

Quantitative volumetric analysis of the optic radiation in the normal human brain using diffusion tensor magnetic resonance imaging-based tractography

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Abstract

To attain the volumetric information of the optic radiation in normal human brains, we performed diffusion tensor imaging examination in 13 healthy volunteers. Simultaneously, we used a brain normalization method to reduce individual brain variation and increase the accuracy of volumetric information analysis. In addition, tractography-based group mapping method was also used to investigate the probability and distribution of the optic radiation pathways. Our results showed that the measured optic radiation fiber tract volume was a range of about 0.16% and that the fractional anisotropy value was about 0.53. Moreover, the optic radiation probability fiber pathway that was determined with diffusion tensor tractography-based group mapping was able to detect the location relatively accurately. We believe that our methods and results are helpful in the study of optic radiation fiber tract information.

Key Words: nerve regeneration; optic radiation; diffusion tensor imaging; diffusion tensor tractography; magnetic resonance imaging; volumetric analysis; probability map; group mapping; visualization; individual variation; neural regeneration

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Introduction

The human visual system consists of two major components, sensory input organs, such as the retina in the eyes, and the visual pathway^[1]. The object information that is captured through the eyes is transmitted by the retina and their axons, which are comprised of nerve fibers, to the optic chiasm^[1-2]. The visual pathway continues to the lateral geniculate nucleus^[1-4]. The optic radiation is a dense fiber tract that emerges from the lateral geniculate nucleus and continues to the occipital visual cortex^[1-4]. Especially, the optic radiation is an important fiber structure that conveys visual information from the lateral geniculate nucleus to the primary visual cortex in the occipital lobe. In recent years, many studies have introduced the anatomical location and features of the optic radiation^[1-10]. Knowing such above-mentioned characteristic information of the optic radiation before operation is important for surgery of the temporal lobe, longitudinal study of patients with optic neuritis, and evaluation of visual function in preterm infants^[5, 7-8, 10-12]. Most of these studies have used diffusion tensor imaging, which is a magnetic resonance imaging technique that is used to examine the directional properties of the diffusion of water molecules^[13-20]. In particular, several studies have been published on these topics related to the optic radiation, and these have described the characteristic information obtained from

diffusion tensor tractography, which is derived from diffusion tensor imaging and is a robust technique that is used for visualizing and evaluating white matter fiber direction in the human brain^[1-2, 7-12, 21]. However, these studies have focused on the anatomical characteristics of optic radiation fiber tracts in individual brains and on comparisons of the anatomical characteristics of the optic radiation fiber tracts between patient and control groups. Therefore, to the best of our knowledge, no diffusion tensor tractography studies of the volumetric information of optic radiation have been conducted without individual brain structure variation.

In the current study, we attempted to analyze the volumetric information of the optic radiation and to investigate the characteristics of the optic radiation in normal human brain with diffusion tensor tractography.

Results

Quantitative data

The values of the counted voxel numbers for the normalized optic radiation fiber tracts, and the percentage of the counted voxel numbers that were divided by whole voxel numbers in the Montreal Neurologic Institute (MNI) echo-planar imaging (EPI) template are shown in Table 1. These values represent the ratio of the optic radiation fiber tract volumetric

Table 1 The counted voxel numbers that were part of the extracted optic radiation fiber tracts, the calculated percentage, and the fractional anisotropy (FA) value for each subject

	Counted voxel	Percentage (%)	FA value
Range (minimum–maximum)	345–419	0.14–0.18	
Mean \pm SD	376.23 \pm 25.12	0.16 \pm 0.01	0.53 \pm 0.02

The counted voxel numbers in the optic radiation fiber tracts of each subject were converted to a percentage of the total voxel numbers in the whole brain of the Montreal Neurologic Institute (MNI) echo-planar imaging (EPI) template. $n = 8$.

information in both hemispheres of normal human brain.

Probability map

The optic radiation probability pathway map, which represents the degree of overlapping optic radiation fiber tracts of all subjects, was overlaid onto a standard MNI EPI template (Figure 1).

