Resolving of Crossing Pathways in the Optic Chiasm of Marmoset Monkey using Diffusion Tractography with High Spatial and Angular Resolution

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Introduction

The structure of the optic chiasm varies widely between the primate and the rodent [1]. The fiber architecture of the marmoset (*Callithrix jacchus*), a New World primate, is close to that of humans [2]; therefore, the marmoset has been used to study the development of the optic chiasm. Further, the body weight of the marmoset (around 300 g) is similar to that of the rat, but its brain-to-body mass ratio is more than 4 times greater than that of the rat (man, 7.5 > marmoset, 1.7 > rat, 0.4 [3]). In addition, the marmoset has a well-developed visual pathway. Because of these factors, the marmoset is an ideal animal model for performing visual research by using a small magnetic resonance imaging (MRI) scanner.

In a previous study, we used manganese-enhanced MRI and diffusion tensor tractography (DTT) to reveal the neuroanatomic features of the visual pathway in the marmoset [4]. However, the DTT technique has some limitations with regard to intravoxel fiber crossing.

Recently, increased angular resolution of diffusion MRI, namely, high angular resolution diffusion imaging (HARDI), has been introduced to overcome this limitation. HARDI tractography is expected to be a method for visualizing the fiber pathway more precisely, particularly in the region of the fiber crossing.

We performed HARDI with increased spatial resolution of the *ex vivo* optic chiasm in the marmoset in order to evaluate the fiber architecture of the optic chiasm.

Materials & Methods

Optic chiasm *ex vivo* models were obtained from post-mortem fixed brains of adult common marmosets (4 females). Each animal was perfused intracardially with 4% paraformaldehyde, and subsequently, the optic chiasm tissues were removed. Two specimens were soaked in phosphate buffered saline solution with 1 mM Gd-DTPA to optimize diffusion MRI [5].

Histological analysis was performed by staining 1 specimen with luxol fast blue (LFB) for evaluation of the myelinated area. Further, another specimen was used for the evaluation of the axon diameter by means of an electron microscope. All the studies were performed in accordance with animal protection laws and were approved by the Animal Ethical Committee of the Central Institute for Experimental Animals.

MRI experiments were performed using a 7T PharmaScan 70/16 system with high gradient strength (300 mT/m). A saddle coil (internal diameter, 22 mm) tuned to 300.5 MHz for proton resonance was used. Diffusion-weighted images (DWIs) were acquired in a 3D DW-SE sequence. The parameters were as follows: TR/TE = 2000 ms/38 ms, spatial resolution = 150(μm)^3, MPG duration time (δ)/separation time (Δ) = 12 ms/20 ms, different 8 b-values of 0–12200 s/mm^2, and MPG directions = 81 (third-order tessellation of the icosahedrons). The software construct used to perform HARDI analysis was an in-house IDL@ program based on spherical harmonics [6]. HARDI Tractography was performed using TrackVis [7] with the fiber assignment by continuous tracking (FACT) algorithm.

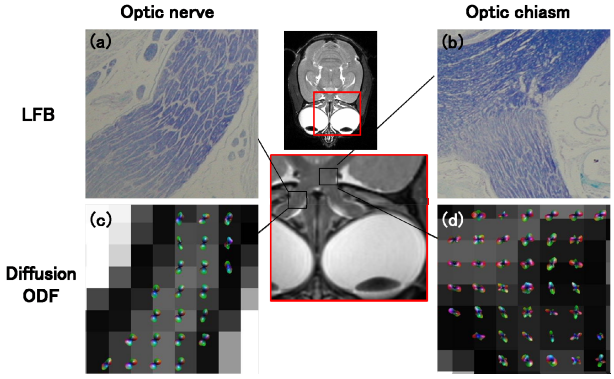

Figure 1. Luxol fast blue (LFB) staining and diffusion orientation distribution function (ODF) of the optic nerve (ON) and the optic chiasm (OC).

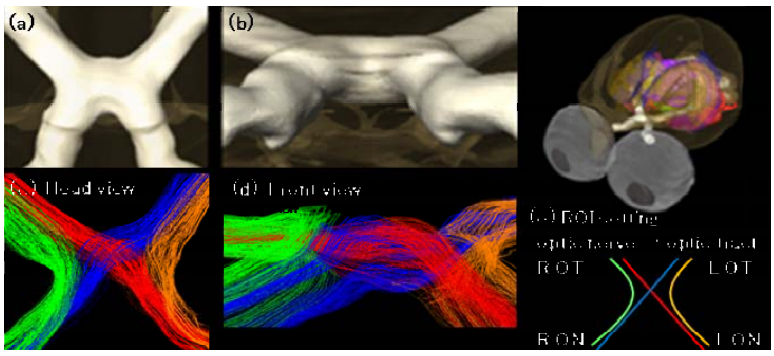

Figure 2. Reconstructed optic chiasm (a and b) and diffusion tractography (c and d).

Results

The optic nerve (ON) fibers in the horizontal section were aligned in a parallel manner, as observed in the LFB staining (Figure 1(a)). The diffusion orientation distribution function (ODF) and the myelinated fibers stained by LFB showed a similar orientation in the same region of the ON. At the optic chiasm (OC), LFB staining failed to reveal the fiber orientation (Figure 1(b)), but we were able to resolve the complex architecture by using diffusion ODF. Further, by using diffusion tractography with 2 region of interests (ROIs) (e.g., R ON→R OT as shown in Figure 2(e)), we were able to resolve the fiber structure in the optic chiasm (b-value, 8000 sec/mm^2).

Discussion

In the primate visual system, the optic nerve fibers from the nasal half of the retina cross in the optic chiasm and pass to the optic tract of the opposite side. Further, the optic nerve fibers from the lateral half of the retina pass directly to the optic tract of the same side. Our results showed that the ratio of the tract counts between the crossing and uncrossing pathways became around half.

We succeeded in visualizing the precise fiber structure in the optic chiasm by using diffusion tractography with increasing spatial and angular resolution. However, diffusion tractography relies on numerical tracking algorithms and not on physiological tracing mechanics. We need to validate our results by using the neurotracing method. We will apply this method to study the optic chiasm in a monkey embryo in order to investigate the development of the visual system.

References: [1] Jeffery G et al., Neurosci, 2008 [2] Neveu MM et al., Eur J Neurosci, 2006 [3] Roth G., Dicke U., Trends Cogn Sci, 2005 [4] Yamada M et al., Radiology, 2008 [5] D'Arceuilet H et al., NeuroImage, 2007 [6] Hess CP et al., Magn Reson Med, 2006 [7] Proc. ISMRM15 (2007)3720