Comparison of Retinal Nerve Fiber Layer Thickness between Amblyopic and Normal Eyes in Unilateral Strabismic Amblyopia using Scanning Laser Polarimetry

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Abstract

***Purpose*:** This study was designed to assess and compare the thickness of the peripapillar retinal nerve fiber layer (RNFL) in amblyopic and normal eyes in unilateral strabismic ambelyopia using scanning laser polarimeter.

***Methods*:** Scanning laser polarimetry was performed on 17 patients with unilateral strabismic amblyopia who had an absence of neurologic diseases or glaucoma with a minimum age of 15 years. A mean retardation map was calculated from separate scans or was considered to be the best scan obtained for each eye. Polarimetric indices were analyzed comparing amblyopic and contralateral normal eyes.

***Results*:** Mean±SD age of patients was 24±4 years (15-32 years). The male:female ratio was 10:7. There were six right and 11 left amblyopic eyes. Mean±SD visual acuity (VA) of amblyopic eyes was 0.57±0.26 logMAR. The average thickness of the nerve fiber layer was 57.01 μm in normal eyes and 58.38 μm in amblyopic eyes (P=0.22). Mean±SD polarimetric indices did not differ significantly between normal and amblyopic eyes with a P-value of 0.98 for total polar average.

***Conclusion*:** There was no statistically significant difference in thickness of the nerve fiber layer between amblyopic and normal eyes in unilateral strabismic amblyopia.

***Keywords*:** Scanning Laser Polarimetry, GDx, Amblyopia NFL, Strabismus

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Introduction

Amblyopia is defined as the unilateral or bilateral underdevelopment of visual acuity (VA) without any organic abnormality of the globe. It is generally attributed to abnormal development of the visual cortex due to strabismus, blurred image due to refractive error, form vision deprivation, or a combination of these factors.[1] Amblyopia remains an important cause of low VA, affecting 2% to 4% of the general population.[2]

Former reports have suggested that some eyes diagnosed with amblyopia may also have abnormalities in the afferent visual system anterior to the striate cortex, including the retina, retinal ganglion cell, retinal nerve fiber layer (RNFL), optic nerve, and lateral geniculate body of the thalamus.[3]

In animal models of visual deprivation amblyopia during the neonatal period, histologic changes have been noted in the lateral geniculate body[4] and cortex.[5] Similar observations have been found in humans.[6] However, in some studies[7,8] it has been suggested that the thickness of the RNFL in eyes with strabismic amblyopia is not considerably different from normal eyes.

In completion to these studies, we compared the RNFL thickness in amblyopic and normal eyes in patients with unilateral strabismic amblyopia, using the GDx Nerve Fiber Analyzer (Laser Diagnostic Technologies, San Diego, California), which previously has been shown to be a useful and noninvasive method for examination of the nerve fiber layer thickness.[9,10]

Methods

In a prospective study, we examined patients who met the inclusion criteria of unilateral strabismic amblyopia. Patients with a neurological disease or ocular diseases such as glaucoma (Glaucoma was diagnosed by high IOP, increased C/D and perimetry and performed automated perimetry in each eye using the Humphrey C-30-2 SITA Standard program)[11] or nystagmus and patients who were too young to cooperate were excluded from this study. Based on these criteria, two patients were excluded because of their nystagmus. Patients with VA difference of less than two lines between amblyopic and normal eyes according to the Snellen chart were also excluded. Informed consent was obtained from all patients. Neurologic consultation was requested if needed.

GDx Nerve Fiber Analyzer (version 5.5.0) was used to measure the thickness of peripapillar RNFL. All polarimetric recordings were obtained with undilated pupils and dim ambient light. For patients with convergent strabismus, temporal base prisms were placed in front of the fixating eye in order to bring the eye under examination into a straight position.

The system accepts the image obtained only if it is focused and has the optic nerve head centered. Only sharp images accepted by the equipment in both eyes were considered for the study. A mean retardation map was calculated when two or more adequate images were obtained.

The data collected using GDx Nerve Fiber Analyzer included nerve fiber analysis (12 parameters, Table 1), polarimetric data analysis (Five parameters), mean sector values (Five parameters), integral ratios (Six parameters), mean ratios (Six parameters), and maximum and median calculations and ratios (Seven parameters). The ellipse quadrants used for the temporal, superior, nasal, and inferior angles were 25°, 145°, 215°, and 335°, respectively.

The GDx software includes a separate parameter, called "The Number" which comprises information from each of the individual parameters. "The Number" is a neural network which has been trained to look at all values obtained when an image is acquired, assigning a number between zero and 100 to each patient. Although "The Number" is quite sensitive to correctly locating and sizing the ellipse, early evaluation of "The Number" indicates that patients who score between zero and 30 are healthy, patients who score over 50 tend to be glaucomatous, and those who score between 30 and 50 tend to be glaucoma suspects.