Discussion

In the current study, we analyzed the volumetric information of optic radiation fiber tracts in the human brain with brain normalization methods with a standard brain template image. In addition, we visualized a probability fiber pathway map in order to investigate the probability and distribution of the optic radiation pathway. Since the introduction of diffusion tensor imaging and fiber tracking methods, these techniques have been widely used to elucidate the anatomical structure and to perform quantitative analyses of neural fiber tracts at the subcortical level^[16-17, 19, 22-38]. Many studies have been conducted on the optic radiation, although the majority of these studies have focused on examining the anatomical structures or landmarks of surgical planning in patients^[3, 4, 9, 11-12, 21, 25]. Scoth et al.^[21] have reported anisotropy changes in blind humans compared to healthy control subjects with diffusion tensor tractography. Winston et al.^[4] have described the use of optic radiation fiber tractography in epilepsy surgical planning and anterior temporal lobe resections. Ciccarelli et al.^[7] have indicated anatomical changes after optic neuritis, and they showed that optic radiation fiber tract location was different between patient and normal control groups. Moreover, some quantitative fiber tracking analyses and approaches have been used in patients with arteriovenous malformations and premature newborns in order to evaluate the optic radiation fiber tracts^[5-6, 26]. In the quantitative analyses, FA values, diffusivity indices, and left-to-right asymmetry indices were measured in these patients.

In this study, we measured the volumetric information of the optic radiation fiber tracts in order to determine the proportion of optic radiation fiber tracts in the whole brain of the normal human brain. The extracted optic radiation fiber tracts were normalized to a standard brain template, the MNI EPI template, in order to remove the individual differences of all of the subjects and to allow for a direct comparison of our volumetric analysis results under the same conditions. The results of this study demonstrated that the

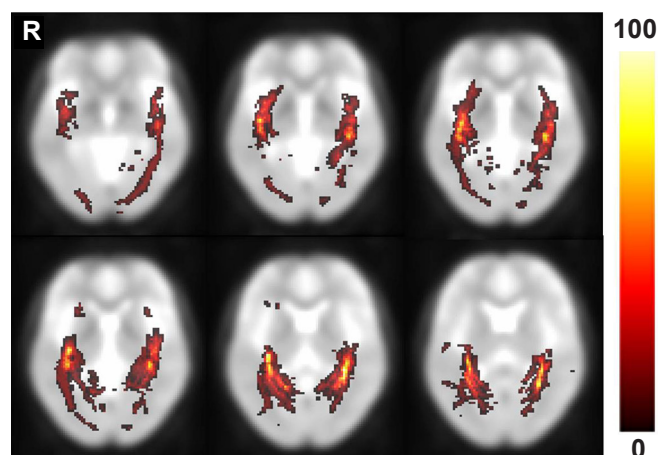


Figure 1 The results of the optic radiation probability pathway map in healthy subjects.

The results were overlaid and shown on the transverse plane of the Montreal Neurologic Institute (MNI) echo-planar imaging (EPI) template. The hot color scale indicates the proportional degree of overlap for all subjects and the probability of a voxel being part of the optic radiation fiber tract pathway. R: Right.

optic radiation fiber tract had a tiny volume of information that was less than 1% of visual performance compared to the volume information of the whole brain. Moreover, the optic radiation probability fiber pathway that was determined with diffusion tensor tractography-based group mapping was able to detect location with relative accuracy.

This study had some limitations. First, a limited number of subjects were enrolled in this study. Based on our results, the 13 healthy subjects exhibited a similar tendency for the percentage of counted voxel numbers. However, these findings are difficult to generalize to our results. In a future study, we plan to study a larger number of subjects. Second, the setting of the region of interest is a user-dependent process. This problem can be solved through fiber tracking that is combined with functional magnetic resonance imaging examinations of visual stimulation in a future study. Third, we evaluated only the optic radiation fiber tract of all of the optic fibers in the human brain. Moreover, the Fuzzy art with Add Clustering Technique (FACT) algorithm, which was used in this study, is used for limited fiber tracking and reconstruction. The FACT algorithm was considered for determining the dominant fiber direction, and the largest eigenvalue components in each voxel were used as an indicator of fiber orientation. Therefore, a fiber-crossing region or a voxel that was eligible for various fiber directions might have resulted in some erroneous points in the FACT algorithm-based fiber tracking. Further study is needed with other fiber tracking and reconstruction algorithms, such as probabilistic approaches or with an advanced fast marching algorithm. The probabilistic fiber tracking algorithm allows for the direction of the tensor in the voxel to be multidirectional, but it is not limited to a dominant direction, as is the FACT algorithm. The advanced fast marching takes into account all of the information that is contained in the diffusion tensor^[2]. Thereby, every tensor is classified as linear, planar, or spherical ellipsoid^[2, 27]. In other words, the method that was described above is able to evaluate brain areas that

