Temporal and spatial evolution of Wallerian degeneration in central nervous system detected using DTI

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Introduction

Wallerian degeneration plays a significant role in many central nervous system (CNS) diseases. Tracking the progression of Wallerian degeneration may provide better understanding of the evolution of many CNS diseases (1,2). In our previous study examining the Wallerian degeneration of mouse visual pathway resulting from the death of retinal ganglia cells demonstrated that in vivo DTI is capable of detecting both proximal (optic nerve) and distal (optic tract) axonal damage at the chronic stage of Wallerian degeneration (3). In order to further validate the capability of DTI to monitor the temporal and spatial evolution of Wallerian degeneration of axons resulting from the death of retinal ganglion cells, in this study, a time course of in vivo DTI was conducted.

Materials and Methods

Five male Swiss Webster mice, 6 – 8 weeks of age underwent transient retinal ischemia (4). Briefly, 100 – 120 mmHg intraocular pressure was applied to the right eye of each mouse for one hour. Reperfusion started immediately after removal of the cannula. The left eye, which was not cannulated, served as the control. For each mouse, in vivo DTI was performed at 1, 2, 3, 5, 9, 14, 28, and 56 days after ischemia. Data were acquired using Oxford Instruments 200/330 (4.7 T) magnet and spin-echo diffusion weighted imaging sequence with TR 1.5 sec, TE 70 ms, b 850 s/mm^2, slice thickness 0.5 mm, field-of-view 3 cm, and data matrix 256 × 256. Relative anisotropy (RA), Tr, $\lambda_{\parallel}$, and $\lambda_{\perp}$ were measured in left and right ON and OT. The effect of retinal ganglion cell death on DTI parameters of the ON and OT was examined using analysis of variance (ANOVA). For parameters that exhibited significant difference ($p < 0.05$), two-sample post hoc t tests were performed to identify days for which left and right visual pathways differed. Differences were considered statistically significant at $p < 0.05$.

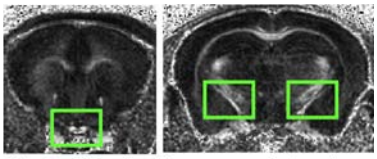

Fig.1 RA of optic nerve optic tract

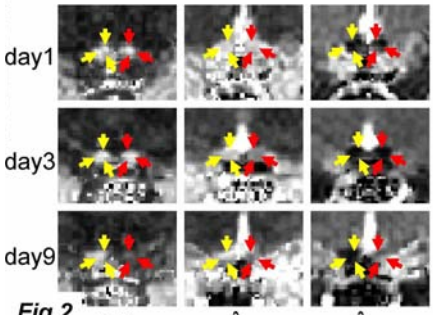

Fig.2

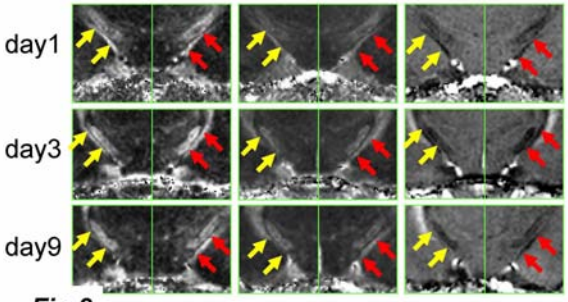

Fig.3

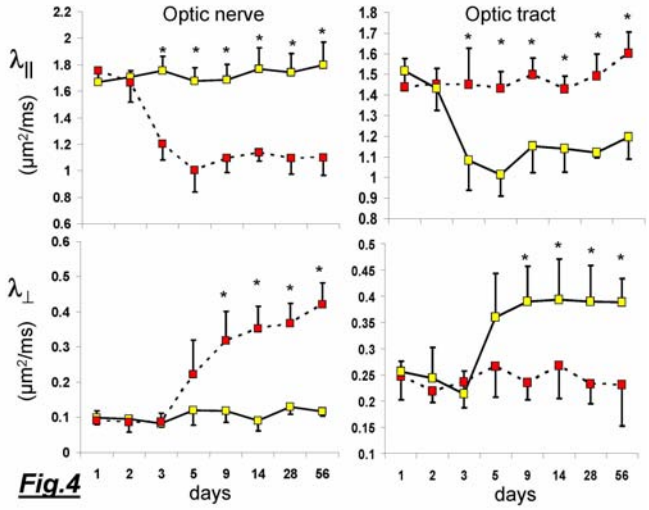

Fig.4

Results

The representative RA maps, which provide great image contrast to characterize white matter tracts, from a normal mouse were shown in Fig.1. The RA, $\lambda_{\parallel}$, and $\lambda_{\perp}$ of the expanded view of the ON and OT (indicated by the green rectangles in Fig. 1) from the same mouse at 1, 3, and 9 days after ischemia were shown in Fig. 2 (ON) and Fig. 3 (OT). The red and yellow arrows pointed to the visual pathways in ipsilateral and contralateral hemispheres respectively. Comparing to the contralateral optic nerve, decreased $\lambda_{\parallel}$ was found at 3 and 9 days in ipsilateral ON. RA and $\lambda_{\perp}$ did not change at 3 day but decreased RA and increased $\lambda_{\perp}$ were found at 9 days. As for OT, there was no difference between left and right OT at 1 day. Decreased $\lambda_{\parallel}$ was found at 3 and 9 days in contralateral OT. In the same tract, decreased RA and increased $\lambda_{\perp}$ were found at 9 days.

The time courses of $\lambda_{\parallel}$ and $\lambda_{\perp}$ from 5 mice were summarized in Fig. 4, where red symbols (dashed-line) and yellow symbols (solid-line) represent the measurements from ipsilateral and contralateral visual pathways respectively. Decreased $\lambda_{\parallel}$ was measured in 3-56 days in both ipsilateral ON and contralateral OT suggestive of the axonal damage. Increased $\lambda_{\perp}$ were found at 9-56 days suggestive of the demyelination.

Discussion and Conclusion

This study demonstrated the capability of $\lambda_{\parallel}$ and $\lambda_{\perp}$ to reflect the temporal and spatial evolution of CNS Wallerian degeneration. The degeneration of mouse visual pathway resulting from retinal ischemia exhibited a pattern of axonal damage followed by the myelin damage as demonstrated by the early decrease of $\lambda_{\parallel}$ (at 3 days) followed by the later increase in $\lambda_{\perp}$ (at 9 days). Interestingly, no time delay was observed in the progression of the Wallerian degeneration spreading from proximal sections (optic nerve) to the distal sections (optic tract) of the visual pathway. Both optic nerve and tract exhibited the changes in $\lambda_{\parallel}$ (axonal damage) and $\lambda_{\perp}$ (myelin damage) at the same temporal evolution and comparable severity. Further histological validations are being pursued to confirm these findings.

References

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