Evaluation of Traumatic Optic Neuropathy in Patients with Optic Canal Fracture Using Diffusion Tensor Magnetic Resonance Imaging: A Preliminary Report

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Key Words
Traumatic optic neuropathy · Diffusion tensor magnetic resonance imaging · Diffusion tensor fiber bundle imaging · Fractional anisotropy · Mean apparent diffusion coefficient

Abstract
Objective: To investigate the role of diffusion tensor magnetic resonance imaging (DT-MRI) in the evaluation of traumatic optic neuropathy (TON). Methods: Six patients with TON underwent DT-MRI prior to decompression surgery. DTV 2 and Volume One 1.44 software were used to measure the fractional anisotropy (FA) and the mean apparent diffusion coefficient (ADC) of the optic nerves. White matter fiber bundle tracking was used to display optic nerves. Results: Visual acuity was improved in 1 of the 6 patients after surgery. The mean FA of the injured eye declined significantly with regard to that of the normal eye (0.2438 ± 0.0670 vs. 0.4524 ± 0.0531; t = 8.711; p = 0.000). The mean ADC on the injured side increased significantly compared with that on the normal side [(1.4172 ± 0.1208) × 10^{-3} mm²/s vs. (1.0866 ± 0.1179) × 10^{-3} mm²/s; t = -5.316; p = 0.003]. The continuity of the intracanalicular segment of the optic nerve was interrupted in 3 patients without improved postoperative visual acuity. In 1 patient with improved postoperative visual acuity, the fiber bundle of the optic nerve was somewhat less dense in the injured eye than in the normal eye. Conclusions: DT-MRI provides valuable information for evaluating the fibers of optic nerves in TON.

Introduction

Traumatic optic neuropathy (TON) is primary fracture or secondary neuron apoptosis and necrosis of the optic nerve due to trauma, which might subsequently cause partial or total vision loss. Studies have shown that accurate pathological classification, early detection of the reversibly injured optic nerve with recovery potential, and timely administration of medicine and surgical therapy might fully, or at least partly, salvage the visual acuity of the eye with TON [1, 2]. With no reliable in vivo ex-
amination method, though, little progress has been made in the diagnosis and treatment of TON. Diffusion tensor magnetic resonance imaging (DT-MRI) is currently the only noninvasive method that can show the microstructure and pathological state of the white matter fiber bundle in vivo [3, 4].

We want to address the role of DT-MRI in vivo in detecting histopathological changes in TON immediately after trauma by relevant clinical radiological observation. Some clinical studies had reported the application of DT-MRI to image the optic nerve in healthy volunteers and patients with optic neuritis [5, 6]; to our knowledge, a report on the in vivo evaluation of the injured human optic nerve by DT-MRI has not yet been published.

Materials and Methods

Clinical Data

Six patients with unilateral TON who were treated at the Department of Otorhinolaryngology of the Third Hospital of Sun Yat-sen University from June 2007 to October 2008 were selected. Diagnosis of unilateral TON was confirmed by clinical manifestations and imaging examination results in each of these patients, and all of them underwent optic nerve decompression under nasal endoscopy. All of the patients were male. There were 5 cases of injury to the right eye and 1 case of injury to the left eye. Visual acuity was lost entirely after injury (no light perception). The time from injury to examination ranged from 1 day to 13 days, and the average duration was 5.2 days. The visual acuity of the contralateral eye was normal in all of the patients (table 1). All of the patients underwent preoperative spiral CT, MRI and DT imaging examination. All received steroid pulse therapy for 3 days before surgery (dexamethasone 30 mg/day) and showed no improvement before receiving optic nerve decompression under nasal endoscopy. Each of the patients was informed of the purpose of the study and signed the informed consent form. This study was approved by the ethics review board of the Third Hospital of Sun Yat-sen University.

