Thicknesses of the Fovea and Retinal Nerve Fiber Layer in Amblyopic and Normal Eyes in Children

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Purpose: This study was designed to assess and compare the thicknesses of the fovea and the retinal nerve fiber layer in normal children and children with amblyopia.
Methods: Optical Coherence Tomography (OCT) was performed on 26 children (52 eyes total) with unilateral amblyopia that was due to anisometropia or strabismus. OCT was also performed on 42 normal children (84 eyes), for a total of 136 eyes. Retinal thickness measurements were taken from the fovea, and the retinal nerve fiber layer thickness measurements were taken from the superior, inferior, nasal and temporal quadrants in the peripapillary region.
Results: The average age of the normal children was 8.5 years, and the average age of the children with amblyopia was 8.0 years. The average thickness of the fovea was 157.4 μm in normal eyes and was 158.8 μm in amblyopic eyes. The difference between the two groups was not statistically significant (p=0.551). The thicknesses of the superior, inferior, nasal and temporal quadrants of the retinal nerve fiber layer between the normal children and the children with amblyopia were also not statistically significant (p=0.751, 0.228, 0.696 and 0.228, respectively). However, for the children with anisometropic amblyopia and the children with strabismic amblyopia, the average thicknesses of the fovea were 146.5 μm and 173.1 μm, respectively, and the retinal nerve fiber layer thicknesses were measured to be 112.9 μm and 92.8 μm, respectively, and these were statistically significant differences (p=0.046, 0.034, respectively).
Conclusions: Normal thicknesses of the fovea and the retinal nerve fiber layers were established, and there were no differences in the fovea and the retinal nerve fiber layer thickness found between normal children and children with amblyopia. *Korean Journal of Ophthalmology 20(3):177-181, 2006*

Key Words: Amblyopia, Foveal thickness, Optical coherence tomography, Retinal nerve fiber layer thickness

Amblyopia is defined as the unilateral or bilateral under-development of visual acuity without any organic abnormality of the globe. Amblyopia is generally detected in 2-5% of the general population,[1] and the current known causalities of amblyopia are abnormal binocular interaction and the deprivation of vision and accurate images. This deprivation can be due to starismus, anisometropia, a difference in refractive error, ptosis, or other abnormalities. 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.[2] Amblyopia is a curable disease if treated early.

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 and the visual cortex.[3] Wiesel and Hubel[4] revealed that in infant cats and monkeys, deprivation of visual stimulation via unilateral lid suture induced anatomical and electrophysiological changes of the lateral geniculate body and the visual cortex. Baddini-Caramelli et al[3] and Wiesel and Hubel[4] also reported that in humans, the ipsilateral lateral geniculate body that developed for the amblyopic eye showed severe atrophy, however, alteration of the anatomical structure of the retina was not detected.

In Korea, Kang et al[5] reported the alteration of the macula thickness in normal adults older than 20 years by performing Optical Coherence Tomography (OCT). Until now, however,

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the thicknesses of the fovea and the retinal nerve fiber layer in children have not been sufficiently measured. In this study, the fovea and the retinal nerve fiber layer thicknesses were assessed in normal children and these were compared with the fovea and retinal nerve fiber layer thicknesses of children with amblyopia performing OCT.

Materials and Methods

This study was performed from January 2004 to May 2004 on 42 normal children (84 eyes) and 26 children (52 eyes) who were diagnosed with unilateral amblyopia. Both groups of children had visited Dongsan Medical Center. The causes of amblyopia in these children were diagnosed as either 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 Han Chun Suk visual acuity charts. Anisometropia was diagnosed in those patients whose spherical equivalence showed 2.0 diopters or greater difference between the two eyes. 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 42 normal children's parents.

To measure the thicknesses of the fovea and the retinal nerve fiber layer, Optical Coherence Tomography from Zeiss (OCT version 3.0, Zeiss Humphrey, Dublin, USA) was used. The measurement of the fovea and the retinal nerve fiber layer thickness was performed by the same examiner. Prior to the examination, the pupils were dilated with alcaine, 1% cyclogyl or atropine, and phenylephrine to measure the thicknesses of the fovea and the retinal nerve fiber layer and to identify the presence of anisometropia.

