

Fusion and stereopsis in children with refractive amblyopia

Fusión y estereopsis en niños con ambliopía refractiva

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Abstract

Objective: To determine the binocular function in patients with refractive amblyopia. **Method:** Cross-sectional study in patients between 5 and 18 years old with refractive amblyopia treated for the first time in the pediatric ophthalmology and strabismus consultation of the Instituto Cubano de Oftalmología Ramón Pando Ferrer. **Results:** No significant correlation was found between the depth of amblyopia and the magnitude of anisometropia in the right eye ($p = 0.217$) or in the left eye ($p = -0.130$), and neither between the magnitude of anisometropia and stereopsis ($p = 0.260$). Patients with isoametropic amblyopia reached a subnormal stereopsis $>100''$ in 53.3%. **Conclusions:** There is no association between the magnitude of anisometropia and the depth of amblyopia, fusion and stereopsis. In most patients with refractive amblyopia, stereopsis is deteriorated, thus affecting binocular function.

Keywords: Amblyopia Anisometropia. Isoametropia. Stereopsis. Fusion.

Resumen

Objetivo: Determinar la función binocular en pacientes con ambliopía refractiva. **Método:** Estudio transversal en pacientes entre 5 y 18 años con ambliopía refractiva atendidos por vez primera en la consulta de oftalmología pediátrica y estrabismo del Instituto Cubano de Oftalmología Ramón Pando Ferrer. **Resultados:** No se halló correlación significativa entre la profundidad de la ambliopía y la magnitud de la anisometropía en el ojo derecho ($p = 0.217$) ni en el ojo izquierdo ($p = -0.130$), y tampoco entre la magnitud de la anisometropía y la estereopsis ($p = 0.260$). El 53.3% de los pacientes con ambliopía isoametrópica alcanzaron una estereopsis subnormal $> 100''$. **Conclusiones:** No se presenta asociación entre la magnitud de la anisometropía y la profundidad de la ambliopía, la fusión y la estereopsis. En la mayoría de los pacientes con ambliopía refractiva se deteriora la estereopsis, afectándose así la función binocular.

Palabras clave: Ambliopía. Anisometropía. Isoametropía. Estereopsis. Fusión.

Introduction

Amblyopia is derived from the Greek word *amblyos*, which means "lazy, clumsy" and *ops*, meaning "eye" for what is commonly called "lazy eye".¹

Over the years it has had numerous definitions²⁻⁶ according to the different authors and the study objectives, but the vast majority agree that amblyopia is "a visual deficit with no organic or anatomical cause to justify it."

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An uncorrected refractive error is the main cause of visual impairment (43%), followed by cataract (39%)⁷. An early and undiagnosed refractive error in early childhood can lead to a reduction in visual acuity. Visual development is a process that requires adequate visual stimulation in the first years of life, which can be interrupted by the presence of non-physiological refractive disorders that produce a blurred image, favoring the development of refractive amblyopia. The detection of refractive errors from an early age is important to make the decision on whether or not to prescribe the refraction, for which the age and amount of the refractive error must be taken into account, based on correction guidelines that vary according to different authors^{2,3-8}.

Naidoo, et al.⁹ point out that uncorrected refractive errors were the cause of visual impairment in 101.2 million people and 6.8% of blindness in 2010.

It is estimated that worldwide there are 285 million people with some type of visual impairment, of which 19 million are children under 14 years of age^{7,10}. A total of 153 million people in the world have visual disturbances secondary to uncorrected refractive errors, and of these, 12.8 million are children between the ages of 5 and 15¹⁰.

Binocular single vision is the state of simultaneous vision, achieved by the coordinated use of both eyes, from two retinal images that are fused by motor and sensory processes that culminate in the perception of a single image in stereoscopic depth. The main advantage of binocular vision is the single vision that results in stereopsis¹¹.

Binocular single vision is divided into three degrees of fusion^{1,12}:

- First degree: simultaneous macular perception, in which both eyes receive the image at the same time.
- Second degree: fusion (ability of the visual cortex to fuse the images received by each eye into a single image); it can be sensory or motor.
- Third degree: stereopsis.