Methods of MRI Examination

Instrument. A GE Sigma Twin 1.5T superconducting magnetic resonance scanner was used. The 8-channel neurovascular head and neck phased array coil was adopted, the gradient field strength was 40 mT/m, and the gradient switching rate was 120 mT/m/s.

MRI Examination. Patients were instructed to close their eyes and avoid intentional eye movement during the examination. The scanning plane was parallel to the optic nerve. A routine MRI scan was performed first. After the 3 planes were positioned, the array spatial sensitivity encoding technique was used for calibration. The axial view was: fast spin echo T1-weighted imaging, T2-weighted imaging, diffusion-weighted imaging (b = 1,000 s/mm²); DT-MRI axial scans used a single-shot spin-echo echo-planar imaging sequence. Further parameters were: repetition time = 6,000 ms; echo time = 60.1 ms; field of view 240 × 240 mm; b = 1,000 s/mm²; number of excitations = 2; 13 nonlinear diffusion directions; matrix 128 × 128; slice thickness = 2 mm, and pitch = 0; scan time was about 17 min.

Data and Postprocessing of Images

The raw data from the DT-MRI scanning, in the DICOM (digital imaging and communications in medicine) format, were input into the computer and processed using the DTV 2 and Volume One 1.72 fiber bundle tracking imaging software developed by Masutani (Tokyo University, Japan). The target regions were selected from the same region of the intraorbital segment of the optic nerve in both the horizontal and coronal planes, and the fraction anisotropy (FA) and apparent diffusion coefficient (ADC) of bilateral optic nerves were measured. The measurement was repeated three times at each position, and the mean calculated. Then, the mean values in the horizontal and coronal planes were calculated. Finally, an intraindividual comparison between the left and the right eye (the normal eye and the injured eye) was performed. Diffusion tensor tractography was used to set up a series of ‘seeds’ to track nerve fiber bundles at different levels of the horizontal or coronal planes of the optic chiasm and bilateral optic nerves. The optic nerve, optic chiasm and some of the fibers of the optic radiation were tracked and observed.

Optic Nerve Decompression under Nasal Endoscopy

Under general anesthesia, all of the patients underwent routine optic nerve decompression under nasal endoscopy. The detailed procedures were performed as follows:

1. After a sphenoethmoidectomy with preservation of the nasal turbinates, the course of the optic nerve and prominence of the internal carotid artery are identified in the sphenoidal sinus.

2. Then the optic tubercle is visualized; approximately 1 cm before this (i.e. anterior), the lamina papyracea is carefully lifted off from front to back and dissected between this and the peri-orbita up to the optic tubercle.

3. Usually one already sees the circularly running fibers of Zinn’s corona here; with a special diamond grinder, the bone above the optic tubercle and further along the optic canal is now carefully thinned out from the middle to the point that it can be removed completely with suitable instruments; the optic nerve and its sheath should be exposed medially almost to 180°.

4. A fine sickle knife pierces into the upper aspect of the exposed nerve sheath, opening this from back to front until just past the fibers of Zinn’s corona.

Statistical Analysis

All statistical analyses were performed using SPSS software version 13.0. The paired t test was used to compare ADC and FA between injured eyes and normal eyes. p < 0.05 indicated a statistically significant difference. A tendency chart was also plotted.

Results

Relationship between Surgical Effects and DT-MRI

All 6 patients underwent optic nerve decompression under nasal endoscopy. The average postoperative fol-
low-up period was 19 months, and visual acuity was improved in only 1 case (16.7%; the final visual acuity was 0.02). This patient was case No. 1. There were no improvements in visual acuity in the other cases. The results showed that surgical effects were related to the continuity of the optic nerve fibers, and that DT-MRI can provide relevant information.

