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ORIGINAL ARTICLE

Unilateral amblyopia: Optical coherence tomography findings

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Abstract *Purpose:* This study was performed to measure the macular and the retinal nerve fiber layer (RNFL) thicknesses using optical coherence tomography (OCT) in patients with unilateral amblyopia.
Methods: Measurement of the Retinal nerve fiber layer and Macular Retinal Layer thickness for both amblyopic and normal fellow eyes by (OCT) was carried out at king Abdulaziz University Hospital, Riyadh, Saudi Arabia.
Results: Ninety-three patients with unilateral amblyopia between the ages of 5 years and 12 years were included. The macular retinal thickness and the RNFL thickness were measured using OCT. The mean macular retinal thickness was 259.3 μm and 255.6 μm, and the mean RNFL thickness was 112.16 μm and 106 μm, in the amblyopic eye and the normal eye, respectively. OCT assessment of RNFL thickness revealed a significantly thicker RNFL in amblyopic eye ($P < 0.0001$), but no statistically significant difference was found in macular retinal thickness ($P = 0.195$).
Conclusion: The amblyopic process may involve the RNFL, but not the macula. However, further evaluation is needed.

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1. Introduction

Amblyopia is defined as the unilateral or bilateral under development of visual acuity without any organic abnormality of the globe that is associated with the presence of strabismus, anisometropia, or form deprivation early in life. If the same disorders occur later in life, amblyopia does not develop (Jin, 2001). The neural sites that are influenced by visual deprivation are still under investigation. Nevertheless, it has been reported by several studies on humans and animals that, during the neonatal period, visual deprivation has an effect on the growth of cells in the lateral geniculate body that receives input from the amblyopic eye and a shift in the dominance pattern in the visual cortex (Baddini-Caramelli et al., 2001). Amblyopia occurs during the period when the neuronal network between the retina and the cerebral cortex is developing and maturing. Thus this condition is frequently developed during the first 2–3 years of the postnatal period; however, it may be developed up to the age of 8–9 years. Amblyopia is a curable disease if treated early (Jin, 2001). During fetal development, there is a rapid decline in cell density in the retinal ganglion cell layer toward the end of gestation. In humans, the total population of cells in the ganglion cell layer is highest (2.2–2.5 million cells) between approximately weeks 18 and 30 of gestation. After this, the cell population declines rapidly to 1.5–1.7 million cells (Provis et al., 1985). The number of axons in the human optic nerve also decreases during gestation (Provis et al., 1965). At 16–17 weeks of gestation, the estimated number of axons was 3.7 million. The number of axons in the human adult optic nerve is 1.1 million. If amblyopia affects the process of postnatal reduction of ganglion cells; RNFL thickness may be thicker than that in the normal eye (Greenfield et al., 2000).

It was our plan to investigate macular and retinal nerve fiber layer thickness (RNFLT) in amblyopic eyes to determine whether it is thicker.

Several techniques to evaluate the RNFLT, such as red-free ophthalmoscopy, scanning laser polarimetry (SLP) and optical coherence tomography (OCT) have been described. OCT is a noninvasive, noncontact technique that measures RNFLT (Huang et al., 1991; Schuman et al., 1996). The RNFLT measured by OCT corresponds to the RNFLT measured histologically (Huang et al., 1991). Because OCT is based on near-infrared interferometry, the thickness measurement is not affected by refractive status or axial length of the eye, or by light changes in nuclear sclerotic cataract density (Schuman et al., 1996).

The purpose of our investigation is to use optical coherence tomography to measure macular and RNFLT in patients with unilateral amblyopia, and to compare the macula and RNFL thicknesses of the amblyopic eye and the normal eye in patients with anisometropic or strabismic amblyopia .

2. Methods

This study was performed from January 2009 to December 2010 on 93 amblyopic patients between the ages of 5 years and 12 years who were diagnosed with unilateral amblyopia to measure the Retinal nerve fiber layer and Macular Retinal Layer for both amblyopic and normal fellow eyes by (OCT). Patients were recruited from the pediatric ophthalmology clinics of King Abdul-Aziz University Hospital Riyadh, Saudi Arabia, after Institutional Review Board (IRB) approval. Amblyopia in these children was diagnosed as anisometropia, strabismus, or a mix of the two. The included subjects were patients whose difference in visual acuity was at least two lines between the normal and amblyopic eye on the snellen visual acuity charts.

Anisometropia was diagnosed in those patients whose spherical equivalence showed 1.5 diopters or greater difference between the two eyes in hyperopia and 3 diopters or greater difference in myopia.

Eligibility testing included visual acuity, cycloplegic refraction, manifested refraction, fundus examination, and ocular motility test. Patients with a neurological disease or ocular diseases such as glaucoma or nystagmus, patients who were too young to cooperate, and patients whose pupillary dilation was not sufficient were excluded from this study. Informed consent was obtained from the children's parents.

The measurement was performed by the same examiner. Prior to the examination, the pupils were dilated with 1% cyclopentolate and phenylephrine.