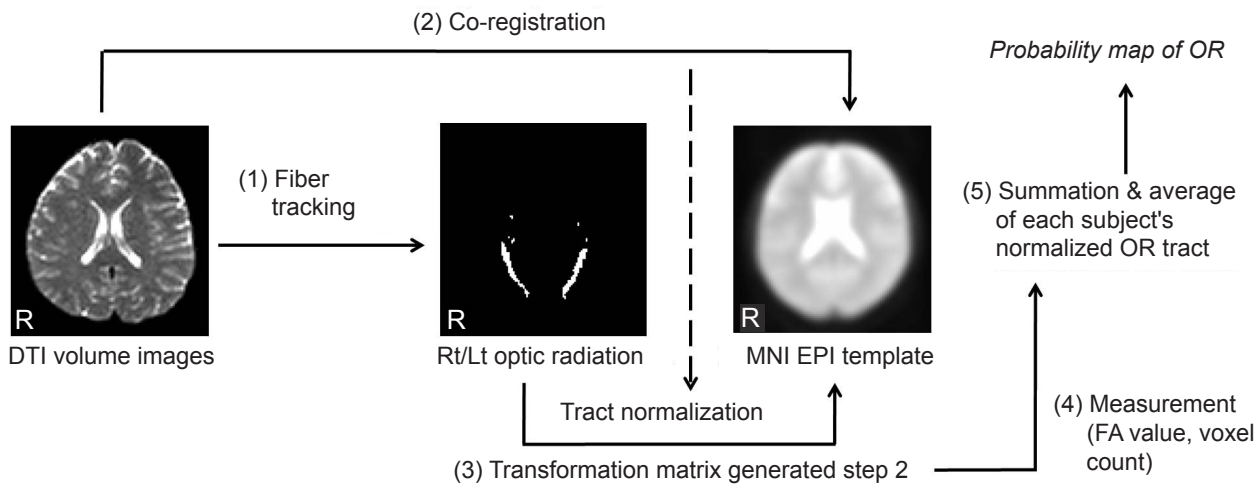


Figure 2 The procedure for the quantitative measurement and probability pathway map reconstruction of the optic radiation (OR) fiber tract. The OR fiber tracts from all subjects were extracted with diffusion tensor imaging (DTI) datasets, and brain normalization processes were performed in order to reduce individual variation and to allow for a comparison of the results under the same conditions without individual variation and to increase accuracy. The Montreal Neurologic Institute (MNI) echo-planar imaging (EPI) template was used to normalize the individual brains and extracted optic radiation fiber tracts. The volumetric analysis was performed with a voxel-count technique. The voxels through which the optic radiation fiber tract passed were counted and a percentage of their counted numbers according to whole-brain voxel numbers in the MNI EPI template was calculated. With the extracted optic radiation fiber tracts, the fractional anisotropy (FA) values were calculated, and a probability pathway map was acquired by averaging the normalized data for each subject for the OR fiber tract. Rt/Lt: Right/left; R: right.

contain fiber-crossing regions, such as the optic chiasm. They have important implications for more accurate fiber tracking for all of the optic nerve that is not limited to the optic radiation, which is a topic for future research.

In conclusion, we analyzed and measured the volume information of the optic radiation fiber tract in the normal human brain and found that the optic radiation fiber tract had a relatively small range of volume information compared to that of the whole brain. To the best of our knowledge, this is the first volumetric analysis study of the optic radiation fiber tract with diffusion tensor tractography and of whole-brain volume information. We believe that our approaches provide preliminary data for researchers who are studying treatments for patients with diseases that are related to the visual pathway in the brain.

Subjects and Methods

Design

An observational neuroimaging study.

Time and setting

This experiment was performed at the Department of Physical Medicine and Rehabilitation, Yeungnam University Hospital, Republic of Korea in June 2009.

Subjects

Thirteen healthy subjects (men, 6; age, 35 ± 2.16 years) were recruited into this study through advertisements. They had no previous history of neurological disease, optic nerve pathology, head injury, or physical disease. All subjects understood the purpose of the study and provided written informed consents prior to their participation. This study was approved by the Institutional Review Board of Yeungnam

University Hospital in Republic of Korea.

