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Functional and Anatomical assessment of Amblyopic Eyes

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Abstract

Purpose: To compare peripapillary retinal nerve fiber layer (RNFL) thickness and visual Potential (VEP) of non amblyopic and amblyopic eyes and to correlate between VEP and visual acuity.

Participants: Sixty two patients aged 12 to 30 years with unilateral anisometropic, Strabismic or combined amblyopia presenting to the out patients Clinic OF Mansoura University Ophthalmic Center were include in this study.

Methods: Retinal nerve fiber layer thickness was measured with optical coherence tomography. latency and amplitude of p 100 wave was measured with visual evoked potential (VEP).

Measures: Mean RN FL thickness and latency & amplitude of wave P100.

Results: For the 60 patients (mean age 14±3.5 years) in whom both eyes were. imaged. The median thickness of RN FL of the non amblyopic eye was 98.8 µm (range from 74 -108 µm) and of amblyopic eye was 80.6 µm range from70-95 urn) and the average difference (sound - amblyopic) eye was 18.2 µm The RNFL thickness in the non amblyopic eye was more thicker than that of the amblyopic eye in 58 patients. The revers was noted in only one patient, while in one patient, the thickness in both eyes was the same.
As regards VEP, there was statistically significant decrease of average amplitude of P100 wave of VEP and prolongation of latency of this wave in amblyopic eyes.

Conclusion: Small (but not clinically significant) difference in RNFL thickness was found between amblyopic and non amblyopic eyes, whether the amblyopia was strabismic, ansioametropic or combined. This mean that the defect does not lie in RNFL. In amblyopia the amplitude of pattern reversal VEP was decreased and latency was prolonged.

Keywords: Retinal Nerve Fiber Layer; Amblyopic Eyes; Optical Coherence Tomography

Introduction

For verbal patients, clinical amblyopia is defined as interocular difference of two or more lines in best corrected visual acuity [1]. In addition, amblyopia is defined as best corrected visual acuity in one or both eyes used by abnormal visual experience during critical period of visual development. It is generally attributed to abnormal development of the visual cortex due to strabismus, image blur from refractive error, from deprivation or combination of these factors However, some have suggested that some eyes diagnosed with amblyopia may also have abnormalities in the afferent visual system anterior to th striate cortex, including the retina, retinal ganglion cells. retinal nerve fiber layer (RNFL), optic nerve. and lateral geniculate body of the thalamus [2].

Optical coherence tomography (OCT) is an imaging technology that produces cross- sectional images of the retina and other ocular structures [3,4]. Peripapillary nerve fiber layer NFL thickness as a total measurement of both macular and peripheral NFL has been reported to be the best surrogate marker for the assessment of the optic nerve in patients with glaucoma." Wollstien and associates applied optical coherence tomography to measure peripapillary NFL thickness in glaucoma. It was found that the NFL loss is better and more sensitive than automated visual Field [5]. VEP is a gross electrical signal generated at the visual cortex in response to visual stimulation. YEP reflects the electrical activity of central visual field of the patient. Latency of YEP provides a sensitive means of detecting subclinical lesions of visual pathway [6].

The purposes of this study were to examine the feasibility of OCT testing in amblyopic eyes and to compare of RNFL and VEP between sound and amblyopic eyes and to correlate between visual acuity and VEP.

Patients And Methods

All subjects were recruited from patients aged 12 to 30 years presenting to Outpatient Clinic Mansoura Ophthalmic Center from January 2020 to November 2021. Patients were recruited with the diagnosis of strabismic amblyopia, anisometropic amblyopia or both.

Exclusion Criteria

Patients with myopia in either eye or hypermetropia greater than 5 diopters were excluded that might" have additional diseases. Patients with neurological, metabolic. vascular or other disorders were also excluded.

The diagnosis was confirmed with comprehensive eye examination with pupillary dilation and completion of visual acuity testing. All subjects received a full ophthalmic examination including refraction, best corrected visual acuity. assessment of ocular alignment, slit lamp biomicroscapic examination and dilated fundus examination, OCT and VEP.

RNFL thickness measurement

Measurements of RNFL thickness were obtained with OCT (Topcon, 3D OCT- 1000 USA). low coherence interferometry is used to measure the time delay of backscattered light from of the retina. RNFL is differentiated retinal layers by using thresholding algorithm is measured in an automated fashion.

In this study., three circular samples are taken. disc with a diameter of 3.44 mm. Internal fixation was used in all cases and centration was verified by direct observation of fundus in video - screen. Satisfactory quality was defined as good centration on the optic disk and, signal –noise ratio more than 50. The instrument software calculates average thickness values from the three Scans for each quadrant (superior, nasal, inferior, temporal), each clock hour and the RNFL as a whole.

