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The Differences of Optical Coherence Tomography (Oct) and Pattern Electroretinogram (P-ERG) in Adult Patients with Anisometropic and Strabismic Amblyopia Might shows a Difference Injure in Visual Pass-Way

Yinglong Li[1,6], Xiaoning Peng[1], Guoke Yang[1], Chen Shao[1], Wei Hu[1], Rongfeng Liao[5], Jiang Jiang[1,6], Shuai Liu[1*] and Wen Wen[2,3,4]

[1]*Department of Ophthalmology, Hefei First People's Hospital, China*
[2]*Department of Ophthalmology and Visual Science, Eye and ENT Hospital, Shanghai Medical College, Fudan University, China*
[3]*Department of Ministry of Health, Key Laboratory of Myopia, Fudan University, China*
[4]*Department of Ophthalmology, Shanghai Key Laboratory of Visual Impairment and Restoration, Fudan University, China*
[5]*Department of Ophthalmology, The First Affiliated Hospital of Anhui Medical University, China,*
[6]*Department of Ophthalmology, BinHu Hospital, China*

Abstract

Objective: To investigate the changes of retinal thickness and P-ERG signals in adult patients with anisometropic and strabismic amblyopia.

Methods: Sixty patients with monocular adult amblyopia, including 30 Anisotropic Amblyopes (AA group) and 30 Strabismic Amblyopes (SA group), were enrolled in our study at the outpatient clinic of The Hefei First Peoples Hospital of Anhui medical University from June 2019 to November 2020. Retinal Nerve Fiber Layer (RNFL) thickness was measured within 3.4 mm diameter range surrounding the optic nerve, and Ganglion Cell Complex (GCC) layer thickness within 6 mm diameter range surrounding the fovea by an Optovue RTVue Optical Coherence Tomography (OCT) in both amblyopic and fellow eyes. The amplitude and latency of P50 and N95 in Pattern-Electroretinogram (P-ERG) were recorded by a Roland electrophysiology instrument under two stimulation conditions with different temporal and spatial frequencies that were designed to bias the parvocellular and magnocellular pathways respectively. Data between amblyopic and fellow eyes was statistically analyzed by paired t test. The correlation between axial length and parameters of OCT and P-ERG was examined by Pearson correlation test.

Results: Changes in RNFL thickness: In the AA group, RNFL thickness in temporal sector was significantly thinner ($p=0.033$), while that in the nasal, superior and inferior sectors increased ($p<0.05$) compared with fellow eyes. In SA group, no significant difference (each sector $p>0.05$) was found between amblyopic eyes and fellow eyes. Changes in GCC thickness compared with fellow eyes, in the AA group, GCC layer thickness of amblyopic eyes was significantly increased ($p=0.039$), whereas in the SA group, we did not find a significant difference between amblyopic eyes and fellow eyes ($p>0.05$). P-ERG stimulated mode biased the parvocellular pathway when compared with fellow eyes ($n=15$), in the AA group, the amplitudes of P50 ($p=0.004$) and N95 ($p=0.038$) were significantly decreased in amblyopic eyes, but no significant latent time difference ($p>0.05$) was found. In the same stimulus pattern, no statistically significant difference ($n=15$, $p>0.05$) between amblyopic eyes and fellow eyes was found in the amplitude and latency of P50 and N95 in the SA group. P-ERG stimulated mode biased the magnocellular pathway the amplitude and latency of P50 and N95 showed no statistically significant difference ($p>0.05$) in either the AA group or the SA group. We found no significant correlation between axial length and OCT, P-ERG parameters ($p>0.05$) in either group.

Conclusion: Our results showed that the alterations in structure and function of retina that could be seen in adult anisometropic amblyopia were not found in adult strabismic amblyopia group. We thought the functional loss in anisometropic amblyopia was more bias to the parvocellular pathway. These findings indicated that the pathological mechanisms were different between anisometropic and strabismic amblyopia.

