Macular and retinal changes in unilateral amblyopia using optical coherence tomography

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Received 26 June 2022
Revised 26 September 2022
Accepted 10 October 2022
Published 09 March 2023

Journal of Current Medical Research and Practice
2023, 8:52–56

Purpose

To identify changes in macular parameters, such as central macular thickness and volume, using optical coherence tomography in cases of unilateral amblyopia and to compare that with their normal fellow eyes.

Design

A prospective, cross-sectional study was performed.

Patients and methods

This study included 62 eyes of 31 participants with unilateral amblyopia who were classified into four categories: anisometropic myopic, anisometropic hypermetropic, strabismic esotropic, and stabismic exotropic amblyopia. Comparison was done with their sound fellow eyes by spectral domain optical coherence tomography regarding changes in macular parameter (central macular thickness and macular volume).

Results

The amblyopic eyes had significantly higher central subfield thickness versus the normal fellow eyes (251.84 ± 44.90 vs. 225.32 ± 53.47 μm; $P = 0.03$), but both groups had insignificant differences regarding average macular volume (7.84 ± 0.72 vs. 7.94 ± 0.82 mm^3; $P = 0.58$).

Conclusion

In this study, we had documented significant changes in central macular thickness and insignificant changes regarding macular volume in amblyopic eyes among cases of unilateral amblyopia in comparison with their sound fellow eyes.

Keywords:
amblyopia, macular changes, optical coherence tomography

J Curr Med Res Pract 8:52–56
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2357-0121

Introduction

Amblyopia is known as unilateral or bilateral diminution of visual acuity with no detectable anatomical or pathological abnormality of the visual pathway. Amblyopia occurs in early childhood, so the normal maturation of the visual pathway is interrupted. This is known as the ‘critical period’ [1].

The worldwide prevalence of amblyopia is ~1–5%. There are 19 million children under the age of 15 years who are visually impaired; 12 million of those are impaired due to uncorrected refractive errors and amblyopia as estimated by the WHO [2–5].

Amblyopia can be caused by many factors, including uncorrected refractive errors, strabismus, and central visual axis obstruction (amblyopia exanopsia). These factors cause blurring or obscuring of the received image by one or both eyes. This in turn leads to an abnormal binocular cortical interaction and could affect visual acuity, contrast sensitivity, and positional disorder [6]. Therefore, amblyopia could be caused by anisometropia, misalignment of one eye (strabismus), or sensory deprivation. It is thought that in amblyopia there is arrest in the physiological postnatal reduction (apoptosis) of retinal ganglion cells as hypothesized by Yen *et al.* [7]. The normal maturation of the macula and the movement of Henle’s fibers away from the foveola would be affected, which results in increase in the foveal thickness [8].

Optical coherence tomography (OCT) is an imaging method with noninvasive-high resolution properties and produces a two-dimensional image (lateral and axial coordinate) based on interruption between signals from an investigated object and the reference signal [9].

Patients and methods

This was a prospective cross-sectional study conducted at the Ophthalmology Department of Assiut University Hospital from June 2019 to August 2021. This study included 62 eyes of 31 participants with unilateral amblyopia.

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Ethical considerations

Consent for participation in this study was obtained from the patients. This study was approved by the Faculty of Medicine Ethics Committee, Assiut University, (the Institutional Review Board local approval number: 17100938).

Inclusion criteria

The study included cooperative patients with unilateral amblyopia, patients having two-line difference in visual acuity between both eyes, either anisometropic or strabismic amblyopia.

Exclusion criteria

Uncooperative patients, patients with mental retardation, patients with any structural abnormality, patients with history of intraocular surgeries, and patients with pathological myopia (more than −8.00 D) were excluded.

Methods

All patients had detailed ophthalmic examination, including measurement of best-corrected visual acuity with Snellen's chart; manifest and cycloplegic refraction by Huvitz HRT-7000 autorefractometer; spherical equivalent (SE) (which is the algebraic sum of the spherical power and half of the cylindrical power); best-corrected visual acuity, which was then converted to LogMAR scale; anterior segment evaluation via slit lamp; fundus examination via an indirect ophthalmoscope; and axial length measured by E-Z Scan AB5500+ Sonomed. Macular thickness and volume were estimated by spectral domain (SD-OCT, RS-3000°CT Retina Scan ADVANCE; Nidek Inc., California, USA). It provides 53 000 A-scans/sec with about 120 images, demonstrating the detailed layers of the retina. Mapping a wide area (9 mm × 9 mm) providing color-coded map, thickness analysis of retinal layers. The *x–y* map of the macula and the disc protocols of scanning were done for all participants in this study. When the patients focus on a fixed central target, the center point of the map coincides with the minimum foveal thickness [10]. Application of the Early Treatment Diabetic Retinopathy Study (ETDRS) grid was done, which included 1-, 3-, and 6-mm three concentric rings of diameters and two lines dividing the macula into nine regions. The average thickness of the macula in the central 1-mm ETDRS grid is defined as central subfield thickness (CST), also known as foveal thickness [11,12]. Macular volume is defined as the sum of all volumes of all nine sections. All spectral domain optical coherence tomography (SD-OCT) images were performed by the same examiner with exclusion of any low-quality images and artifacts.

