



Retinal nerve fiber layer thickness profiles associated with ocular laterality and dominance



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HIGHLIGHTS

- Different relationships between the inferior and superior RNFLs were observed according to ocular dominance and laterality.
- The right eyes had a thicker RNFL, except in the superior quadrant, than the left eyes.
- Regardless of laterality, inferior RNFL was thicker than superior RNFL in the dominant eyes.
- This is the first reported study demonstrating the RNFL characteristics associated with ocular dominance.

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ABSTRACT

Although human anatomy is arranged symmetrically based on a central vertical axis, the majority of persons will use one side of their body more readily than the other. Interestingly, these lateral body dominances including ocular dominance are all rightward. The asymmetry in retinal nerve fiber layer (RNFL) thickness between the right and left eyes in healthy subjects has been reported in several studies, and the reason for this structural difference between right and left eyes is unclear. In the manuscript, we hypothesized that the characteristics of ocular dominance are reflected in the RNFL profile and may be related to inter-ocular structural differences between right and left eyes. In this study, ocular dominance occurred mostly in right eyes (right vs. left: 78.77% vs. 21.22%; $P < 0.001$). According to ocular dominance and laterality, different relationships between the inferior and superior RNFLs were observed. The right eyes had a thicker RNFL, except in the superior quadrant, than the left eyes. Regardless of laterality, inferior RNFL was thicker than superior RNFL in the dominant eyes. To our knowledge, this paper is the first report demonstrating the RNFL characteristics associated with ocular dominance.

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1. Introduction

Most people tend to use one side of their body more readily, and with greater frequency and facility, for skilled activities, although human anatomy is generally symmetrical, based on a central vertical axis [1,2]. Interestingly, these lateral body dominances are all rightward: handedness ~90%, footedness ~80%, and eyedness ~70% [3].

The significance of ocular dominance differs from hemispheric laterality. While lateral body dominance maybe related to dominance of one cerebral hemisphere, the human retina exhibits

semi-decussation; thus, right and left ocular signals are similarly represented in both hemispheres [2]. Also, the correlation between ocular dominance and handedness is weak [2,4]. Despite the anatomical distinctness of ocular dominance, ocular dominance has been reported to be accompanied by greater cerebral cortical activity in response to the dominant eye than to the non-dominant eye in studies using functional MRI and visual evoked potentials [5–8].

In terms of the structural aspects of the eye, the retinal nerve fiber layer (RNFL) profiles between each eye are not symmetrical, although there are strong correlations in RNFL thickness between the right and left eyes [9–12]. However, the reason for this structural difference between right and left eyes is unclear. It may be associated with lateral body dominance, particularly ocular dominance [11].

Neurotrophins, synaptic survival and growth factors, are expressed in a region-specific manner and modulated by neural activity in the region [13]. Due to inter-neuron communication and

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dependence, trans-neuronal degeneration can occur from the disruption of input from or output to other nearby neurons [14]. In the visual pathway, too, there is evidence of trans-neuronal degeneration. The pathology of glaucoma has been examined extensively at the level of the retina, optic nerve head (ONH), intracranial optic nerves, lateral geniculate body, primary visual cortex, and cerebral nervous system beyond the visual cortex [15,16]. In patients with cerebral infarction [17,18], Parkinson's disease [19], and Alzheimer's disease [20,21], thinning of the RNFL has been observed.

In this regard, we hypothesized that the characteristics of ocular dominance may be reflected in the RNFL profile and may be related to inter-ocular structural differences between right and left eyes. Thus, in the present study, we investigated the characteristics of RNFL profiles associated with ocular dominance, along with the inter-ocular comparison between right and left eyes.

2. Patients and methods

2.1. Study subjects

Medical records of all consecutive patients who underwent pre-operative examinations for refractive surgery between September 2012 and October 2012 at the Gangnam BS Eye Center (Seoul, Korea) were reviewed retrospectively.

This study was performed according to the tenets of the Declaration of Helsinki. The study protocol was approved by the institutional review/ethics boards of Catholic University, Seoul St. Mary's Hospital (Seoul, Korea). The institutional review board waived the need for written informed consent from the participants, because of the retrospective design.

All subjects underwent a full ophthalmic examination, including measurements of visual acuity (VA) and refraction, intraocular pressure (IOP) using Goldmann applanation tonometry, axial length (AL) using laser interference biometry (IOL Master; Carl Zeiss Meditec, Inc., Dublin, CA), dilated fundus examination, stereo disk photography, fundus photography using a digital retinal camera (CR-1 Mark II; Canon, Tokyo, Japan) after maximum pupil dilatation and standard perimetry (24-2 Swedish Interactive Threshold Algorithm SAP, Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc.), and optical coherence tomography (OCT; Cirrus HD-OCT; Carl Zeiss Meditec, Inc.).

