Early Pathological Changes in the Optic Nerves of Type-I Diabetic Rats Revealed by Directional Diffusion-Weighted MRI

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Introduction Diabetic retinopathy (DR) is a major complication of diabetes and a leading cause of blindness [1]. In animal models of diabetes, increased apoptosis of the retinal neural cells begins at about one month after induction of diabetes [2]. The optic and peripheral nerves of diabetic animals start to show axonal transport impairment and axonal loss at 4-12 weeks after diabetes induction [3-5]. Directional diffusion imaging is a simplified version of diffusion tensor imaging, which has been widely used to assess morphological and structural changes of white matters having oriented fiber structures such as the optic nerves [6-8]. With this method, the water diffusivities parallel and perpendicular to the nerve fiber tracts are measured, which are thought to reflect axonal injuries and myelin sheaths damages respectively. In this study, the directional diffusion imaging technique was applied to investigate the pathological changes in the optic nerves of rats at 4 weeks (4w) and 10 weeks (10w) after the induction of type-I diabetes.

Materials and methods Eight-week old male Sprague-Dawley rats, weighing 220-270 g, received intraperitoneal injections of either 62 mg/kg streptozotocin (STZ) dissolved in 0.01 M sodium citrate buffer (pH 4.5) or the same amount of saline (control group). The treated animals were considered to be diabetic if their fasting blood glucose levels were higher than 226 mg/dl. Directional diffusion imaging was conducted on a 4.7 T/30 cm Bruker Biospec scanner with a 5-cm diameter saddle coil at 4w and 10w after diabetes induction. A spin-echo sequence was used with the following acquisition parameters: TR 1000 ms, TE 28 ms, matrix size 256×256, FOV 3.0 cm×3.0 cm, slice thickness 1 mm, Δ 14 ms, δ 5 ms (b= 0 and 500 s/mm^2) and 4 averages. The diffusion-weighting gradients were applied on two orthogonal directions that were parallel ($DW_{//}$) and perpendicular ($DW_{\perp}$) to the pre-chiasmtic sections of the optic nerves (2 mm anterior to the chiasm), respectively. Averaged directional apparent diffusion coefficients of the optic nerves, $ADC_{//}$ and $ADC_{\perp}$, were calculated and compared between the diabetic and control groups with Student's *t*-tests.

Results Figure 1 shows diffusion-weighted images acquired from coronal slices of a control rat and a STZ-treated rat. Figure 2 plots the quantitative changes of $ADC_{//}$ and $ADC_{\perp}$. Compared to the control animals, the STZ-treated rats showed little diffusion abnormalities in the optic nerves at 4w, but decreased $ADC_{//}$ (1.40±0.15 vs. 1.65±0.12 $\times 10^{-3}$ mm^2/s) and $ADC_{\perp}$ (0.32±0.15 vs. 0.59±0.12 $\times 10^{-3}$ mm^2/s) in the optic nerves at 10w. The changes in $ADC_{\perp}$ at 10w were statistically significant (p <0.05), but not those in $ADC_{//}$.

Discussion The optic nerves of the diabetic rats showed little changes in water diffusivity at 4w after the induction of diabetes, suggesting that the structural integrity of the nerves was still well maintained at this stage. This is consistent with previous reports showing that diabetic retinopathy only starts to occur at 1 month after STZ-induced diabetes [2]. The diabetic animals showed significantly reduced $ADC_{\perp}$ and a trend of reduced $ADC_{//}$ in the optic nerves at 10w after diabetes induction, indicating that axonal atrophy or degeneration may have already occurred by this time. The imaging results obtained in this study agreed well with the histopathological findings in the same animal model of diabetes, showing that diabetes-induced damages in the optic and peripheral nerves are characterized by reduced myelinated fiber size and loss of axonal neurofilaments [9,10].

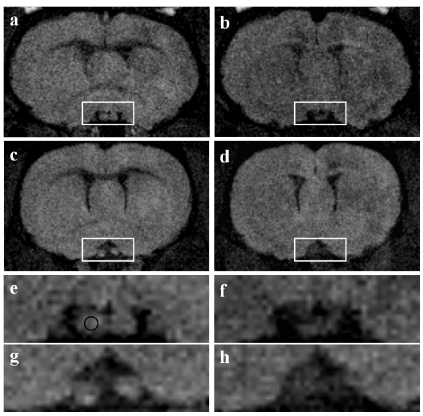

Figure 1. Diffusion-weighted images acquired from coronal slices of a control rat (a and b) and a STZ-treated rat (c and d) at 10w. (a) and (c): $DW_{\perp}$; (b) and (d): $DW_{//}$. Enlargements of the regions within the white rectangles in (a-d) are shown in (e-h), respectively. The region of interest for the optic nerve is delineated by the back circle in (e).

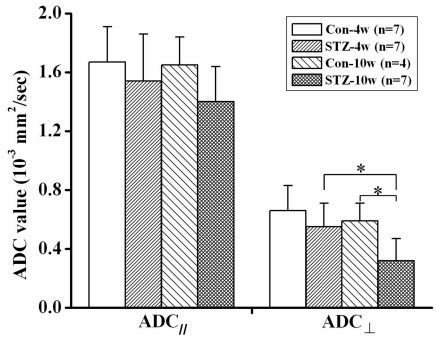

Figure 2. Averaged $ADC_{//}$ and $ADC_{\perp}$ in the pre-chiasmatic optic nerves of the control rats (Con) and STZ-treated rats at 4w and 10w. *p<0.05, compared to Con-10w and STZ-4w.

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References [1] Barber AJ, Neuro-Psychopharmacol Biol Psychiatry, 2003, 27:283-290. [2] Barber AJ, et al, J Clin Invest, 1998, 102(4):783-791. [3] Medori R, et al, Proc Natl Acad Sci, 1985, 82(22):7 716-7 720. [4] Scott TM, et al, J Anat, 1986, 144:145-152. [5] Ino-Ue M, et al, Invest Ophthalmol Vis Sci, 2000, 41:4 055-4 058. [6] Song SK, et al, Neuroimage, 2003, 20(3):1 714-1 722. [7] Wu QZ, et al, Neuroimage, 2007, 37(4):1 138-1 147. [8] Xu J, et al, NMR Biomed, 2008, 21(9):928-940. [9] Ino-Ue M, et al, Brain Res, 1998, 800(2):319-322. [10] Yagihashi S, Am J Pathol, 1990, 136(6):1 365-1 373.