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Evaluation of Retinal Nerve Fiber Layer and Macular Thickness in Amblyopia

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Abstract

Purpose: To investigate the differences in macular and nevre fiber layer thicknesses between amblyopic and fellow eyes.

Method: One hundred and twenty two eyes of 61 patients were enrolled for this study. All patients underwent complete ocular examination, cover test, prism test and also RNFL, macular thickness measurements (CMT; central macular thickness, TMT; total macular thickness) were obtained with OCT. 61 amblyopic (30 strabismic, 31 anisometropic) eyes and 61 fellow eyes were compared. A comparison of all amblyopic eyes versus fellow eyes was conducted. Amblyopic subgroups were also compared with both each other and fellow eyes, respectively.

Results: There was slightly elevated RNFL in strabismic group comparing to anisometropic group, but the difference was not significant. The strabismic group had both lower values in CMT and TMT than the anisometropic group but only the difference in TMT values was statistically significant (p: 0.043). Although the all amblyopic group had elevated RNFL, CMT and TMT values were lower comparing fellow eyes, but none of the differences were statistically significant.

Conclusion: The only significant result in our study between strabismic and anisometropic groups was TMT. The evaluation between amblyopes and fellow eyes revealed no differences. Amblyopia does not seem to have prominent effect on retinal structures.

Introduction

The meaning of the word Amblyopia is blurred vision (Amblyos: blurred, Opia: vision). Amblyopia is a disorder where visual acuity does not develop properly in one or both eyes during childhood. It is the most common cause for decreased vision in children with 1-5% [1].

Amblyopia can be associated with strabismus, anisometropia or disruption of normal development of the lateral geniculate body during the neonatal period [2]. In 1963 Wiesel and Hubel revealed that in infant cats and monkeys, deprivation of visual stimulation by suturing unilateral lid, induced anatomical and electrophysiological changes of the lateral geniculate body and the visual cortex [3].

It also has been suggested that abnormalities in the retinal ganglion cells may be attributable to the effect of amblyopia on the process of postnatal reduction of ganglion cells [4]. Red-free ophthalmoscopy, scanning laser polarimetry (SLP), and optical coherence tomography (OCT) can evaluate retinal nerve fiber layer (RNFL) and macular thickness. In several studies which were investigating the relationship between amblyopia and retinal anatomy, RNFL was found thicker comparing control patients [5,6]. On the other hand, in various studies, macular thickness was found elevated in amblyopic patients comparing to controls while in many studies no differences were found in RNFL and macular thickness between the amblyopic and healthy individuals [7-12].

There are many controversial results in literature about morphological changes in macular thickness and RNFL in amblyopic patients. The aim of our study is to investigate differences between amblyopic and fellow eyes in RNFL and macular thickness with OCT.

Material and Method

The study was conducted at department of opthalmology at (****). 122 eyes of 61 patients (61 amblyopic eyes, 61 fellow eyes) were enrolled to the study. The amblyopic group consisted 31 anisometropic and 30 strabismic eyes. All patients underwent complete ocular examination including visual acuity, biomicroscobic examination, cover test, prism test, retinal examination using optical coherence tomography. The amblyopic eye was defined as an eye that has a visual acuity of at least two lines worse than the normal eye with Snellen chart, having no ocular problem in the visaul axis such as leukoma or cataract or macular disease. Anisometropia was defined as a cycloplegic spherical equivalent difference greater than 2.00 diopters between fellow eyes.

We used Optical Coherence Tomography device from OPKO (Spectral OCT SLO, Opko, Florida USA) for measuring the thicknesses of the fovea and the retinal nerve fiber layer. The measurement of the fovea and the retinal nerve fiber layer thickness was performed by the same masked examiner (a doctor from our clinic). OCT images were obtained using spectral domain OCT after pupillary dilatation with 1% cyclopentolate hydrochloride. Two different values were noted about macula; central 1 mm diameter area was defined central macular thickness (CMT) and 6 mm diameter area is total macular thickness (TMT), RNFL scan was performed with three peripapillary scans with the protocol of having diameter of 3.4

mm centered on the optic disc. The instrument software calculates average thickness values for two quadrants (superior, inferior) and average RNFL automatically.

Patients with systemic or ocular disease (glaucoma, leukoma) or had previous ocular surgery, nystagmus and patients with spherical equivalent difference smaller than 2.00 diopter were excluded from this study. Written informed consent was also obtained from each patient or their parents. The study was conducted with accordance of declaration of Helsinki.

Statistical analysis

The statistical analysis for the comparison of the fovea and the retinal nerve fiber layer thicknesses between the amblyopic eye and fellow (control) eye was performed using the T test. P values less than 0.05 were considered to be statistically significant. SPSS software version 21.0 (SPSS, Inc., Chicago, IL) was used for statistical analyses. Analysis of variance was used to compare the differences between the three groups. Sample T test was used to determine whether differences between values of the amblyopic eyes and nonamblyopic eyes were significant.