Methods

Diffusion tensor imaging acquisition

All diffusion tensor imaging datasets were acquired with a 1.5-T magnetic resonance imaging system (Gyrosan Intera, Philips Healthcare, Best, the Netherlands) with a six-channel phased-array sensitivity-encoding (SENSE) head coil by using single-shot echo-planar imaging (EPI) with parallel acquisition in the transverse plane. The imaging parameters were as follows: repetition time/echo time, 10,726/76 ms; matrix, 128×128 ; field of view, 221 mm; slice thickness, 2.3 mm; and reduction factor for SENSE, 2. Diffusion weighting was applied along 32 non-collinear diffusion-sensitizing gradients with a b -value of $1,000 \text{ s/mm}^2$. We obtained 63–67 contiguous transverse slices that covered the entire brain with no slice gaps. During the acquisition, radiologists routinely checked for gross head movement or other motion in real time^[25].

Diffusion tensor imaging analysis

Eddy current corrections of the diffusion tensor imaging data were performed with the tool in FSL 4.0.1 (Analysis Group, FMRIB, Oxford, UK) with a 12-parameter affine registration^[4-5, 12, 25, 39]. Each diffusion-weighted image was registered to non-diffusion weighted images ($b = 0$). The diffusion tensor imaging datasets were analyzed with DtiStudio 3.0.3 (Department of Radiology, Johns Hopkins University, Baltimore, MD, USA), which was based on the fiber assignment by the continuous tracking (FACT) algorithm^[22, 40-43]. Propagation in each fiber tract was terminated if a voxel with a fractional anisotropy (FA) value less than 0.25 was reached or if the turning angles of 2 consecutive vectors were over

70° during tracking^[10]. An FA threshold of 0.25–0.35 for fiber tract reconstruction has been recommended by Mori et al. and Stieltjes et al.^[10,23,44]. A relatively large angle threshold was used so that the optic radiation course in acute angles could be examined^[10,26]. The region of interest was manually drawn in both lateral geniculate nucleus on the transverse plane at the level of the transition from the posterior limb of the internal capsule to the cerebral peduncle on a color-coded FA map, and the volume of the region of interest was standardized for all subjects (9 voxels)^[3,7]. The color-coded FA map showed the fiber pathway directions with 3 colors as follows: red (left-right direction), green (anterior-posterior), and blue (superior-inferior)^[45-46].

Quantitative measurements and probability map of the optic radiation

After both optic radiation fiber tracts were extracted with the region of interest described above, we performed quantitative measurements and created a probability pathway map of the optic radiation. These methods were conducted based on the brain normalization method in order to avoid individual brain variation. The procedure is shown in Figure 2 and is described as follows. (1) Each subject's non-diffusion image ($b = 0$ image) was co-registered to the standard Montreal Neurologic Institute (MNI) space with an EPI template with SPM2 (Wellcome Department of Cognitive Neurology, London, UK). (2) The transformation matrices for each subject that were created with the coregistration process in (1) were then applied to the extracted optic radiation fiber tracts of each subject for normalization to the MNI space. (3) For the quantitative measurements, the voxels that the optic radiation fiber tract passed through in the normalized brain of each subject were counted with ImageJ (US National Institutes of Health, Bethesda, MD, USA) software. We calculated the percentage of the optic radiation fiber tracts with the counted voxel numbers divided by the whole-brain voxel numbers in the MNI EPI template. (4) In order to assess optic radiation fiber tracts quantitatively, the FA values in the extracted optic radiation fiber tracts for each subject were measured. (5) Finally, each individual normalized optic radiation was averaged pixel-by-pixel and overlaid on the MNI EPI template in order to obtain and investigate the optic radiation probability pathway map with MRicro (Chris Rorden, USA, <http://www.mricro.com>) software.

Author contributions: Lee DH participated in study conception, design and analysis and manuscript development. Park JW contributed to data acquisition and analysis. Hong CP contributed to study design, manuscript development, oversight and research supervision. All authors approved the final version of this paper.

Conflicts of interest: None declared.

Peer review: This study was designed to provide information about the average size and degree of diffusion anisotropy of the optic radiation in addition to a probability map describing the likelihood of optic radiation pathway. The proposed analysis was applied to 13 healthy subjects with a mean age of 35 years and the results were demonstrated according to the analysis. This type of analysis and results are considered to be an addition to the field of diffusion tensor imaging because of inaccurate diffusion tensor im-

aging measurement, approximate tensor model and relatively low resolution diffusion tensor imaging. The difficulties are to verify the segmented optic radiation using various tractography segmentation algorithms. Quantitative measurements of optic radiation probability map and the estimated optic radiation size and anisotropy can help identify healthy subjects and be used as a reference for comparing healthy to pathological subjects.

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