Quantitative DTI of White Matter Abnormalities upon Early Postnatal Visual Impairments

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INTRODUCTION: Visual impairments are among the main causes of childhood disabilities in developed countries. Understanding the neural mechanisms of visual impairments can shed light not only on the plastic rearrangements that take place when vision is loss, but also on the functional organization of the sighted brain itself (1). To date, limited studies have been performed to systematically examine the effect of early visual impairment and blindness on the microstructural integrity in the cerebral white matter (2,3). The present study examines in vivo the effect of 4 types of early postnatal visual impairments on the development and plasticity of rat visual pathways using diffusion tensor imaging (DTI).

MATERIALS AND METHODS: Animal Preparation: Sprague-Dawley rats (N=30) were prepared and divided into 5 groups. In Groups 1 and 2 (n=6 each), neonatal binocular enucleation (BE) and monoculear enucleation (ME) to the right eye were performed respectively at postnatal day (P) 1. In Group 3 (n=6), monocular deprivation (MD) was performed by suturing the eyelids of the right eyes at the time of eyelid opening at P15. In Group 4 (n=6), animals were kept in a dark room for dark-rearing (DR) since birth. Six other animals were untreated and acted as a control (CTRL). DTI was performed to all animals at 6 weeks old. **MRI Protocol:** All MRI measurements were acquired utilizing a 7 T Bruker scanner. T2WI were acquired using 2D RARE pulse sequence. For DTI, 4-shot SE-EPI diffusion weighted images were acquired with FOV = 32x32 mm^2, MTX = 128 x 128, slice thickness = 1 mm, no. of slices = 15, TR/TE = 3750/30 ms, b = 0 and 1000 s/mm^2 and 30 diffusion directions. **Data Analysis:** DTI parameters, including FA, $\lambda_{//}$, $\lambda_{\perp}$ and diffusion trace were obtained using DTIStudio v2.30 after co-registration. The DTI parameters along the major visual pathways projected from the left eye [left prechiasmatic optic nerve (L-PON), and right anterior (R-AOT) and posterior optic tract (R-POT)] and from the right eye [right prechiasmatic optic nerve (R-PON), and left anterior (L-AOT) and posterior optic tract (L-POT)] were measured using ImageJ v1.43u. DTI parameters of each optic segment were compared between each experimental (BE, ME, MD, DR) group and CTRL group using unpaired t-tests. Results were considered significant when $p<0.05$.

RESULTS: In the anatomical T2WI, dramatic shrinkage of SC and LGN was observed in both hemispheres of BE rats and in the left hemisphere of ME rats (data not shown). In the FA maps in Fig. 1, the PON, AOT and POT could be visualized in both hemispheres in each animal group. Figs. 1 and 2 indicated a significantly lower FA in the visual pathways projected from both eyes in BE rats, and from the right eye in ME rats compared to CTRL rats. A small but significantly lower FA could also be observed in the left POT of MD rats, whereby a significantly higher FA was found in the left PON of ME rats. The lower FA observed in PON and AOT in the BE and ME rats was mainly attributive to an increase in $\lambda_{\perp}$ compared to the CTRL rats, while the lower FA observed in the POT of BE, ME and MD rats was apparently attributive to a decrease in $\lambda_{//}$ compared to CTRL rats. No apparent difference was observed in DR group along either visual pathway.

DISCUSSIONS AND CONCLUSION: The results of this study documented in vivo the varying degrees of microstructural alterations along the visual pathways in 4 rat models of early postnatal visual impairments. The lower FA and higher $\lambda_{\perp}$ observed in the PON and AOT of BE and ME rats were likely ascribed to anterograde degeneration of the afferent fibers projected from the enucleated eyes (4), while the lower FA and $\lambda_{//}$ observed in the POT of BE, ME and MD rats might be partially related to apoptosis of retinocollicular and retinogeniculate synapses at the posterior visual brain nuclei (4,5). Previous studies demonstrated that both diffuse illumination by MD and total light deprivation by DR might cause structural and functional changes in the posterior visual brain nuclei (5-8). Our observations of no apparent DTI parametric changes in DR but MD rats appeared to support the hypothesis that the effect from DR on the visual pathway was less deleterious than that from MD (6,7). Whether the higher FA in left PON of ME rats was related to the retention of optic nerve axons from the ipsilaterally projecting retinal ganglion cells of the left eye (4) remained to be elucidated. Future DTI studies are envisioned that measure the development and reorganization of the impaired visual pathways after early interventions in longitudinal studies.