Statistical analysis

Recorded data were analyzed using the Statistical Package for the Social Sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± SD and compared with Student t test in case of two groups and analysis of variance test in case of more than two groups. Qualitative data were expressed as frequency and percentage and compared with χ^2 test. Level of confidence was kept at 95%, so *P* value was significant if it was less than 0.05.

Results

A total of 62 eyes (31 amblyopic and 31 normal fellow eyes) of 31 patients with unilateral amblyopia were included in this study.

Mean age ± SD of studied participants was 23.35 ± 5.57 years, with range between 10 and 30 years. Majority (18 patients, 58.1%) of patients were females, and 13 (41.9%) patients were males (Table 1).

The most frequent type of amblyopia in this study was anisometropic myopia (14 patients) (45.2%) followed by strabismic esotropia and anisometropic hypermetropia (six patients for each) (19.4%), then strabismic exotropia (16.1%) (Fig. 1).

Axial length was significantly higher among amblyopic eyes (23.59 ± 1.82 vs. 22.81 ± 1.12 mm; *P* = 0.04) in comparison with normal eyes. It could be due to the higher number of myopic patients included in this study (Table 2).

Optical coherence imaging of the macula in all amblyopic groups and their normal fellow eyes

The amblyopic eyes had significant higher CST versus the normal fellow eyes (251.84 ± 44.90 vs. 225.32 ± 53.47 μm; *P* = 0.03), but both groups had insignificant differences regarding the average macular volume (7.84 ± 0.72 vs. 7.94 ± 0.82 mm^3; *P* = 0.58) (Table 3).

Optical coherence tomography findings in each group of amblyopia separately

Optical coherence imaging in anisometropic myopic amblyopia

We found that eyes with anisometropic myopic amblyopia

Table 1 Age and sex of studied patients

	n=31
Age (year)	23.35±5.57
Range	10-30
Sex	
Male	13 (41.9)
Female	18 (58.1)

Data expressed as frequency (percentage), mean (SD), range.

Table 2 Axial length in amblyopic and normal eyes

	Amblyopic eyes (*n*=31)	Normal eyes (*n*=31)	*P*
Axial length (mm)	23.59±1.82	22.81±1.12	0.04*

Data expressed as mean (SD). *P*<0.05. *Student *t* test was used for comparison.

had significantly higher CST in comparison with their normal fellows (268.71 ± 53.55 vs. 227.57 ± 51.87; P = 0.03) but insignificant changes in the macular volume (7.72 ± 0.67 vs. 7.97 ± 0.68; P = 0.26) (Fig. 2).

Optical coherence imaging in anisometropic hypermetropic amblyopia

We found that eyes with anisometropic hypermetropic amblyopia and their fellows had insignificant differences regarding CST and macular volume (P > 0.05).

CST was 264.33 ± 32.75 in anisometropic hypermetropic amblyopia versus 263.50 ± 30.19 in normal fellow eyes, with P = 0.86, and macular volume was 8.15 ± 0.41 in anisometropic hypermetropic amblyopia versus 8.29 ± 0.36 in their normal fellow eyes, with P = 0.54 (Fig. 3).

Optical coherence imaging in eyes with strabismic exotropic amblyopia

We found that eyes with strabismic exotropic amblyopia and their fellows had insignificant differences regarding CST and macular volume (P > 0.05).

CST was 241 ± 50.82 versus 222.40 ± 69.88, with P = 0.66, and macular volume was 7.51 ± 1.10 versus 7.34 ± 1.35, with P = 0.83 (Fig. 4).

Optical coherence imaging in eyes with strabismic esotropia amblyopia

We found that eyes with strabismic esotropic amblyopia and their fellows had insignificant differences regarding different parameters of OCT (P > 0.05).

CST was 255.67 ± 33.95 versus 233.50 ± 42.01 μm, with P = 0.20.

Macular volume was 8.05 ± 0.67 versus 8.02 ± 0.84 mm^3, with P = 0.65 (Fig. 5).