To measure the thickness, the examiner focused a scanning beam on the fovea by inspecting the fundus with an infrared sensing camera. Subsequently, the images were obtained by performing a macula scan. The macula scan consisted of 6 radial scans that had the maximal 1,024 pixels focused on the fovea, and each scan was rotated by a 30 degree interval. Using the images obtained by the 6 scans, the macular thickness map equivalent to a central 20 degrees of vision (a 6-mm diameter map) or to a central 10 degrees of vision (a 3.45-mm diameter map) was then prepared for each eye. The thick areas of the retina appeared as bright colors (white and red) and the thin areas appeared as dark colors (blue and black).[6,7] The map of the macula thickness was composed of three concentric circles: a central circle, an inner ring and an outer ring. In the case of the 6-mm diameter map, the diameters of the concentric circles were 1 mm, 3 mm, and 6 mm, and in the case of the 3.45-mm diameter map, the diameters of the concentric circles were 1 mm, 2.22 mm and 3.45 mm. In addition, each concentric circle was divided again into 4 quadrants and this is shown as 9 sections. The location of the vitreoretinal interface and the retinal pigment epithelium defined the inner and outer boundaries. These two boundaries were generated by the high contrast in the optical reflectivity between the relatively nonreflective vitreous and the reflective neurosensory retina and between the minimally reflective photoreceptor outer segments and the highly reflectively retinal pigment epithelium.[7,8] The distance between photoreceptor outer segments and retinal pigment epithelium was defined as the thickness of retina. In this study, by using a 6-mm diameter map, measurements from a total of 10 areas, including the fovea, were obtained in μm units: All children were measured three times, and their average values were obtained.

The statistical analysis for the comparison of the fovea and the retinal nerve fiber layer thicknesses between the normal children and the children with amblyopia was performed using the Dunnet test, ANOVA and a post-hoc procedure. P values less than 0.05 were considered to be statistically significant.

Results

The population of normal children used in this study contained 21 males and 21 females, and their mean age was 8.5 years (age range: 4-17 years). The population of children with amblyopia included 14 males and 12 females, and their mean age was 8 years (age range: 4-12 years). The cause of amblyopia was identified as anisometropia in 15 cases, strabismus in 6 cases, and a mix of the two in 5 cases. Of the patients with anisometropia, hyperopia was noted in 5 cases and myopia was noted in 10 cases. Among patients with strabismus, esotropia was noted in 3 cases and exotropia

Table 1. Clinical data of the 26 amblyopic patients

	No. of patients	Diagnosis	No. of patients
Anisometropia	15	Spherical hyperopia	5
		Spherical myopia	10
Strabismus	6	Esotropia	3
		Exotropia	3
Mixed	5	Spherical hyperopia+ Exotropia	2
		Spherical myopia+ Exotropia	3

Table 2. Retinal nerve fiber layer thickness (μm) in normal and amblyopic patients

	Normal	Amblyopic patients	p value
Superior	134.8±22.5	135.5±25.2	0.751
Inferior	136.7±20.8	134.2±23.2	0.228
Nasal	77.6±20.5	76.8±21.0	0.696
Temporal	82.7±16.1	82.4±17.0	0.228
Total	108.8±11.3	107.2±16.2	0.615

Table 3. Retinal nerve fiber layer thickness (μm) in the amblyopic patients

	Normal eyes	Amblyopic eyes	p value
Superior	142.3±20.5	135.5±25.2	0.055
Inferior	132.5±11.5	134.2±23.2	0.262
Nasal	77.8±17.9	76.8±21.0	0.458
Temporal	86.3±16.5	82.4±17.0	0.307
Total	106.7±16.5	107.2±16.2	0.810

Table 4. Fovea and retinal nerve fiber layer thicknesses (μm) in amblyopic eyes of 15 anisometropic and 6 strabismic amblyopia patients

	Anisometropic amblyopia	Strabismic amblyopia	p value
Fovea thickness	146.5±26.2	173.1±34.1	0.046
NFL* thickness	112.9±10.8	92.8±25.2	0.034

*: nerve fiber layer.

was noted in 3 cases. In the mixed cases, there were 2 cases in which anisometropic hyperopia and exotropia were concomitantly present, and there were 3 cases in which anisometropic myopia and exotropia were concomitantly present (Table 1).

The mean total thickness and thicknesses of the four quadrants of the retinal nerve fiber layer from the normal children and the children with amblyopia are shown in Table 2. There was no statistically significant difference found when comparing the thickness of the retinal nerve fiber layer of the normal children and that of the children with amblyopia.

In the normal fellow eye of the children with amblyopia, the mean total thickness and thicknesses of the four quadrants of the retinal nerve fiber layer are shown in Table 3. There were no statistically significant difference between the thickness of the retinal nerve fiber layer of the normal fellow eyes and that of the amblyopic eyes in the children with amblyopia.

The mean age of the children with anisometropic amblyopia and strabismic amblyopia was 6.3 years and 8 years, respectively. The mean thicknesses of the fovea and the retinal nerve fiber layer of the amblyopic eyes of the children with anisometropic amblyopia and strabismic amblyopia are shown in Table 4, and there was a statistically significant difference.