Visual evoked potential (VEP)

Visual evoked response was obtained with (LKC technologies, Inc. utas –E2000)

The forehead was cleaned by pieces of cotton soaked in alcohol to remove any dirt. Then electrocardiogram (ECG) adhesive electrode was applied to the forehead then a pinch connection was connect to the nipple of ECG electrode (referred to as ground electrode). The ear lobule was scrub by piece of cotton soaked in alcohol then ear clip was filled with gel and applied to it (referred to as negative electrode), while positive electrode is cup. Shaped silver- electrode which was fixed with collodion to back of head (one finger below inion which is projection at middle of back of head) after cleaning of back of head and separation of hair at hair line.

The stimulation was monocular with occlusion of contralateral eye visual stimuli were checkerboard patterns (black and white checker small size, contrast 80%, mean luminance 110 ed.m2 (this luminance was constant to eliminate the effect of stray light on VEP) generated on. television monitor (23.3 cm high x 20.8 cm wide): reversed in contrast at the rate of two reversals per second at viewing distance of 114 cm, 6 mm -red target was placed in the center of the stimulus field to maintain stable fixation. The VEP response is characterized by a series of waves with sub sequential peaks of negative (N) then, positive (P) then negative polarity (N).

Statistical analysis

Data were analysed by SPSS (statistical package for social science). Qualitative data were presented as number and percent. Chi square (x') test of significance was used for comparison. Quantitative data were represented as mean standard deviation, range and median. Krauskal-. Wallis, Munn Whitney and kolmogorov-smimov tests were used for comparison. Spearman's correlation coefficient was used to calculate correlation between variances.

Results

Sixty-two amblyopic patients. 12 to 30 years old were studied. The cause of amblyopia was strabismus (n = 21), anisometropia (n = 12) and combined anisometropia and strabismus (n = 33). The visual acuity was measured. The mean uncorrected acuity of non amblyopic eyes were 0.66 (range from 1-0.5) and of amblyopic eyes were 0.1 (range, from 0.016 to 0.25). The RNFL of all non amblyopic eyes could be imaged, whereas 2 amblyopic eyes couldn't be accurately imaged. The scan path for one patient (strabismic amblyopic) couldn't be centered correctly around the optic nerve image whereas the other patient (combined amblyopia), the scan was of insufficient quality to asses. So, the two patients were excluded from the study. For the 60 patients in whom both eyes were imaged, the mean age was 14±3.5 (Table 1).

Table 1: Demographic data Charactricteristic

Age	**Mean ± SD**	**14± 3.5**
	Range	**12-30**
Gender		
	Female	**27(45%)**
	Male	**33(55)%**

D = standard deviation

The median thickness of non amblyopic eye RNFL was 98.8 μm (range from 74. μ m to 108 μm). The median thickness of amblyopic eye RNFL was 80.6 μm (range from 70 - 95 μm) (Figure 1). The average difference was 18.2 μm (P= 0.2). The non amblyopic eye was 5 μm or more thicker than amblyopic eye in 58 patients, the amblyopic eye was 5 μm or more thicker than the non amblyopic eye in one patient. The thickness in both eyes was the same in one patient. RNFL thickness measurements were recorded for the temporal, inferior, nasal and superior quadrants. The difference between the non amblyopic and amblyopic eyes was small and insignificant (Table 2).