Results

Two major groups were compared in this study; amblyopic group and their fellow eyes (control). The amblyopic group included 61 eyes; 30 strabismic and 31 anisometropic. There were 15 boys and 15 girls in strabismic subgroup and 16 boys and 15 girls in anisometropic subgroup, respectively. The strabismic group contains 12 esotropic and 18 exotropic patients. The anisometropic group had 9 myopic and 22 hyperopic anisometropes. Mean ages were 13.5+2.12 (range 6-25) in the strabismic subgroup and 11.21+2.44 (range 7-15) in the anisometropic subgroup. There was no statistically significant difference in ages between those groups. The average visual acuity with Snellen charts in anisometropic group was 0.49 and 0.44 in strabismic subgroup. On the other hand it was 0.96 in control group.

When comparing amblyopic subgroups eachother, the strabismic group had slightly thicker RNFL than the anisometropic group, while the anisometropic group had thicker central macular area than strabismic group, but neither of the differences were statistically significant. But, as comparing total macular thickness values, the anisometropic group had higher macular thickness than strabismic group. Althought this difference was not clinically significant (254 vs 276 microns), it was found to be statistically significant (p: 0.043) (Table 1).

	Strabismic (n:30)	Anisometropic (n:31)	P value
RNFL µm	105.9000 ± 15.59918	102.4516 ± 14.43107	0.374
CMT µm	147.8667 ± 65.33296	151.8710 ± 67.68394	0.815
TMT µm	254.0667 ± 40.59041	276.8387 ± 45.00600	0.043
TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer			

Table 1: Comparison of the two amblyopic subgroups eachother with central macular thickness, total macular thickness and RNFL values.

Amblyopic subgroups were also compared with their fellow eyes, respectively. The strabismic group had slighlty thicker RNFL (106 µm) comparing to control group (104 µm), but CMT and TMT values were found smaller respectively. On the other hand, none of them were found significantly different (Table 2).

(N:30)	Strabismic	Control (fellow eyes)	P value
RNFL µm	105.9000 ± 15.59918	104.1667 ± 13.75922	0.650
CMT µm	147.8667 ± 65.33296	151.6000 ± 53.88980	0.810
TMT µm	254.0667 ± 40.59041	262.7000 ± 27.56703	0.340
TMT: Total Macular Thickness ; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer			

Table 2: RNFL, CMT and TMT values in Strabismic group and fellow eyes.

Table 3 shows a comparison of RNFL, CMT and TMT measures between anisometropic subjects and their fellow eyes. The RNFL and CMT were found smaller in anisometropic group comparing to fellow eyes, although TMT was slightly elevated (276 µm). No statistically significant difference were found in all values between groups (p>0.05) (Table 3).

(N=31)	Anisometropic	Control(fellow eyes)	P value
RNFL µm	102.4516 ± 14.43107	103.0645 ± 12.69103	0.860
CMT µm	151.8710 ± 67.68394	162.9032 ± 63.10486	0.509
TMT µm	276.8387 ± 45.00600	269.5806 ± 23.11100	0.428
TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer			

Table 3: RNFL, CMT and TMT values in Anisometropic group and fellow eyes.

A total evaluation of all amblyopic subjects (anisometropic +strabismic) comparing to control group (fellow eyes) was also conducted. The RNFL values in the amblyopic group was little higher than control group but again, the difference was not statistically significant. When comparing central and total macular thickness, although control group had higher values in both CMT and TMT measures, none of the differences were found statistically significant (Table 4).

(N:61)	Amblyopic	Control	P value
RNFL µm	104.1475 ± 14.99204	103.6066 ± 13.12793	0.832
CMT µm	149.9016 ± 66.01280	157.3443 ± 58.54254	0.511
TMT µm	265.6393 ± 44.05528	266.1967 ± 25.42428	0.932
TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer			

Table 4: A comparison of RNFL, CMT and TMT values between amblyopic and control Groups.

Discussion

The reason of amblyopia is still certainly unknown. There are many possible causes that might promote for amblyopia development. It was

once considered as a situation associated with an abnormality of the retina [13]. However, amblyopia-induced cerebral changes were later shown in the visual cortex and the lateral geniculate body.

In 1977, von Noorden et al. reported that, several changes occured after amblyopia development with suturing one lid, such as; an arrest in the lateral geniculate body cell growth, an abnormal distribution of the cerebral cortex, and a decrease in the size and density of parafoveal ganglion cells [14]. Wiesel and Huble have reported that atrophy of the neurons in the cerebral cortex and lateral geniculate body was detected; nevertheless, it had no influence on the retina [3].

One of the major consequences of amblyopia is reduction in the ganglion cells and optic disc. Lempert et al. showed that in a presumed amblyopia, visual impairment may cause optic disc hypoplasia [4]. Such changes may affect retinal nevre fiber layer and foveal thickness after all.

In several studies, retinal changes were investigated in amblyopic patients. Both RNFL and macular thickness were evaluated and different results were obtained from those studies. RNFL thickness in amblyopic patients were found either thicker, thinner or unchanged comparing to control groups.