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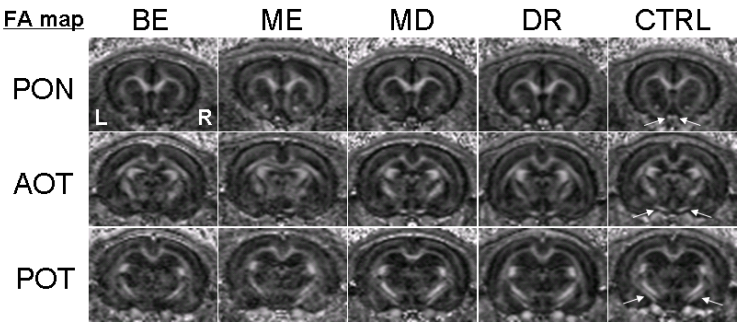

Fig. 1: Fractional anisotropy (FA) maps of the experimental groups (BE, ME, MD, DR) and the control group (CTRL) at the levels of prechiasmatic optic nerve (PON), anterior optic tract (AOT), and posterior optic tract (POT) (arrows in CTRL).

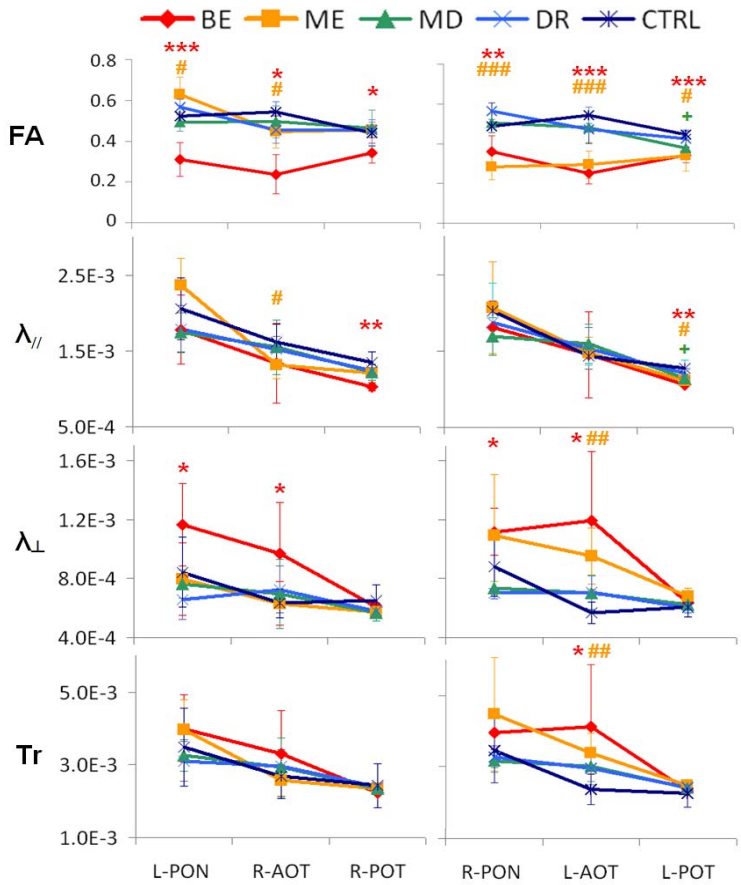

Fig. 2: Comparisons of DTI parameters along visual pathways projected from the left (1st column) and right (right column) eyes between each experimental group (*BE, #ME, +MD, ^DR) and the control group (Two-tailed unpaired t-test, *.#,+,^$p<0.05$; **.##,++,^^$p<0.01$;***.###,+++,^^^$p<0.001$).