**Diffusion Tensor MRI**

A total of 8 DT-MRI examinations were performed on the 6 patients. Two of the examinations failed; 6 of them yielded effective data, from both normal and injured eyes. In 2 patients, the images of the intracanicular segment of the optic nerve were of poor quality because of interference by sinus air and surrounding fat, which hindered measurement of ADC and FA using the intracanicular segment of the optic nerve as a marker. However, the intraorbital segment of the optic nerve, the optic chiasm, and the optic radiation showed up very well in all of the patients. Therefore, in order to avoid interference by the aforementioned factors, the plane for ADC and FA data collection was positioned at the intraorbital segment of the optic nerve close to the orbital opening of the optic canal (with good DT-MR images). The entire optic nerve fiber bundle was tracked and successfully imaged. The results indicated that the data obtained from there were significantly different than those collected on the uninjured side (p values are listed in Table 2).

It is noteworthy that the DT-MRI fiber tracking map showed continuous nerve fibers on the injured side in case No. 1 only. In the remaining 5 cases, discontinued nerve fiber signals on the injured side were revealed by the nerve tracking.

**Measurement of Optic Nerve Data**

The average FA values for the intraorbital segment of the optic nerve were 0.2438 ± 0.0670 and 0.4524 ± 0.0531 on the injured side and the normal side, respectively. The ADC values were 1.4172 ± 0.1208 × 10^-3 mm²/s and 1.0866 ± 0.1179 × 10^-3 mm²/s. The two groups were compared using the paired t test, and all of the p values were lower than 0.05, indicating that the two groups were significantly different with respect to those values (Table 2). The tendency chart shows that the FA values of the injured eyes decreased significantly in relation to those of the normal eyes, and that the ADC values of the injured eyes increased significantly in relation to those of the normal eyes (Fig. 1, 2).

**Optic Nerve Fiber Bundle Tracking and Display**

Whole-course tracing and display of the bilateral optic nerve fiber bundle was achieved in 4 of the 6 patients.
The spatial integrity and continuity of the optic nerve in vivo were shown directly and three-dimensionally. The traveling of the normal eyes’ optic nerve fiber bundles (including the intracanalicular segments) was continuous in 4 patients, and the fiber bundles were plump. In the injured eyes, though, the continuity of the optic nerves was interrupted in 3 patients (fig. 3). In 1 patient (case No. 1), though the optic nerve fiber bundles on the injured side were continuous, they were sparse, and there were significantly fewer nerve fibers than on the normal side. In some patients, the nerve fibers of the optic chiasm and optic radiation could also be tracked (fig. 4).

**Discussion**

The primary purpose of using routine imaging examinations (CT and MRI) in cases of TON is to determine the 'macro'-morphological changes in the optic nerve. The examinations are not sensitive to the 'micro' changes in density and signal in the optic nerve. In our experience, conventional MRI is of limited utility in the diagnosis of TON. It can only detect whether the optic nerve is swelling. Conventional CT can reveal only whether there is an optic canal fracture. Routine imaging examinations cannot provide detailed information about injury; in particular, they do not offer direct and valuable
quantitative analyses of the severity of the histopathological damage to the optic nerve. DT-MRI is a quantitative functional MRI technique that operates at the molecular level. It utilizes the anisotropy of water molecule diffusion in tissue to quantitatively analyze changes in the microstructure of nerve tissue and to indirectly delineate the fiber bundles. This could help to elucidate the pathophysiological mechanism of the disease and reveal the spatial direction of traveling and the continuity of the white matter fiber bundles. To date, DT-MRI is the only noninvasive approach that can show the traveling, direction, alignment, tightness and myelination of white matter fiber bundles in live neural tissue. In measuring the ADC and FA values of the nerves, it offers objective, dynamic and quantitative information about the subtle pathological changes in white matter nerve bundles. At the same time, nerve fiber bundle tracking in vivo can show the spatial integrity and continuity of nerves directly and three-dimensionally [3]. Currently, the technique is mainly used in studies of the brain and spinal cord white matter fiber bundles [7]. Due to technical limitations, it is used only infrequently in studies of the optic nerve, and no studies have been reported in which it was applied to TON. Recently, Wheeler-Kingshott et al. [5], Hickman et al. [8], Miller [9] and Sun et al. [10] have conducted exploratory research with DT-MRI on the normal optic nerve, optic neuritis and optic atrophy, and reported some progress. In this study, we preliminarily found that the technique offers significant potential in studies of TON.