Keywords: Amblyopia • Anisometropic • Strabismic • Parvocellular pathwaye

Introduction

Abnormal visual input in critical period, commonly due to anisometropia or strabismus, results in amblyopia (mostly unilateral), with an incidence rate of 1% to 5% [1]. Causes for amblyopia include strabismus, anisometropia, form deprivation, and uncorrected refractive errors during the sensitive period of visual system development, but the pathophysiological mechanism of amblyopia is still unclear [2]. Bo Li et al and Wiesel TN [3-4] found that amblyopia could affect the development of lateral geniculate body cells, leading to abnormal cell morphology. These geniculate body neurons are responsible for receiving the eyes' visual signals and project signals onto the visual cortex. Previous Pattern Reversal Visual Evoked Potentials (PVEP) studies also showed that the amplitude and latency time of P100 wave were significantly decreased in amblyopic eyes. These studies revealed that in amblyopia, structural and functional alterations could be seen in the visual cortex and subcortical area.

Are there any structural and functional changes that can be found in the retina in patients with amblyopia? In recent years, the wide application of the Spectral Domain Optical Coherence Tomography (SD-OCT) has made it possible to measure the thickness of the retinal nerve fiber layer [5]. Nishi and Rajavi Z [6-7], with the use of an OCT, found no significant

**Address for Correspondence:* *Shuai Liu, Department of Ophthalmology, Hefei First People's Hospital, China, Email: anhuiliushuai@163.com*

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difference in Retinal Nerve Fiber Layer (RNFL) thickness in patients with anisometropic amblyopia when comparing their amblyopic eyes with the fellow eyes. However, Kasem MA also used OCT to examine children ages 5 to 12 with anisometropic amblyopia and found that these patients' RNFL thickness increased in the amblyopic eyes when compared to the fellow healthy eyes. The above-mentioned research reflects contradictory results of RNFL thickness changes in amblyopic eyes. The present consensus regarding structural changes in the retina of patients with amblyopia mainly focuses on the ganglion cells alternations after birth [8]. The Ganglion Cell Complex (GCC), comprising the nerve fiber layer, ganglion cell layer, and inner plexiform layer, is a good indicator of ganglion cells status. Park and Tugcu measured amblyopic patients' GCC thickness but arrived at opposite results. Park et al. found GCC thickness in amblyopic eyes reduced when compared to fellow healthy eyes. Tugcu on the other hand, found that patients with anisometropic amblyopia had a significant increase in GCC thickness in the amblyopic eyes.

Pattern-Electroretinogram (P-ERG) reflects the function of retina, especially the ganglion cells function. Arden et found that P50 amplitude of amblyopia eyes in 6 to 28 year old patients with anisometropic and ametropic amblyopia is smaller than that of normal control eyes; but other researchers such as Guttob and Hess reported that the amblyopic eyes, comparing to normal control group, showed no significant difference in P-ERG in any type of amblyopia. (Table 1)

Table 1. Characteristics of Two amblyopic groups.

	AE		FE	
	AA	**SA**	**AA**	**SA**
Age	21.32 ± 2.81		22.43 ± 1.47	
Gender (percent female)	52.63%		47.14%	
Race (percent Asians)	100%		100%	
BCVA (log MAR)	0.509 ± 0.330	0.511 ± 0.277	-0.039 ± 0.094	-0.001 ± 0.027
Spherical equivalent	1.75 ± 0.56	-2.00 ± 0.48	-2.13 ± 1.03	-1.79 ± 0.80
AL (mm)	24.2 ± 0.586	24.7 ± 0.443	25.1 ± 0.514	25.4 ± 0.112

AE: amblyopic eye; FE: fellow eye; AA: anisometropic amblyopia group; SA: strabismic amblyopia group; BCVA: best corrected visual acuity; AL: axial length.

Data were presented as Mean ± SD

Whether or not structural or functional changes of the retinal are present in amblyopia has been of interest to many researchers, but results have been conflicting.

With the goal to explore retinal changes of adult amblyopia, we used OCT and PERG to investigate the functional and structural alternations of retinal in anisometropic and strabismic amblyopes.