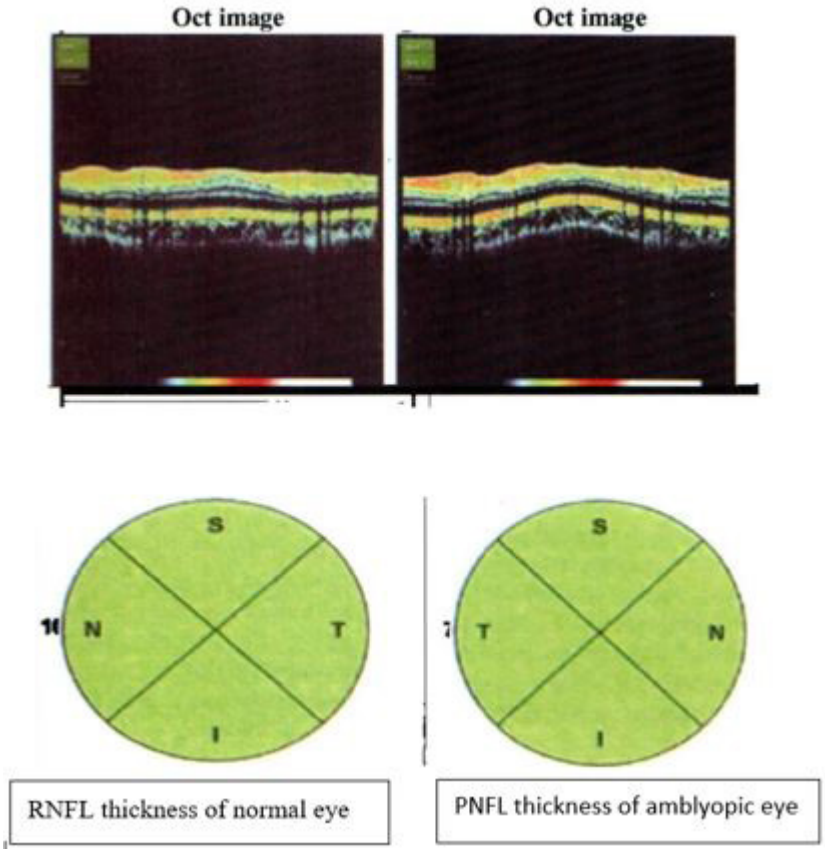

Figure 1: Insignificant difference in RNFL thickness is noted between normal and amblyopic eyes. Normal RNFL thickness in both amblyopic and non amblyopic

Table 2: OCT Measurements among groups in micron

Sound eye	**Median**	**98.8**	**114.9**	**113**	74.75	**66**
	Mean±SD	**90 ± 15**	**110 ± 10**	**109 ± 16**	**70 ± 15**	**60± 14.3**
	range	**74 - 108**	**95 - 130**	**92 - 130**	**52 - 106**	**51 - 100**
Amblyopic eye	**Median**	**80.6**	**101.5**	**95.6**	**62.6**	**57.5**
	Mean±SD	**85 ± 20**	**100 ± 15**	**90± 17**	**60 ± 10**	**55 ± 14**
	range	**70 - 95**	**82 - 134**	**78 - 113**	**42 - 99**	**42 - 71**
Difference	**Median**	**18.2**	**13.4**	**17.4**	**12.55**	**8.5**
(Sound-Amblyopic) amblyopia)	**Mean±SD**	**5±5**	**10 ± 5**	**19± I**	**10± 6**	**5 ± 0.3**
	Range	**4 - 13**	**3 - 13**	**14 - 17**	**7 - 10**	**9 - 29**
P		**0.2**	**().022**	**0.1**	**0.0**	**0.1**
		Average	SUPERIOR	Inferior	Nasal	Temporal

There is insignificant difference in NFLT

As regards the VEP, the median amplitude of p100 of visual evoked potential of the non amblyopic eye was 14 μv (range 10-20 μv) while that of the amblyopic eye was 7μv (range 3-8 μv Table 3 and Figure 2) and the average difference was 7 μv (range 7-12 μv), P= 0.00 I. The median latency of VEP of the sound eyes was 100 ms (range 95 - 110 ms) and of the amblyopic eyes was 120 ms (range 112 - 145 ms) and the difference was 20 ms (range 17- 35 ms) (Table 3).

There was significant prolonged latency & smaller amplitude in amblyopic eyes compared with fellow normal eyes P=0.002.

Table 3: VEP Parameters

YEP parameters		PI00 amplitude	P 100 latency
		μv±	(MS)
Sound	Median	14	100
	Mean ± SD	12± 5	94 ± 10
	range	(10 -20)	(95 -110)
Amblyopic	Median	7	120
	mean± SD	5±4	113± 30
	range	3-8	(112-145)
Difference	Median	7	20
	mean± SD	7±1	19±20
	range	7-12	17-35