TON can lead to severe damage to the visual function in patients. Optic nerve decompression is a classic surgical approach to the treatment of TON, but its success rate varies greatly in the literature. Evidence-based medicine has not yet determined whether surgery is effective in treating TON [11]. The timing of surgery, surgical techniques, surgical indications and surgical effects are still very controversial, and as a result, surgery has a certain blindness [2, 12]. Based on our cumulative experience during long-term clinical practice, the aforementioned problems are primarily due to the lack of a reliable method for the pathological diagnosis of optic nerve injury. Doctors rely on the pathological classification of optic nerve injury when determining the appropriate timing of surgery and surgical indications. It is possible that even successful decompression surgery cannot salvage vision after primary laceration and mutilation of the optic nerve. However, timely and appropriate decompression surgery can be therapeutically effective in treating swelling, compression and ischemia of the nerves caused by

Fig. 3. Optic nerve fiber bundle tracking showing discontinued optic nerve fibers in the injured eye (right, R) and a continuous and plump optic nerve in the normal eye (left).

Fig. 4. Whole-course visual pathway fiber bundle tracking showing that the optic nerve fiber bundles were significantly less dense in the injured eye (right, R) than in the normal eye (left).
secondary injury. While there is currently no non-invasive, objective and accurate examination method by which to determine the pathology of living optic nerves, the emergence of DT-MRI offers some hope of resolving the aforementioned problems. The optic nerve is composed of myelinated nerve fibers and, similar to the white matter fibers in the brain and spinal cord, it is a tract of the central nervous system. Theoretically, changes in ADC and FA values measured by DT-MRI can reflect, quantitatively and sensitively, subtle pathological changes to the white matter fiber bundles, and can indirectly reveal the spatial integrity and continuity of the living nerves. Hickman et al. [8] have recently shown that DT-MRI can be used to detect the severity of optic nerve axon injury in patients with optic neuritis. Chabert et al. [13] used non-CPMG (Carr-Purcell-Meiboom-Gill) fast spin echo to study DT-MRI and found the technique to be of great value for pathological diagnosis of optic neuropathy or nerve compression. In conclusion, DT-MRI can provide sensitive and valuable pathological information regarding the injury to, and the repair process in, optic nerve fiber bundles.