Discussion

Currently, the causative mechanism of amblyopia is thought to be the lack of adequate visual stimulation to the fovea during infancy, the abnormal binocular interaction or incongruency of visual information received by the two eyes, or a mixture of these problems.[9] 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.[10] von Noorden et al[11] 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 the based on animal experiments by Rasch et al[12] and Chow et al,[13] internal plexiform layer thinning and nucleolar volume diminution in the ganglion cell cytoplasm were demonstrated, and Chow[14] reported the reduction in optic nerve size. von Noorden et al[15] 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 Huble[4] 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[3] 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[16] Kanai et al[17] measured 47 eyes in 47 cases by performing OCT and reported the fovea thickness as 142±15 μm. Ling et al[18] reported 146.34±8.58 μm in 60 cases with 120 eyes, Gobel and Kretzchmar-Gross[19] reported 153±15 μm in 60 cases with 120 eyes, and Hee et al.[6] have reported 174±18 μm in 41 cases with 73 eyes. Comparing the fovea thickness of the 42 normal children (84 eyes) in our study (mean age: 8.5 years) to these data, our result was thicker than Kanai's measurement,[17] similar to Gobel and Kretzchmar-Gross's measurement,[19] and thinner than Hee's measurement.[6] 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. Hence, further studies on these issues are required.

Varma et al[20] reported that in 312 individuals whose mean age was 52 years (age range: 40-79 years), the total thickness of the retinal nerve fiber measured by OCT was 132.7±14.4 μm, and thicknesses of the superior, inferior, nasal and temporal quadrants were 157.7±17.8 μm, 159.8±18.9 μm, 109.3±19.1 μm, and 102.5±19.0 μm, respectively, showing thickness in the superior and the inferior quadrants and thinness in the temporal and the nasal quadrants. Schuman et al,[21] Bowd et al,[22] and Liu et al[23] reported that the nasal quadrant is thinner than the temporal quadrant. In our study, compared with the thickness of the retinal nerve fiber layer of normal children whose mean age was 8.5 years, the superior and the inferior quadrants were thicker than the temporal and the nasal quadrants, and the nasal quadrant was thicker than the temporal quadrant, which is consistent with above the mentioned studies.[20-22]

Baddini-Caramelli et al[3] 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, and the thickness of the superior and the inferior quadrants of the amblyopic eyes and the normal eyes was 74.71±15.67 μm, 76.29±15.51 μm, 84.52±17.19 μm and 83.43±17.01 μm, respectively, showing no statistically significant difference. Colen et al[24] 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[25] 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. In our study, in the comparison of the retinal nerve fiber layer thickness of the amblyopic eyes and the normal fellow eyes in 26 children with amblyopia (mean age: 8 years), the difference was not statistically significant between the amblyopic eyes and the normal fellow eyes. The results are in agreement with those reported by Baddini-Caramelli et al[3] and Colen et al[24] but are different from the results reported by Yen et al.[25] To clarify whether the cause of such a difference is due to the measurement error among examiners, the difference between scanning laser polarimetry and OCT, or the difference in subjects' age, comparison studies having a larger number of subjects with more diverse ages are required.

In our study, the thickness of the fovea and the thickness of the retinal nerve fiber layer of the amblyopic eyes of the 15 children with anisometric amblyopia (mean age: 6.3 years) and the 6 children with strabismic amblyopia (mean age: 8 years) were compared, and it was found that the fovea was thicker in the children with strabismic amblyopia while the retinal nerve fiber layer was thicker in the children with anisometric amblyopia. In relation to this, Yen et al[25] reported that the difference in thickness of the fovea and the retinal nerve fiber layer according to type of amblyopia is due to the different mechanisms responsible for the development of amblyopia. To assess these different mechanisms via the examination of visual functions, hyperacuity studies using the vernier acuity are frequently conducted. The vernier acuity associated with cerebral function is not affected in anisometric amblyopia as the retinal images are optically blurred, but this acuity is a severely decreased in patients with strabismic amblyopia.[10] In addition, during the measurement of the vernier acuity in strabismic amblyopia, a crowding effect was detected that was absent in those patients with anisometric amblyopia.[2] This might explain the difference in the thickness of the fovea and the retinal nerve fiber layer according to type of amblyopia. Nevertheless, histological studies are needed to see whether the difference of the thickness has a clinical significance, and further studies with a larger number of children with amblyopia are also required.

The limitations of this study are that, in the comparison among children with amblyopia, the number of children with strabismic amblyopia was small. In the future, studies on the correlation between refractive error and the thicknesses of the fovea and the retinal nerve fiber layer according to spherical equivalence in children with anisometric amblyopia are required.

There were no statistically significant differences in the thicknesses of the fovea and the retinal nerve fiber layer between the normal eyes of normal children, the amblyopic eyes of children with amblyopia, or normal fellow eyes of the children with amblyopia. Therefore, it was found that amblyopia does not have an effect on the thickness of the fovea and the retinal nerve fiber layer. 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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