Diffusivity Evaluation of Optic Nerve in Aged Rhesus Monkeys
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Introduction: The optic nerve is the continuation of the axons of ganglion cells in the retina. Changes during aging have been observed in the optic nerve in postmortem studies of human subjects and non-human primates (NHP) [1-5]. Diffusion Tensor Imaging (DTI) provides a non-invasive means for evaluating optic nerve abnormality and has demonstrated its sensitivity in several studies of optic nerve development and disorders in humans and animals [6-12]. NHPs are most closely similar to human in brain structure and functionality and are the preferred models for studying optic nerve aging. In this study, the diffusivity in optic nerve was investigated in aged rhesus monkeys to assess aging related changes.

Materials and Methods: Aged female rhesus monkeys (n = 9, 20-24 years old) were scanned with a multi-shot double-echo DTI sequence on a Siemens 3T Trio with the extremity CP knee coil. The MRI parameters were: TR/TE = 6970/90 ms, FOV = 141 mm × 141 mm, matrix size = 128 × 128, slice thickness = 1.1 mm (voxel size: 1.1 mm isotropic), 60 directions, b-value = 0, 1000 s/cm². Animals were immobilized with a head holder under anesthesia (1-1.5% isoflurane), EtCO₂, inhaled CO₂, O₂ saturation, blood pressure, heart rate, respiration rate and body temperature were monitored continuously and regulated. DTI data was preprocessed with distortion and motion correction using FSL and SPM5. Region of interests (ROIs) were drawn manually using MRIcro on the slices located between the anterior and posterior quarters of the optic nerve (Fig. 1 (a)). Mean values of MD, λ₂, λ⊥ and FA in the ROI were calculated from each optic nerve. Fiber tractography was carried out using FSL with multiple masks (n = 2) (Fig.1 (b)). Pearson correlation was used for statistical analysis.

Results and Discussion: Female animals were used in this study in order to minimize any possible gender bias because the nerve fiber degeneration with age in male and female may be different [9]. As shown in Fig. 2, the mean diffusivity (MD) and axial diffusivity (λ₂) of optic nerves increased significantly in the animals from 20 to 24 years old. Radial diffusivity (λ⊥) also increased (p = 0.053). These are in agreement with the DTI findings on white matter aging in human brain [10-12].

On the other hand, no significant correlation was observed between either the fractional anisotropy (FA) or the fiber tract number with age. This is consistent with previous ex-vivo studies of rhesus monkey optic nerves [3], in which fiber number didn’t correlate significantly with age for monkeys at ages from 20 to 29 years old (p = 0.65).

The results suggest that DTI is a sensitive tool to study the normal aging of optic nerve and diffusivity parameters are more sensitive to age-related change than FA and fiber tract number. Sullivan and colleagues also found that aging effects were more evident in diffusivity than FA measures from white matter study of human brain [10].

Conclusion: The optic nerves in aged female rhesus monkeys were investigated systematically with DTI. The data revealed that MD and λ₂ increased significantly during aging, with no significant changes in FA and fiber tract number. The elevation of MD, λ₂ and λ⊥ is consistent with the DTI findings on white matter in aged human brains. The unchanged FA and fiber tracts number are in agreement with the ex-vivo study of optic nerve aging in rhesus monkeys. The results suggest that DTI is sensitive for characterizing the optic nerve aging and the diffusivity parameters may be potential markers to evaluate the optic nerve disorders during aging.

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