Some studies showed that RNFL was found thicker in amblyopic patients. Such as, Wu et al. reported that anisometropic amblyopes had thicker RNFL values in the amblyopic eye than in the fellow eye based on OCT [15]. Also Yen et al. hypothesized that amblyopia affects the postnatal maturation of the retina, including the postnatal reduction of retinal ganglion cells, which would cause an increase in the RNFL thickness in amblyopic eyes [16]. In their study, they measured RNFL thickness in patients with unilateral amblyopia (strabismic and refractive amblyopia) and found no significant difference between strabismic amblyopic and normal eyes, although the RNFL was significantly thicker in eyes with refractive amblyopia.

Similarly Chen et al. found that, in amblyopic group, RNFL were significantly thicker than the emmetropia group. However, they explained that the significance of this difference disappeared after adjustment for axial length and refractive error [17]. Yoon et al. measured the peripapillary RNFL in patients with anisometropic amblyopia. They reported that the RNFL in patients with amblyopia was significantly thicker [6].

Unlike these studies, some others showed no significant difference in RNFL thickness between amblyopic groups and controls. Fırat et al. found no statistically significant difference for RNFL thickness among the amblyopic and control eyes although it was slightly thicker in amblyopic patients. They suggested that amblyopia does not affect on RNFL [10]. Yalcin et al. reported that the difference in RNFL thickness between amblyopic eyes, fellow eyes of the amblyopic patients, and normal eyes of the emmetropic subjects was not clinically significant [8]. On the other hand, Ersan et al found that, RNFL thickness did not differ between strabismic amblyopic and anisometropic amblyopic patients and fellow eyes but they found temporal RNFL quadrant in the hypermetropic anisometropic group, and superior RNFL quadrant in the myopic anisometropic group were significantly thinner in amblyopic eyes compared to their fellow eyes [9].

In our study, RNFL was found thicker in strabismic group comparing both anisometropic group and fellow eyes. Also, all amblyopic patients had slighlty thicker RNFL comparing all controls. But none of the differences were not statistically significant. Similar to Yalcin et al., Altintas et al. and Fırat et al., our study revealed no significant difference in RNFL between amblyopic and fellow eyes [8,18,10].

There is another region in retina that has been investigated with imaging devices in amblyopia. Macular thickness was also compared in amblyopic eyes and control groups. There are various results obtained from different studies in literature.

Another study performed by Yoon et al. used OCT to measure the peripapillary RNFL and foveal thickness in patients with anisometropic amblyopia. Even though RNFL in patients with amblyopia was found significantly thicker, there was no significant difference in macular thickness [6].

In another study, Xu et al. reported the fovea and the central sector of the retina in amblyopic eyes were slightly but not significantly thicker than those in the normal fellow eyes in children aged seven to 14 years [19]. Huynh et al. found increase in macular region among amblyopic patients but it was not statistically significant [20]. In another study Yalcin et al. reported that the mean foveal thickness for amblyopic patients was 220 ± 38.25 microns; for fellow eyes, it was 202.87 ± 31.01 microns, and for healthy subjects, 198.91 ± 22.50 microns. They found a statistical difference between groups (P=0.025). The difference between amblyopics and fellow eyes was statistically significant (P=0.038). There was also a significant statistical difference in macular thickness between amblyopics and healthy subjects (P=0.028) [8].

Tugcu et al. conducted similar study about amblyopic and control patients but they both evaluated persistant and resolved amblyopia. They found that foveolar thickness was significantly increased in both resolved and persistent amblyopia groups compared with the control group (p=0.031). However, there was no difference between amblyopic groups [21]. Al-Haddad et al. demonstrated that the mean macular thickness was significantly increased in amblyopic eyes versus the fellow eye while the mean the RNFL thickness was similar. The mean macular thickness was significantly increased in the amblyopic (273.8 μm) vs fellow eyes (257.9 μm) in their study (p=0.001). This difference remained significant in the anisometropic group (p=0.002) but not the strabismic group [7].

In our study, we compared macular thickness of strabismic amblyopes, anisometropic amblyopes and fellow eyes. The anisometropic subgroup had slightly thicker macula, while the strabismic subgroup was thinner comparing their fellow eyes. When comparing all amblyopic patients to their fellow eyes, the mean macular thickness is 265 μm in amblyopic group and 266 μm in fellow eyes, respectively. But the difference was not significant (p: 0.932).

Our study aimed to investigate to report the difference in RNFL and macular thickness between ambliyopic and fellow eyes. OCT was used to obtain the data like other studies but the differences between devices and the examiners, the patients ages and their refractive situations may explain the differences between studies. The only statistically significant result came out of our study is the difference in macular thickness between strabismic and anisometropic amblyopes, which the anisometropic group was found significantly thicker.

One of the limitations of our study is not evaluating the relationships between RNFL, macular thickness, and age/refractive errors. We did not obtain data from patients after they overcome amblyopia with treatment. The mechanism of amblyopia and the differences between normal eyes is not totally understood yet. Further studies, including histopathological and instrumental studies with a

greater number of patients, are required to investigate the differences between amblyopic and normal eyes.

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