



Distinguishing and quantification of the human visual pathways using high-spatial-resolution diffusion tensor tractography[☆]

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ARTICLE INFO

Article history:

Received 18 August 2013

Revised 8 March 2014

Accepted 3 April 2014

Keywords:

Diffusion tensor imaging
Diffusion tensor tractography
High spatial resolution
Human visual system
Visual pathways
Retinogeniculocalcarine tract
Optic nerve
Optic chiasm
Optic tract
Optic radiations
Calcarine cortex
Occipital lobe

ABSTRACT

Quantification of the living human visual system using MRI methods has been challenging, but several applications demand a reliable and time-efficient data acquisition protocol. In this study, we demonstrate the utility of high-spatial-resolution diffusion tensor fiber tractography (DTT) in reconstructing and quantifying the human visual pathways. Five healthy males, age range 24–37 years, were studied after approval of the institutional review board (IRB) at The University of Texas Health Science Center at Houston. We acquired diffusion tensor imaging (DTI) data with 1-mm slice thickness on a 3.0-Tesla clinical MRI scanner and analyzed the data using DTT with the fiber assignment by continuous tractography (FACT) algorithm. By utilizing the high-spatial-resolution DTI protocol with FACT algorithm, we were able to reconstruct and quantify bilateral optic pathways including the optic chiasm, optic tract, optic radiations free of contamination from neighboring white matter tracts.

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1. Introduction

The human visual pathway consists of two neuron chains that traverse the brain anteroposteriorly in an axial plane. Optic nerve fibers project from the retina to the lateral geniculate nucleus (LGN) of the thalamus via the optic chiasm and optic tracts [1]. From the LGN, fibers emerge as the optic radiation carrying information from the contralateral visual field (geniculocalcarine tract or the genic-

lostriate pathway) and traverse the retrolenticular portion of the internal capsule on their way to their destination in primary visual cortex in the occipital lobe [2,3].

Challenges in mapping and progress toward quantification of the entire living human visual pathways or retinogeniculocalcarine tracts are historically documented [1]. In particular, imaging the optic nerve (ON) due to its small volume and tortuous geometry, and the harsh MRI environment surrounding it remain challenging [4].

Early reviews and comparison of acquisition parameters and quantitative results between methods have been provided elsewhere [5–8]. Diffusion-sensitized MRI methods applied to the human visual pathways have utilized regions of interest [9,10], deterministic [11–14] and probabilistic tractography [15–17] on separate components of the visual system including optic nerves [9,18], optic chiasm [19–21], optic tracts [10], and optic radiations [11–14] including Meyer loop [7,8]. Qualitatively, the methods adopted to-date to quantify components of the human visual system using diffusion-weighted imaging were different on several aspects

[☆] Presented in abstract: "Kamali A, Kramer LA, Hasan KM. Feasibility of Visual Pathways Tractography Using High-Resolution Diffusion Tensor Tractography Data on 3 T. Presented at the 47th Annual ASNR Meeting, in cooperation with the ASPNR, ASHNR, ASPNR, ASSR and SNIS, Vancouver Convention and Exhibition Centre, Vancouver, BC, May 18–21, 2009."

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including spin history preparation (i.e. fat, cerebrospinal fluid and outer volume suppression), k-space sampling (i.e. conventional spin echo, stimulated echoes, line scan, echo-planar imaging), in addition to differences in spatial resolutions (1–4 mm), *b*-factor (300–1000 s mm⁻²), signal-to-noise ratio (i.e. diffusion encoding, averaging, main magnetic field B_0), plane of acquisition, and scan time [21].

Diffusion tensor imaging (DTI) methods have been applied to various clinical conditions including ischemic injury of optic pathways [22], multiple sclerosis and optic neuritis [9,18,23–26], neuromyelitis optica [27], diabetes mellitus [28], glaucoma [29–31], amblyopia [32], blindness [33,34], cerebral palsy [35], and in neoplastic involvement of optic pathways [36,37]. Three-dimensional (3D) tractography of the entire human visual system might be more useful in preoperative and/or intraoperative neurosurgical planning to preserve structural integrity and avoid visual field defects by mapping the optic radiations [38,39] as well as for quantitative assessment of visual recovery after surgery [3,40–44] or in congenital lesions [45,46].

Neuroimaging DTI studies of the human visual pathways including the optic tracts, pretectal fibers and those between the deep gray nuclei and cortex have so far been limited due to inadequate spatial resolution (in-plane and slice thickness 2–5 mm) and poor signal-to-noise ratio (SNR) [46,47]. The use of large voxel sizes increase partial volume averaging [47–49] and contamination from neighboring fiber pathways, in particular, the occipito-pontine tract (OPT). Low SNR results in overestimation of anisotropy and increases errors in eigenvector estimation. This leads to inaccurate white matter connections [47–49] and false-positive results which has been a challenge in tracking the optic tracts and the pretectal fibers in particular. The ability to quantify the volume and corresponding diffusion tensor metrics of the optic pathways across the healthy human lifespan and in various aforementioned clinical scenarios would provide objective useful neuroimaging markers for therapy or modeling the neurobiology of injury or plasticity due to age, training, disease, neurotoxins, high-elevation or even microgravity in long space travels [50].