To measure the thickness, the examiner focused a scanning beam on the fundus with an infrared sensing camera. Subsequently, the images were obtained by performing an (MM6) for macula scan. RNFL 3.45 scan was used for retinal nerve fiber layer thickness measurement for each eye. The map of the macula thickness measurement was composed of three concentric circles: a central circle, an inner ring and an outer ring. The diameters of the concentric circles were 1 mm, 3 mm, and 6 mm for the macula and the diameters of the concentric circles were 1 mm, 2.22 mm and 3.45 mm in the case of (RNFL 3.45) scan.

In this study, measurements from total areas were obtained in μm units. All children were measured three times, and their average values were obtained. The results were analyzed statistically using SPSS version16 and medcalc version8. Comparison was performed using student's *t*-test. *P* values less than 0.05 were considered to be significant.

3. Results

Total of 93 patients with unilateral amblyopia were enrolled in this study. They included 48 (51.6) males, and 45 (48.4%) females, and their mean (SD) age was 8.72 years (2.21) (age range 5–12 years). The identified amblyogenic factor was strabismus in 36 (38.7%), anisometropia in 33 (35.4%), and mixed type in 24 (25.8%). Of the patients with strabismus, esotropia was noted in 24 cases and exotropia was noted in 12 cases. Among patients with anisometropia, hyperopia was noted in 25 cases and myopia was noted in 8 cases. In the mixed cases, there were 11 cases of anisometropic hyperopia and esotropia, 4 cases of anisometropic myopia and esotropia, 1 case of anisometropic hyperopia and exotropia, and 8 cases of anisometropic myopia and exotropia (Table 1).

The mean total thickness of retinal fiber layer, macula, and fovea for all patients are shown in Table 2. There was statistically significant difference found when comparing the thickness of RNFL in amblyopic eyes and normal fellow eyes, although no statistically significant difference was found when comparing the thickness of the macula and fovea in amblyopic eyes and normal fellow eyes.

For strabismic amblyopic patients the mean total thickness of retinal fiber layer, macula, and fovea are shown in (Table 3). There was statistically significant difference found when comparing the thickness of RNFL in amblyopic eyes and normal fellow eyes, but there was no statistically significant difference found when comparing the thickness of both macula and fovea in amblyopic eyes and normal fellow eyes.

For anisometropic amblyopic patients the mean total thickness of the retinal fiber layer, macula, and fovea are shown in Table 4. There was statistically significant difference found when comparing the thickness of RNFL, macula, and fovea in amblyopic eyes and normal fellow eyes. The results of RNFL, macular and fovea thickness in mixed type of amblyopia are shown in Table 5.

Table 1 Clinical data of the patients.

	No. of patients	Diagnosis	No. of patients
Strabismus	36 (38%)	Esotropia	24
		Exotropia	12
Anisometropia	33 (35%)	Spherical hyperopia	25
		Spherical myopia	8
Mixed	24 (25%)	Spherical hyperopia + Esotropia	11
		Spherical myopia + Esotropia	4
		Spherical hyperopia + Exotropia	1
		Spherical myopia + Exotropia	8
Total			93

Table 2 Measurement of retinal nerve fiber layer thickness, macular thickness, and foveal thickness (μm).

		No of patients	Amblyopic eye	Normal eye	*P*-value
RNFLT	mean ± SD	93	112.16 (12.67)	106 (8.91)	< 0.0001
MT	mean ± SD	93	259.3 (16.67)	255.6 (21.34)	0.195
FT	mean ± SD	93	192.88 (25.72)	186.31 (32.31)	0.127

RNFLT: retinal nerve fiber layer thickness, MT: macular thickness, FT: foveal thickness.

Table 3 Retinal nerve fiber layer thickness, macular thickness, and foveal thickness (μm) in the strabismus amblyopic patients.

	RNFLT		MT		FT	
	A	N	A	N	A	N
Mean ± SD	112.69 (15.12)	107.47 (10.31)	265.31 (17.33)	264.39 (16.84)	204.31 (33.81)	199.39 (39.31)
P-value	0.029		0.758		0.306	

A: amblyopic eyes, N: normal eyes, RNFLT: retinal nerve fiber layer thickness, MT: macular thickness, FT: foveal thickness.

Table 4 Retinal nerve fiber layer thickness, Macular thickness, and Foveal thickness (μm) in the anisometropic amblyopic patients.

	RNFLT		MT		FT	
	A	N	A	N	A	N
Mean ± SD	113.76 (12.89)	106.91 (9.13)	256.76 (14.15)	246.61 (27.39)	187.12 (14.55)	177.61 (20.55)
P-value	< 0.0001		0.050		0.039	

A: amblyopic eyes, N: normal eyes, RNFLT: retinal nerve fiber layer thickness, MT: macular thickness, FT: foveal thickness.

Table 5 Retinal nerve fiber layer thickness, macular thickness, and foveal thickness (μm) in the mixed amblyopic patients.