There is significant delay in latency in amblyopic eye

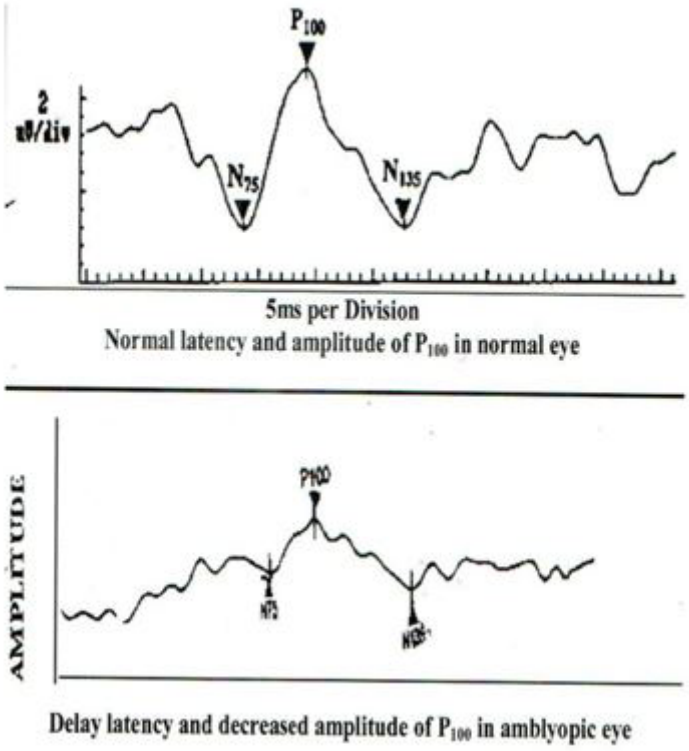

Figure 2: The Difference between normal and amblyopic eyes with VEP

Table 4: correlation between VEP parameters and visual acuity

Visual cuity (V.A)	P100 amplitude	P100 latency
	R=0.8	R=0.3
	P=0.005	P=0.001

R= correlation coefficient. r>5 good correlation, R<5 weak correlation
There is weak correlation between p100 latency and V.A,Strong correlation between VA and amplitude of p100

Table 5: Correlation between VEP parameters and OCT

VEP		RNFL	
P100	amp	R	p
		0.4	0.01
P100	latency	0.3	0.05

There is insignificant correlation between VEP AND OCT Parameters

Discussion

In this study, the non amblyopic eyes of the patients were used as the control to test the hypothesis of a difference between sound and amblyopic eyes. This analysis reduces the effect of age and gender on the comparison.

In this study, RNFL thickness in the peripapillary region of sound and amblyopic eyes was measured employing a technique similar to that used in glaucoma [8,9].

Testing was easily performed despite the reduced acuity of the patients. This varies from the findings of Hess and associates who studied children with glaucoma and found some difficulty in fixation [10].

Small but not statistically significant difference in average NFL thickness between amblyopic and non-amblyopic eyes was found in this study.

This is in agreement with previous reports of NFL thickness in eyes with strabismic amblyopia using scanning laser polarimetry in which there was no clinically important difference between amblyopic and non-amblyopic eyes [11,12].

These research groups did not include anisometropic amblyopia, which has been suggested by lempert to often involve abnormalities of the optic nerve [13]. In addition, Repka et al found small insignificant difference between amblyopic and non-amblyopic eyes [14,15].

Previous studies of OCT and amblyopia reported different results. Yen and associates found the RNFL with OCT to be thicker in amblyopic eyes compared with sound eyes of children with anisometropic amblyopia but no difference in children with strabismic amblyopia [16].

As regards VEP, there was a statistically significant difference between p100 and decrease in amplitude of p100. This component (p100) of pattern - onset VEP was evaluated quantitatively because it is the most commonly measured.17 This prolongation in latency and decrease in amplitude of p100 in amblyopic eyes is in agreement with other studies. Shan et al found that amplitude of VEP was selectively reduced in anisometropic amblyopic eyes [17].

Similiarly, Kryzstkowa, *et al.* [18] found a statistically significant decrease of the amplitude of the amblyopic eye at stimulation with small pattern. Also Hene – petrinovic, *et al.* [19] noticed VEP amplitude side difference (between amblyopic and better fellow eye) were significant, with first positive wave (Pl00) being invariably lower on the amblyopia."

Also, Hamurcu, *et al.* found reduction in p100 amplitude in amblyopic eye compared with control [20-22] In addition, Shawkat, *et al.* [23] and spekreigse, *et al.* [24] found that the amblyopic children showed longer p100 latency than their normal fellow eye.

In contrast, Davis et al found that there was no significant difference in VEP latency or amplitude between amblyopic and fellow eyes across all contrast levels for the early onset amblyopia (i.e starting before age 18 months), but in late onset amblyopia (after 18 months old), latencies were significantly longer and amplitudes smaller in amblyopic eyes [25].

In this study, there was a correlation between visual acuity and amplitude of Pl00. The decrease of V.A. is accompanied by a decrease of Pl00 amplitude, while the change in Pl00 latency did not correlate with visual acuity. Fishman and sokel and other found that the amplitude correlates with visual acuity particularly for small checks size [26,27]. Oncer et al found Pl00 amplitude of P-VEP test parallel the improvement in subjective visual acuity in amblyopic eyes [28].

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