As mentioned above, several prior DTI tractography studies attempted to trace components of the visual tracts [5–8]. Lack of adequate spatial resolution resulted in partial volume averaging and false-positive and false-negative results. Also susceptibility artifacts and limited spatial resolution have been major drawback in the prior DTI studies [4,21]. These limitations resulted in inability to trace the subcomponents of the optic tract such as the pretectal fibers [6] or anterior aspect of the optic radiation known as the Mayer's loop in the prior DTI tractography studies [38]. Furthermore, to our knowledge, no illustration of the major neighboring fiber pathways of the visual tracts has been demonstrated by prior DTI tractography studies.

DTI acquisition methodology can be improved by sequence optimization with respect to shorter echo time, decreased partial volume averaging effects and reduced geometrical distortions [4,10,21]. This will be advantageous to the study of the delicate fibers of the optic pathway in relation to adjacent major white matter fiber tracts such as the posterior thalamic radiation (PTR) or occipito-pontine tract [14]. The aim of this study is to demonstrate the feasibility of delineation and quantification of the human visual system using high-resolution diffusion tensor tractography at higher magnetic field strength and the ability to distinguish the visual tracts from major neighboring fiber tracts [48].

2. Subjects and methods

2.1. Participant demographics

This work was institutional review board (IRB) approved and complied with the Healthy Insurance Portability and Accountability

Act (HIPAA). Five right-handed healthy males (age range of 24–37 years) were included in this study and written informed consent was obtained from all the subjects.

2.2. Conventional MRI data acquisition

All MRI studies were performed on a 3-Tesla Philips Intera clinical MRI scanner with a dual-quasar gradient system with maximum gradient amplitude 80 mT/m, maximum slew rate 200 mT/m/ms and an eight channel SENSE-compatible head coil (Philips Medical Systems, Best, the Netherlands).

The conventional MRI (cMRI) protocol included axially prescribed 3D spoiled gradient echo imaging (repetition time (TR) = 8 ms; echo time (TE) = 4 ms) with a square field-of-view (FOV) = 256 × 256 mm and a matrix of 256 × 256 pixels. The slice thickness for the MRI sequences was 1.0 mm with 120 contiguous axial slices covering the entire brain from foramen magnum to vertex [51].

2.3. Diffusion-MRI data acquisition

Diffusion-weighted imaging (DWI) data were acquired axially from the same graphically prescribed cMRI volumes using a single-shot multi-slice 2D spin-echo diffusion-sensitized and fat-suppressed echo-planar imaging (EPI) sequence, with balanced Icosa21 tensor encoding scheme [51]. The *b*-factor was 500 s/mm² and TR/TE = 14,460/60 ms. The spatial coverage for DTI data matched the 3D cMRI spatial coverage (field-of-view = 256 mm × 256 mm and slice thickness/gap/no. of slices = 1 mm/0 mm/120). The EPI phase encoding used a SENSE k-space undersampling factor of two, with an effective k-space matrix of 112 × 112 and an image matrix after zero-filling of 256 × 256. The acquisition spatial resolution for DTI data was ~2.29 × 2.29 × 1 mm and the digitally interpolated spatial resolution after k-space image construction was 1 mm × 1 mm × 1 mm. The number of *b*-factor ~0 (b_0) magnitude image averages was 4. The DTI acquisition was ~7 min and was repeated three times to enhance SNR for a total of 21 min. The selection of the *b*-factor, parallel imaging, TR and TE enabled entire brain coverage using single-shot and interleaved EPI. The thin slice acquisition in space and replication of data in time combined with the DTI encoding provided several quality control options to study SNR and partial volume effects [48,49] on DTI tracking results [52]. The SNR in the non-diffusion-weighted data was ~26–31.

2.4. White matter fiber tracking

The imaging data in this study were acquired to cover the entire human brain. As the acquisition data were not optimized specifically toward the study of the extracranial portion of the optic nerves, the frontal aspect of the calvarium including the intraorbital portions of the skull was masked during post-processing. This prospectively prevented us from performing tractography of the intraorbital portion of the optic nerves. Fiber tracking was performed using DTI Studio software and based on the FACT algorithm with a fractional anisotropy (FA) threshold of 0.22 and angle threshold of 60°. Two regions of interest (ROIs) were applied to obtain each fiber tract and an “AND” operation was performed to include the fibers passing through both of the ROIs [52,53]. The T1-weighted volumes were co-registered with the DTI-derived maps on all five subjects allowing better characterization of the anatomic landmarks for placement of the ROIs using FA-modulated or color-coded principal eigenvector maps [54,55].

2.4.1. Fiber tracking regions of interest

The locations of the ROIs selected for tracing the optic tract (OT) and optic radiation (OR) are demonstrated in Fig. 1. To trace the OT, the first ROI was placed over the optic chiasm in coronal plane. The

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