The inclusion criteria were a healthy ONH without glaucomatous damage (i.e., no disk hemorrhage, thinning, or notching of the neural rim), no visible RNFL defects, and the absence of any glaucomatous visual field (VF) defects. A glaucomatous VF change was defined as the consistent presence of a cluster of three or more points on the pattern deviation plot with a probability of occurring in <5% of the normal population or as having one point with a probability of occurring in <1% of the normal population, and glaucoma hemifield test results outside the normal limits, or a pattern standard deviation of $P < 5\%$ [22].

The exclusion criteria were a best-corrected VA of <20/20, an IOP >21 mmHg in either eye, a history of severe ocular trauma, intraocular or refractive surgery, or any ocular or neurological disease that could have affected the ONH or RNFL, a media opacity or pathological retinal lesion, or a closed or occludable angle.

2.2. Determination of the dominant eye

To determine the dominant eye, we used the hole-in-a-card test [23]. In this test, the patient holds a card with a hole in the middle using both hands and is asked to view a 6-m target through the hole in the card. The observer then occludes each eye alternately to establish which eye is aligned with the hole and the distant

target. The selected eye is considered the dominant eye. The process is repeated; the second time, the subject moves the card slowly toward the face without losing the alignment with the fixation point until the hole is over an eye. This is considered to be the dominant eye.

2.3. RNFL measurement by OCT and adjustment for ocular magnification

A commercially available spectral domain-OCT system was used. Imaging was performed using an optic cube scan consisting of 200×200 axial scans (pixels) of the optic nerve region. Image quality was assessed by an experienced examiner blinded to patient identity and other test results. Only well-focused, well-centered images without eye movement and a signal strength of 7/10 or greater were used. Patients with less than satisfactory OCT image quality were excluded. The OCT parameters (average/quadrant and clock-hour based mean RNFL thickness) were used in the analysis. Additionally, the difference between the inferior and superior RNFL thicknesses in an individual was calculated and designated the I-S difference. Left eye data were converted into right eye format.

To correct AL-related ocular magnification, we used the Littmann formula ($t = p \times q \times s$) [24], as modified by Bennet [25]. In the formula, t is the actual fundus size, s is the size measured on fundus photography, p is a magnification factor related to the camera, and q is a magnification factor related to the eye. The correction factor q can be determined with the formula $q = 0.01306 (x - 1.82)$, where x is AL.

P is instrument-dependent and remains a constant in a telecentric imaging system. As shown in previous studies, both the RNFL peripapillary scan circle and optic disk area are related to camera magnification in the fundus imaging system (p) and the optical dimensions of the given eye (q). Thus, we used the known magnification factor of 3.382 for the analysis of Cirrus HD-OCT parameters (average/quadrant RNFL thickness), which is the same value as calculated with the Stratus OCT system (i.e., actual average RNFL thickness at a 1.73-mm radius circle = $3.382 \times 0.01306 \times [AL - 1.82] \times$ observed average RNFL thickness on the optic disk cube scan) [26].

2.4. Data analysis

Comparisons of parameters between the right and left eyes and dominant and non-dominant eyes were made using dependent-sample t -tests. The patients were divided into two subgroups: those whose ocular dominance was in the right eye (right-eyedness subgroup) and those whose ocular dominance was in the left eye (left-eyedness subgroup).

All analyses were performed using SPSS software (ver. 14.0 for Windows; SPSS Inc., Chicago, IL). $P < 0.05$ was considered to indicate statistical significance.

3. Results

In total, 358 eyes of 179 participants who met the inclusion and exclusion criteria were analyzed (mean age, 28.18 ± 6.38 years; 41.3% males, all Koreans). Ocular dominance occurred predominantly in the right eye (right vs. left: 78.77% vs. 21.22%; $P < 0.001$).

The main characteristics of ocular laterality are shown in Table 1. The dominant eyes showed significantly lower spherical equivalent values than the non-dominant eyes ($P = 0.017$). In the quadrant analysis, the I-S difference was $4.82 \pm 20.64 \mu\text{m}$ in dominant eyes. However, the value was significantly different and reversed in non-dominant eyes ($-2.48 \pm 17.80 \mu\text{m}$, $P < 0.001$; Table 1). In terms of the clock-hour-based RNFL thickness, the dominant eyes showed significantly thicker RNFLs at 6 o'clock than the non-dominant eyes

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