefficient (ADC), fractional anisotropy (FA) and directional diffusivities ($\lambda_{//}$ and $\lambda_{\perp}$) values were measured in WM and GM lesion and their contralateral side at 3 different time points to assess whether DTI can improve the detection of brain injury in infants with a noncystic PVL.

MATERIALS and METHOD

7-day-old Sprague-Dawley rats (n=20, 12g-16g weight) underwent unilateral ligation of left common carotid artery plus exposure to hypoxia for 50 minutes at ambient temperatures of 36°C, in order to create mild H-I models[1].

MRI scanning: DTIs and T2 weighted images (T2WIs) at coronal sections were performed using a 7T animal MRI scanner (70/16 Bruker BioSpin MRI PharmaScan, Germany) and mouse brain coil in day 1, day 3 and day 7 following the H-I insult. DTIs were acquired with a respiration-gated spin echo 4-shot EPI readout sequence. An encoding scheme of 30 gradient directions which are homogenously distributed on the unit sphere was used to acquire DTIs. The imaging parameters were: TR/TE=3000/32 ms, Δ=20 ms (diffusion gradient duration), δ=4 ms (diffusion gradient separation), b value =1000 s/mm^2, NEX=1, field of view (FOV) =2.5 cm^2, slice thickness=1.0 mm, matrix=128×128 (zero filled to 256×256), 10 slices, and acquisition time ≈7 min. T_2WI were acquired using a dual-echo RARE sequence with TR/TE1/TE2 =6000/60/200 ms, RARE factor=12, NEX=2, FOV =2.5 cm, slice thickness = 0.5 mm, matrix = 256×256, 20 slices, acquisition time ≈3 min.

Image analysis: FA, tensor trace (ADC), axial diffusivity ($\lambda_{//}$) and radial diffusivity ($\lambda_{\perp}$) maps were derived using DtiStudio software v2.4. The region-of-interest (ROI) of GM was first manually drawn over the parietal cortical lesion and then mirrored to contralateral side in the ADC maps on D1 post injury. ROIs of WM were manually drawn over external capsule (EC) of each hemisphere in the FA maps on 3 consecutive slices from D7 post injury images. Then, the GM or WM ROIs were respectively placed on identical sites on $\lambda_{//}$ and $\lambda_{\perp}$, FA or ADC maps in other time points. Suitable *t-test* was performed to see if the GM and WM differences between the ipsilateral and contralateral side were significant.

RESULTS and DISCUSSION

12 neonatal rats were successfully created as mild hypoxic-ischemic (H-I) models. The evolution of T2WIs and different DTI maps was showed in Fig.1, and the changes of DTI parameters between the both hemispheres were showed in Fig.2. In day 1 post H-I insult, the ADC, FA and $\lambda_{//}$ values showed significant decrease in GM lesion of ipsilateral parietal cortex, likely resulting from an apparent intracellular edema and subsequent reductions of extracellular space. WM lesion of ipsilateral EC only showed a significant ADC increase likely due to edema, suggesting an enlargement of extracellular space between WM fibers and without a marked breakdown of WM structure. In day 3, the alleviation of cell swelling in GM lesion reduced the difference of ADC and $\lambda_{//}$ values between the ipsilateral and contralateral cortex [1]. Whereas the significant decrease in FA and increase in $\lambda_{\perp}$ likely arose from the disruption of cortical layer, which exhibited as astrocytosis, radial glial organization and neuronal death [3]. In the WM of day 3 post H-I insult, significant increase in ADC and $\lambda_{\perp}$, and dramatic decrease in FA within the ipsilateral EC may indicate dysmyelination or demyelination and vacuolation in lesion. However, axonal caliber and number may not change in mild H-I insult as suggested by the similar $\lambda_{//}$ values in both sides [1, 2]. By day 7, no differences were observed in ADC, FA, $\lambda_{//}$ and $\lambda_{\perp}$ values in both WM and GM between two hemispheres, revealing the developmental changes and postinjury regeneration and adaptation.

CONCULSION

DTI is a sensitive method for characterizing the transient changes after mild H-I insult in neonates, and may provide with the multi-parametric assessment of the microstructural evolution during WM and GM injuries.

REFREENCES

1, Meng S, et al., Pediatr Res 2006;59:554-9 2, Harsan LA, et al., JNR 2006;83:392-402. 3, Sizonenko SV, et al., Cereb Cortex 2007; 17(11):2609-17.

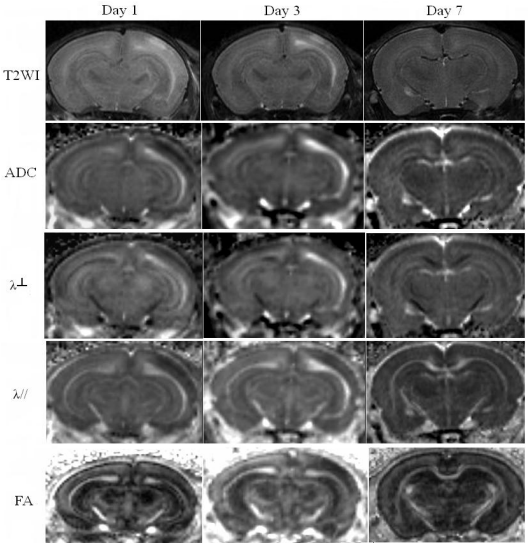

Fig. 1 T2WIs and various DTI maps at three time-points.

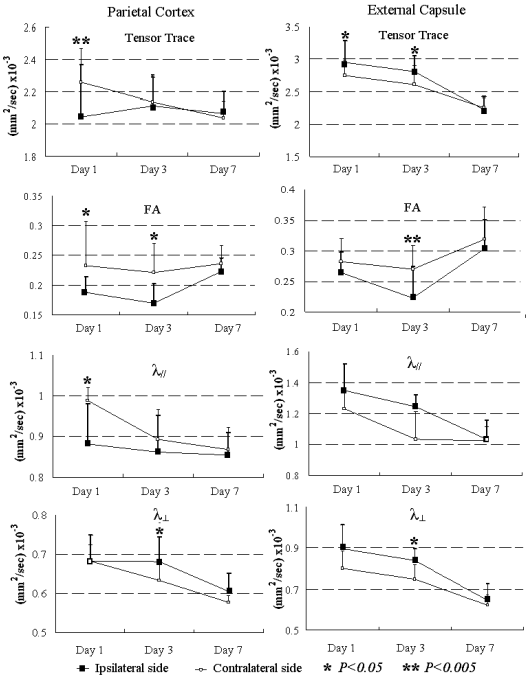

Fig. 2 DTI parameters at different time-points.