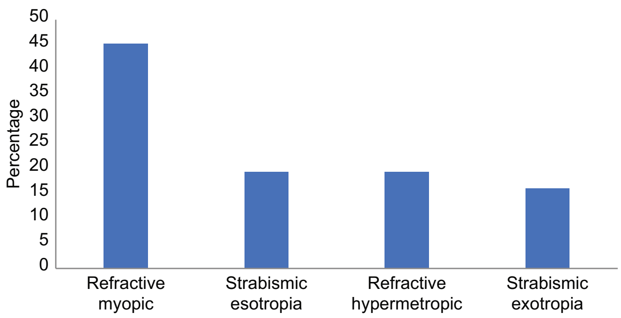
Discussion

Amblyopia is thought to be a disease in which the physiological maturation of the visual cascade from the retina to the visual cortex is interrupted. This in turn may cause various effects on multiple neural levels of the visual pathway, although the precise site of its impact is still debatable [13]. Some authors assumed that functional deficits are first observed at a thalamic level, that of the LGN [14]. On the contrary, some have claimed changes in the microstructures of different layers of the retina in amblyopic eyes such as decrease in the size and density of parafoveal retinal ganglion cells [15], a decrease in the volume of the nucleolus of retinal ganglion cells [16], internal plexiform layer thinning, bipolar synapses number decrease [17], and foveal outer nuclear layer decrease, which makes the involvement of the photoreceptors more likely [13].

In this study, 31 patients with unilateral amblyopia were included and divided into four groups (myopic anisometropia, hypermetropic anisometropia, esotropic strabismus, and exotropic strabismus amblyopia) to study OCT parameter changes regarding macular thickness, macular volume in comparison with their normal fellow eye.

We found that all amblyopic groups had significant higher CST (251.84 ± 44.90 vs. 225.32 ± 53.47 μm; P = 0.03) but insignificant difference regarding average

Figure 1



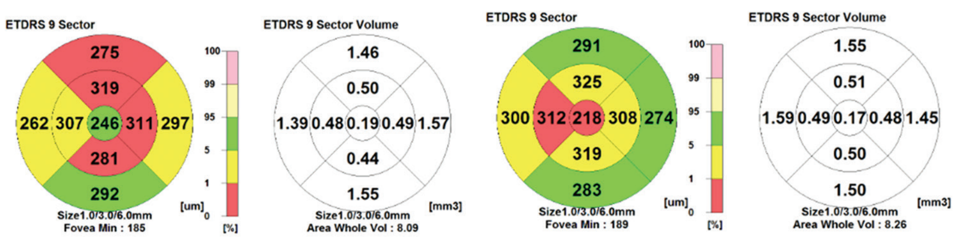
Type of amblyopia in the studied patients.

Table 3 Optical coherence imaging of the macula in amblyopic and normal eyes

	Amblyopic eyes (n=31)	Normal eyes (n=31)	P*
CST (μm)	251.84±44.90	225.32±53.47	0.03*
Macular volume (mm^3)	7.84±0.72	7.94±0.82	0.58

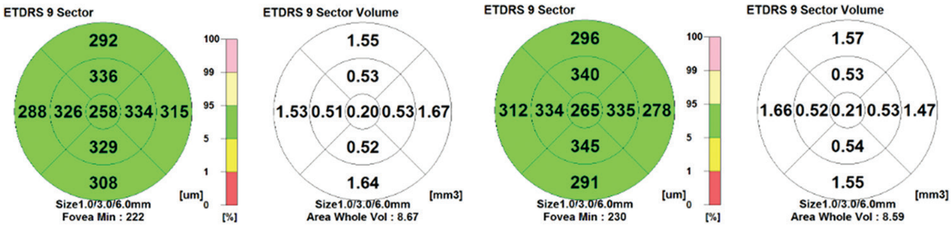
Data are expressed as mean (SD). CST, central subfield thickness. *P<0.05. Student t test was used for comparison.

Figure 2



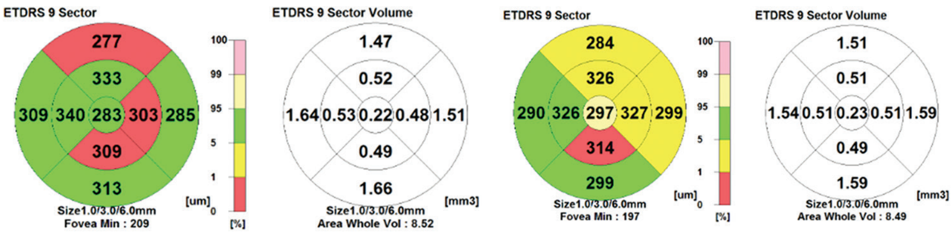
Right macular map of case with right anisometropic myopic amblyopia. Left macular map of case with right anisometropic myopic amblyopia.