Subjects and Methods

Participants

30 cases of adult Anisometropic Amblyopia (AA) and 30 cases of adult Strabismic Amblyopia (SA), age 21.35 ± 2.14 years (Mean ± SD), were recruited at the eye outpatient clinic of the Hefei First Peoples Hospital of Anhui medical University from June 2019 to November 2020. All subjects were of Chinese origin with a male to female ratio close to 1:1. The visual acuity of the amblyopic eyes in the AA group was 0.509 ± 0.330 log MAR, and in the SA group, 0.511 ± 0.277 log MAR. The study was approved by the ethics committee of the Hefei First Peoples Hospital of Anhui medical University and followed the Declaration of Helsinki [9-10]. Written informed consent was obtained from all subjects. (Figure 1)

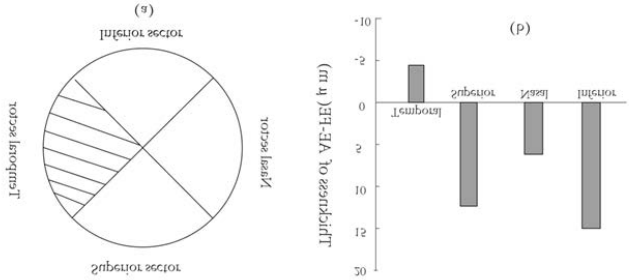

Figure 1. (a): Schemata of amblyopic eyes RNFL thickness in the AA group. The measurement area of RNFL thickness is separated into four sectors: Temporal (T), Superior (S), Nasal (N) and Inferior (I). The striped area represents the sectors in the amblyopic eyes where RNFL thickness is thicker than the contralateral healthy eye.

(b): The Y- axis comes from the thickness of AE subtract FE (mean value, AA group), by a paired t-test, there are statistically significant difference between the AE and FE in AA group. T sector (t=-2.353, p=0.033); S sector (t=3.970, p=0.001); N sector (t=3.307, p=0.005); I sector (t=5.573, p<0.001).

The subjects Best Corrected Visual Acuity (BCVA) in the amblyopic eye was required to be ≥ 0.222 log MAR, and the fellow healthy eyes BCVA was required to be ≤ 0 log MAR. Automatic optometer (Tomey RC-500) was employed and the refraction was measured under cycloplegia. Subjects were excluded if there was any anterior segment, fundus disease, or previous ocular surgery, or if there was any systemic disease that may affect the eyes. Both amblyopic and fellow eye in each subject were required to have normal central fixation.

In the AA group, only subjects with a refractive error difference of spherical power greater than 3.0 D between the two eyes, and cylindrical power difference of greater than 1.0 D, were included. In the SA group, subjects with an inter ocular difference of spherical power ≤ 1.5 D, and cylindrical power difference of <1.0 D, were included. (Figure 2)

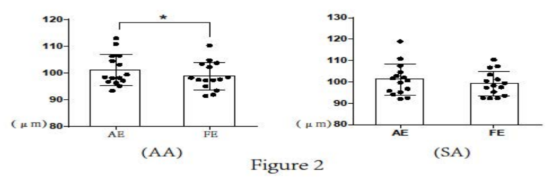

Figure 2. GCC thickness within the 6 mm diameter range surrounding the fovea with the AE and FE represented on the X axis. The Y axis represents the GCC thickness (with error bars). The scatter dots represent all data from the sample. The asterisk shows the significantly statistical difference between the two groups.
AA: GCC thickness in AA patients; SA: GCC thickness in SA patients.
By a paired t test, amblyopic eyes GCC thickness is thicker than that FE (n=15, t=2.264, p=0.039 in the AA group, but in the SA group, there was

no statistically significant difference between two eyes.

Examination methods

Silver chloride skin electrodes were placed on both sides of the lower eyelid and temples as a recording line and forehead acted as a ground reference line. Each stimulus flipped 200 times in a row to be superimposed and recording electrical impedance remained below 5Ω. The recording signal was amplified 50,000 times by the dual differential amplifiers. Filters were set between 1Hz and 30Hz. The computer automatically recorded the steady-state P-ERGs near sinusoidal by Fourier transformation. P50, N95 amplitude and latency were analyzed.