This study selected well-displayed intraorbital segments of the optic nerve in the plane close to the orbital apex for the measurement of FA and ADC values while whole-course fiber bundle tracking and display of the optic nerve were performed. The results from 6 patients showed that, in normal eyes, the mean ADC value of the intraorbital segment was \( (1.0866 \pm 0.1179) \times 10^{-3} \) mm\(^2\)/s, while the mean FA value was 0.4524 \( \pm 0.0531 \). These results are consistent with those of Wheeler-Kingshott et al. [5] and Chabert et al. [13], and they furthermore showed good repeatability. In addition, in the injured eyes, the mean ADC value was 1.4172 \( \pm 0.1208 \times 10^{-3} \) mm\(^2\)/s, and the mean FA value was 0.2438 \( \pm 0.0670 \). These results were significantly different from those in the normal eyes (p < 0.05). Also, in relation to the normal eyes, the ADC values of the injured eyes tended to increase, whereas the FA values tended to decrease. We hypothesized that the increase in ADC and decrease in FA in the injured eyes reflected changes in the quality and volume of the white matter nerve fibers after optic nerve injury due to rupture, ischemia, necrosis or demyelination, which led to changes in the direction and the scope of the local water molecule movement at the site of injury, and ultimately to changes in ADC and FA values. The relationship between these changes and the degree of injury requires further study, however. In addition, although this study measured the adjacent intraorbital segment of the optic nerve rather than the intracanalicular segment, the results for the injured eyes still differed significantly from those for the normal eyes. We speculate that this is related to blood supply disorders after optic nerve injury. Van Overbeke and Sekhar [14] found that the superior hypophyseal artery is the main blood supply to the intracranial and intracanalicular segments of the optic nerve. The ophthalmic artery provides very little blood supply there. The ophthalmic artery passes through the intracanalicular segment and delivers blood mainly to the intraorbital segment of the optic nerve and the eyeball. We believe that the pressure in the optic canal might increase in patients with TON due to bone mass compression or tissue edema, and that this pressure increase can result in either decreased blood supply from the vascular network of the superior hypophyseal artery or discontinued blood supply, affecting the supply to the intracanalicular segment of the optic nerve. Secondly, the blood flow in the ophthalmic artery passing through the intracanalicular segment of the optic nerve drops precipitously or stops altogether, causing either poor blood supply to the entire optic nerve or optic nerve infarction. For this reason, we believe that when the pressure in the optic canal increases, ischemic demyelination or necrosis of nerve fiber bundles may appear, in addition to the primary injury to nerve fibers, due to obstructed blood supply to the entire optic nerve. Such changes might be reflected, within a short period of time, in the increase in ADC and decrease in FA. Decompression of the optic canal might therefore help to restore the blood supply to the intracanalicular segment (the superior hypophyseal arterial network) and the intraorbital segment (the ophthalmic artery) of the optic nerve. The results of this study suggest that optic nerve decompression surgery might be of great importance to the relief of blood circulation disorder of the optic nerve and retrieval of nerve fibers with recovery potential. Here, while 6 patients underwent optic nerve decompression under nasal endoscopy, visual acuity was improved in only 1 patient after surgery. DT-MRI images from that patient suggested that the fiber bundles of the optic nerve were sparse on the injured side but not discontinued, indicating that the optic nerve of the injured eye was not completely mutilated and that some reversible nerve fibers still remained. There was a very good chance that timely surgery would improve visual acuity. The results of this study show that surgical effects are related to whether or not the optic nerve fiber bundle is discontinued, and furthermore that DT-MRI might provide important information and could serve as a basis for adopting surgical treatment for TON in clinical practice. The sample size was small, though, and we
did not compare patients with and without residual vision after surgery. Nor did we compare pre- and postsurgical data. Further work is needed, therefore, to confirm the meaning of the results.

Although reports in the literature and our preliminary results demonstrate that DT-MRI can provide a valuable reference for the early diagnosis of optic nerve injury, assessment of damage and clinical treatment, many technical issues remain to be resolved [15]. In terms of the scanning technique, the sensitivity of the echo-planar imaging sequence may be affected by the fat and cerebrospinal fluid around the optic nerve and the adjacent gas-rich nasal cavity and paranasal sinuses with few water molecules. In addition, this study used 13-direction data collection, and the scanning time was long, which might have increased the probability of involuntary eye movement causing artifacts. Therefore, the intracanalicular segment only yielded good images in 66.7% of patients (4/6), which is not satisfactory. In future studies, we need to further explore methods by which to limit the eye movement, to improve the hardware and to achieve more rapid velocity, better precision and greater processing power, so that all of the intracanalicular segment can be imaged and measured with greater precision. Currently, there is no gold standard for evaluating the outcome of fiber tracking imaging in vivo, and many factors can affect the results of fiber tracking imaging.

In conclusion, this was a preliminary study. Although the method has many deficiencies at the present time, we believe those may be gradually addressed with improvements in the MRI equipment, hardware and software as well as with optimization of the scan parameters.

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Disclosure Statement

All authors declare that there was no conflict of interest, and no financial support or incentive by commercial associations was provided for the manuscript.

References

1 Bloching M: Indications and surgical technique of the endonasal decompression of the optic nerve from an HNO medical viewpoint (in German). Klin Monbl Augenheilkd 2004; 221:927–932.