The Student T-test was applied to mean index values for the comparison of amblyopic and fellow eyes. A P-value of less than 0.05 was considered statistically significant.

Results

The study included 10 men and seven women and their mean±standard deviation (SD) age was 24±4 years (15-32 years). Mean±SD VA was 0.57±0.26 logMAR in the amblyopic eyes (from $^{20}/_{25}$ until $^{20}/_{200}$ in Snellen chart or 0.1 until 1.1 in logMAR). There were six right and 11 left amblyopic eyes. The type of amblyopia in all patients was strabismic.

The nerve fiber analysis parameters (Table 1) were not statistically different between sound and amblyopic eyes with P-values ranging from 0.06 for the superior average to 0.94 for ellipse modulation. The maximum difference between sound and amblyopic eye was observed in superior average (P-value=0.06) although not statically significant. Other 32 parameters measured were not statistically different too, with P-values ranging from 0.23 for the temporal integral to 0.98 for total polar average.

Table 1. GDx nerve fiber analyzer results: Mean (SD)

Parameter	Sound eye	Amblyopic eye	P-value
The Number	15.76 (7.84)	15.59 (8.51)	0.83
Symmetry	0.98 (0.12)	1.01 (0.16)	0.55
Superior Ratio	3.59 (1.38)	3.24 (1.68)	0.48
Inferior Ratio	3.78 (1.08)	3.12 (1.40)	0.14
Superior/Nasal	2.44 (0.43)	2.14 (0.78)	0.18
Max Modulation	2.96 (1.19)	2.42 (1.40)	0.24
Superior Maximum	80.46 (13.99)	82.88 (15.14)	0.38
Inferior Maximum	82.67 (11.92)	81.40 (11.63)	0.64
Ellipse Modulation	3.81 (1.58)	3.77 (1.63)	0.94
Superior Average	68.35 (10.25)	66.33 (10.40)	0.06
Inferior Average	67.67 (9.09)	65.86 (11.24)	0.46
Ellipse Average	57.01 (5.70)	58.38 (7.64)	0.22

Discussion

Currently, the causative mechanism of amblyopia is thought to be the lack of adequate visual stimulation to the fovea during infancy, the abnormal binocular interaction or incongruency of visual information received by the two eyes, or a mixture of these problems.[1] In the past, amblyopia was considered to be a disease with an abnormality of the retina; however, it has recently been reported that the cerebral anatomical alteration caused by amblyopia is primarily in the lateral geniculate body and the visual cortex.[12] Von Noorden et al[13] have reported, in a histological study of patients with anisometric amblyopia, a decrease in cell sizes in the parvocellular layers enervated by the amblyopic eye. This decrease was more pronounced in the lamina that received the crossed nerve fibers. In studies on amblyopia based on animal experiments[14,15] internal plexiform layer thinning and nucleolar volume diminution in the ganglion cell cytoplasm have been demonstrated, and Chow[16] reported the reduction in optic nerve size as well. Von Noorden et al[17] reported that after the induction of amblyopia by performing unilateral lid suture in the Macaca mulatta, there was an arrest in the lateral geniculate body cell growth, an abnormal distribution of the cerebral cortex, and decreases in the density and size of the parafoveal ganglion cells.

Scanning laser polarimetry seems to be a good modality to examine the effect of amblyopia on the retinal fiber layer. The organization of microtubules and other components of the RNFL produces birefringence; the retardance changes the polarization state of passing light. The nerve fiber analyzer measures this change in polarization by scanning the retina with a polarized laser beam. The light reflected from the retina is detected, digitized, and transformed into a video image, composing a retardation map of over 65,000 pixels of the peripapillary area. Wiesel and Huble[18] have reported that atrophy of the neurons in the cerebral cortex was detected; nevertheless, it had no influence on the retina.

Several studies have tried to compare the effect of amblyopia on thickness of RNFL. Baddini-Caramelli et al[8] have reported that there is no significant difference between the GDx parameters of amblyopic eyes compared to normal eyes except for "The Number" parameter, which comprises information from each of the individual parameters. The number is a neural network that has been trained to look at all values obtained when an image is acquired, assigning a number between zero and 100 to each patient. Although the number is quite sensitive to correctly locating and sizing the ellipse, early evaluation of the number indicates that patients who score between zero and 30 are healthy, patients who score over 50 tend to be glaucomatous, and those who score between 30 and 50 tend to be glaucoma suspects.

In agreement with the results reported by Baddini-Caramelli et al[8] and Colen et al[7] but inconsistent with the results of Yen et al[19], we found that the thickness of RNFL is not significantly different in strabismic amblyopic eyes compared to their fellow sound eyes. In our study, “The Number” parameter was not also different between the eyes.

Conclusion

In conclusion, the obtained findings support the previous assumptions that strabismus-induced amblyopia does not affect the thickness of RNFL. However, this finding requires further histopathologic confirmation.

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