	RNFLT		MT		FT	
	A	N	A	N	A	N
Mean ± SD	109.17 (6.57)	102.71 (4.91)	253.71 (16.68)	254.88 (10.40)	183.67 (16.50)	178.67 (28.28)
P-value	< 0.0001		0.798		0.484	

A: amblyopic eyes, N: normal eyes, RNFLT: retinal nerve fiber layer thickness, MT: macular thickness, FT: foveal thickness.

4. Discussion

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 (The Korean strabismus and pediatric ophthalmological society, 2004). Von Noorden et al. (1983) 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, and this decrease was more pronounced in the lamina that received the crossed nerve fibers. In a study on amblyopia that was based on animal experiments by Rasch et al. (1961) and Chow et al. (1957)

internal plexiform layer thinning and nucleolar volume diminution in the ganglion cell cytoplasm were demonstrated, and Chow (1955) reported the reduction in optic nerve size. von Noorden et al. (1977) reported that, after the induction of amblyopia by performing unilateral lid suture in the Macaca mulatta, there was 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. Wiesel and Hubel (1963) have reported that atrophy of the neurons in the cerebral cortex was detected; nevertheless, it had no influence on the retina. However, Baddini-Caramelli et al. (2001) have reported that in visual deprivation amblyopia and strabismic amblyopia, the visual cortex, the lateral geniculate body and the ganglion cells of the amblyopic eyes were damaged. The number and size of the axons on the ganglion cells were decreased as was the thickness of the retinal nerve fiber layer. In normal individuals, the thickness of the fovea was reported to be 130 μm by the histopathological tests performed by Hogan et al. (1971). Kanai et al. (2002) measured 47 eyes in 47 cases by performing OCT and reported the fovea thickness as 142 ± 15 μm. Ling et al. (2000) reported 146.34 ± 8.58 μm in 60 cases with 120 eyes, Gobel and Kretzchmar-Gross (2002) reported 153 ± 15 μm in 60 cases with 120 eyes, and Hee et al. (1998) have reported 174 ± 18 μm in 41 cases with 73 eyes. Comparing the fovea thickness (186.31 Mm) of the 93 normal eyes in our study (mean age: 8.7 years) to these data, our result was thicker than the previous studies. As for the causes of such differences in the thickness, the combination of racial difference, the measurement error among the examiners, different versions of the OCT and the difference of the subjects' ages could be considered.

In the present study, the peripapillary RNFL and macular thicknesses were measured by OCT and the results showed that the macular thickness was not significantly different between the anisometropic amblyopic eyes and the normal eyes, although the peripapillary RNFL was significantly thicker in the amblyopic eyes. Our results corroborate those of a previous OCT study22 that suggested RNFL is thicker in refractive amblyopia and that the amblyopic process may involve the peripapillary RNFL. Baddini-Caramelli et al. (2001) measured the thickness of the retinal nerve fiber layer of the amblyopic eyes and the normal eyes in the children with amblyopia using scanning laser polarimetry. In these 21 patients whose mean age was 15 years (age range: 7–35 years), the total thickness of the amblyopic eyes and the normal eyes was 64.90 ± 13.08 μm and 65.71 ± 13.13 μm, respectively showing no statistically significant difference. Colen et al. (2005) reported that in the children with strabismic amblyopia, as measured by a nerve fiber analyzer, there was no statistical difference in the thickness of the retinal nerve fiber layer between the amblyopic eyes and the normal fellow eyes. However, Yen et al. (2004) reported that in 18 patients with unilateral anisometric amblyopia (mean age: 25.4 years) and 20 patients with strabismic amblyopia (mean age: 27.4 years), the thicknesses of the retinal nerve fiber layer of the amblyopic eyes and the normal fellow eyes were 142.2 ± 18.6 μm, 129.7 ± 18.5 μm, 131.5 ± 12.6 μm and 128.3 ± 21.5 μm, respectively, and there was a statistical difference only in patients with unilateral anisometric amblyopia. The overall thickness of the retinal nerve fiber layer of the amblyopic eyes and the normal fellow eyes of the amblyopic patients was 136.6 ± 16.5 μm and 128.9 ± 19.9 μm, respectively, note that the thickness of the retinal nerve fiber layer of the amblyopic eyes was thicker than that of the normal fellow eyes. The cause of this difference was not clear, though it may have been due to the slow-down of the normal postnatal reduction of ganglion cells. The limitations of this study are that, in the comparison among children with amblyopia, the number of mixed type of amblyopia was small. In the future, further studies with larger number of children with amblyopia are needed.

In conclusion, peripapillary RNFL was significantly thicker in anisometropic amblyopia, whereas the macular thickness was not significantly different between amblyopic and normal eyes. Our results suggest that although the amblyopic process may not have any significant effect on the macula, it may exert a significant effect on peripapillary RNFL. However, more studies on the differences in thickness of the fovea and the retinal nerve fiber layer between children with anisometric amblyopia and children with strabismic amblyopia are required.

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