Statistical analysis

Statistical analysis was performed using SPSS 15.0 (SPSS Inc, Chicago, IL). Significant level of P values is ≤ 0.05. OCT and P-ERG parameters were compared by using paired t test. The correlation between the Axial Length (AL) and parameters of OCT, P-ERG was analyzed by using the Pearson correlation test.

Results

Changes in RNFL thickness

In the AA group, RNFL thickness in temporal sector was significantly thinner (p=0.033), while that in the nasal, superior and inferior sectors increased (p<0.05) compared with fellow eyes. In SA group, no significant difference (each sector p>0.05) was found between amblyopic eyes and fellow eyes. Changes in GCC thickness compared with fellow eyes, in the AA group, GCC layer thickness of amblyopic eyes was significantly increased (p=0.039), whereas in the SA group, we did not find a significant difference between amblyopic eyes and fellow eyes (p>0.05). P-ERG stimulated mode biased the parvocellular pathway when compared with fellow eyes (n=15), in the AA group, the amplitudes of P50 (p=0.004) and N95 (p=0.038) were significantly decreased in amblyopic eyes, but no significant latent time difference (p>0.05) was found. In the same stimulus pattern, no statistically significant difference (n=15, p>0.05) between amblyopic eyes and fellow eyes was found in the amplitude and latency of P50 and N95 in the SA group. P-ERG stimulated mode biased the magnocellular pathway the amplitude and latency of P50 and N95 showed no statistically significant difference (p>0.05) in either the AA group or the SA group. We found no significant correlation between axial length and OCT, P-ERG parameters (p>0.05) in either group

Discussion

Ganglion cell development requires the stimulus of a clear optical image. In anisometropic amblyopia, the eyes' refractive state does not allow a clear image to be projected onto the retina. This may affect the normal development of the ganglion cells leading to structural and functional abnormalities, which may in turn affect the photoelectric signal conversion or signal transmission of the retina, resulting in amblyopia development. In strabismus amblyopia patients, neither GCC nor RNFL thickness was significantly different in the amblyopic eyes compared with the fellow eyes, and also no statistically significant difference existed in amplitude and latency of P50 and N95 when compared with the fellow eyes in our study. Our results are consistent with the results of Kee et al. These findings also support the hypothesis that the mechanism of anisometropic amblyopia is different from strabismic amblyopia. Though with some other measurement we may found differences between amblyopic eye and fellow eye in anisometropic amblyopia, but as far as we found is not, and in some other studies the visual pathway damage of strabismic amblyopia may be mainly in the visual cortex, and the retina may be as normal as the fellow normal eyes.

Since the present study enrolled subjects who were all over the age of 18, the confounding factor of age has been excluded in comparison with previous studies. Axial length was not corrected during analysis because the authors did not find a significant difference between the amblyopic eyes and the fellow eyes in AL. No significant correlation between axial length and OCT, P-ERG indicators was established. These results are consistent with the findings of Szigeti A.

Conclusion and Recommendation

In this study, we found that in the amblyopic eyes in patients with anisometropic amblyopia, relative to the fellow healthy eyes, RNFL in the temporal sector was significantly thinner where the maculopapillary bundle is located, whereas RNFL thickness in the nasal, superior and inferior sectors was increased and the mean GCC layer was thickened as well. Functionally, P-ERG showed that the anisometropic amblyopia eyes had a reduction in the amplitude of P50 and N95 under the parvocellular pathway stimulated mode, indicating changes in the function of the retina in patients with anisometropic amblyopia was selective to parvocellular pathway. No statistically significant difference could be seen in OCT and ERG parameters among patients with strabismic amblyopia. These findings also supported the hypothesis that the pathological mechanisms were different between anisometropic and strabismic amblyopia. The visual pathway damage of strabismic amblyopia may be mainly in the visual cortex.

Acknowledgement

None.

Conflict of Interest

We declare that we have no financial or personal relationships with other people or organizations that could inappropriately influence this work.

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