Figure 3



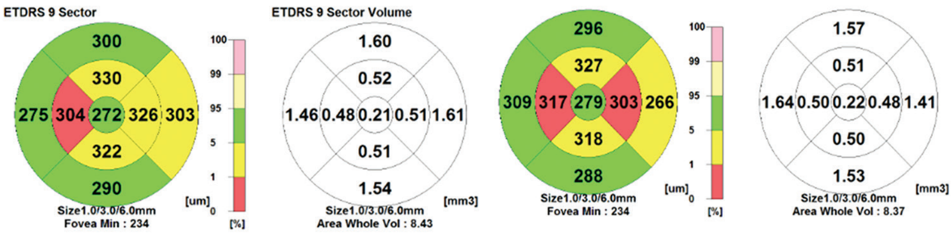
Right macular map of case with right anisometropic hypermetropic amblyopia. Left macular map of case with right anisometropic hypermetropic amblyopia.

Figure 4



Right macular map of case with left strabismic exotropic amblyopia. Left macular map of case with left strabismic exotropic amblyopia.

Figure 5



Right macular map of case with right strabismic esotropic amblyopia, Left macular map of case with right strabismic esotropic amblyopia.

macular volume (7.84 ± 0.72 vs. 7.94 ± 0.82 mm^3; $P = 0.58$) in comparison with their normal fellow eyes. With a special prominence of these results, among the myopic anisometropic group there was significantly higher CST in comparison with its normal fellow eye (268.71 ± 53.55 vs. 227.57 ± 51.87; $P = 0.03$). Although It is thought that the normal macular development could be affected by myopia causing macular dysplasia through the ganglion cell, inner plexiform, and inner nuclear layer potential apoptosis in the macular area [18], this association is only in cases of pathological myopia (myopic spherical equivalent >8 D), which is excluded in our study [19].

These results are consistent with Li *et al.* [20] and Rajavi *et al.* [18], who documented that retinal involvement, especially the macula and thicker foveola, was found in the amblyopic eyes in comparison with control eyes [20]. Aguirre *et al.* [21] also agreed that in moderate to severe amblyopia, the macular thickness was significantly higher compared with their fellow eyes and external controls [21]. Andalib *et al.* [22] also reported that in anisometropic amblyopic eyes the macular thickness was increased, but there were insignificant changes in the strabismic amblyopic group. However, Pang *et al.* [23] focused on patients with high myopic unilateral amblyopia and detected increase in foveal thickness and decrease in inner and outer macular thickness in the amblyopic eye with high myopia in comparison with the fellow sound eye [23]. Altındağ [24] found macular thickness changes in strabismic amblyopia and used that as an early diagnostic method of amblyopia and for early treatment outcome of these cases [24].

Kasem and Badawi reported that there is an increase in central macular thickness and retinal nerve fiber layer thickness in unilateral amblyopic eyes. The precise explanation of these results is still not clear. However, it could be explained by the abnormal postnatal development of the retina and the decline in the number of ganglion cells, which in turn may cause macular changes, such as the displacement of Henle's fibers away from the fovea, so foveal diameter decreases and thickness of fovea increases [25]. On the contrary, Altintas *et al.* [26] had assessed patients with unilateral strabismic amblyopia and stated no differences between the two eyes regarding retinal nerve fiber layer thickness, macular thickness, or macular volume [26]. In line with that were the results of Kee *et al.* [27], who stated that there were no detected changes in the macula and the retinal nerve fiber layer thickness but they had compared amblyopic children with normal ones as external control [27]. The disparity between all of the previous studies may be owing to the variety in the OCT devices, measurement accuracy, different races, various age groups of the participants, wide range of number of participants, and different types of control group either normal group or the normal sound eye of the same patient.

Furthermore, other authors thought that the main detected changes in the amblyopic eye not in the retina itself but it may involve the choroid in the subfoveal region more than the retinal and peripapillary area [28–30].

We found that the axial length was significantly higher among amblyopic eyes (23.59 ± 1.82 vs. 22.81 ± 1.12 mm; $P = 0.04$) in comparison with normal eyes. However, it could be owing to the higher number of myopic patients included in this study, but a direct correlation between axial length and macular parameter could not be detected. Moreover, we could not find a direct relation between the age of the participants and the retinal parameter changes.

Conclusions

Although it was thought that amblyopia only attributed to functional and anatomical changes in the visual cortex and LGN due abnormal visual stimulation, recent studies have found that the amblyopic eye may involve the visual pathway from retina to visual cortex.

In this study, we documented significant increase in the central thickness of the macula and insignificant changes regarding macular volume in amblyopic eyes among cases of unilateral amblyopia in comparison with their fellow sound eyes.

This in turn could be used as an early diagnostic method and prognostic factor for treatment response or resistance.

Financial support and sponsorship

Nil.

Conflicts of interest

No conflicts of interest.

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