To evaluate the state of binocular function, fusion and stereopsis are considered. In the case of fusion (second degree of binocular vision), Worth's lights are used, and for the exploration of stereopsis (third degree of binocular vision), the Titmus test.

Achieving quality vision not only depends on achieving 20/20 visual acuity in distance vision, but also on having good contrast vision and adequate stereopsis. Stereopsis enables simple depth perception and is considered the only property of binocular vision that allows the perception of depth and solidity in visual space. In

people with normal visual acuity, it is around 40 or 60"¹³.

As levels of anisometropia vary, suppression and stereopsis change. Normal development allows good binocular vision. Blurred vision at an early age causes a particular pattern of functional loss that leads to sub-normal binocular vision.

The objective of this study was to determine binocular function in patients with refractive amblyopia, relating the magnitude of anisometropia with the depth of amblyopia, fusion and stereopsis, as well as determining fusion and stereopsis in patients with isoametropic amblyopia.

Methods

A cross-sectional study was carried out in 27 patients (54 eyes) with refractive amblyopia who were taken by their parents for the first time to the pediatric ophthalmology and strabismus department of the Instituto Cubano de Oftalmología Ramón Pando Ferrer, during the period between July and December of 2019. The small sample size was due to the inclusion and exclusion criteria, as the research was affected by the COVID-19 pandemic.

We included children between 5 and 18 years old, whose legal guardians voluntarily agreed to participate in the study, with a best-corrected visual acuity (BCVA) of 20/30 (0.18 logMAR) or less in one or both eyes, or a difference of at least 2 logMAR lines, that had not previously received any prescription, with the following refractive errors: myopia ≤ -0.50 D, hyperopia ≥ 0.50 , astigmatism ≥ 0.50 D and anisometropia ≥ 1 D. Patients with allergy to cycloplegics, presence of any ocular disorder that decreased visual acuity (surgical aphakia, pediatric cataract, palpebral ptosis), mental retardation, infantile cerebral palsy or Down syndrome were excluded.

Amblyopia was divided by type into isoametropic (AI, refractive error of equal magnitude in both eyes) and anisometropic (AA, interocular difference of spherical or cylindrical refractive error of 1 D or more)¹⁴.

Depth of amblyopia was based on BCVA measured with the Snellen chart and converted to logMAR. The classification scale used was: mild, 20/30-20/40 (0.18-0.30 logMAR); moderate, >20/40-20/80 (0.30-0.60 logMAR); and severe, >20/80 (0.60 logMAR)³.

The magnitude of anisometropia was classified as mild, 1.00-3.00 D; high, >3.00-6.00 D; and very high, >6.00 D¹⁵.

For stereopsis evaluation, the Titmus test (Stereo Optical Co., Inc., Chicago, IL, USA) was used, despite the monocular cues, as it is easier to interpret in children. Stereopsis was examined at near distance (40 cm), with optical correction and polarized glasses, and it was classified as normal up to 40", subnormal >40-100" and abnormal >100", according to the classification used by Sapkota¹⁶.

Fusion was explored with Worth four light test (Worth 4-Dot Attachment, Richmond Products, Albuquerque, NM, USA), at 6 m, with red-green lenses (Original Bernell Model Red/Green Goggles; Bernell VTP, Mishawaka, IN, USA), over the corrected refractive defect. We established sensory fusion if the patient saw all four lights and suppression if they saw three green lights or two red lights.

To carry out this work, data from the patient's medical records were taken. The information was entered by the primary investigator in a spreadsheet prepared for this purpose.

The study began by interviewing patients, specifying age, previous ocular consultations and treatments, followed by the determination of BCVA and performance of the alternate cover test and the near and far cover-uncover test with an accommodative target to detect any deviation in primary gaze position.

Subsequently, the cycloplegic refraction was evaluated with a TOPCON KR8800 Auto Kerato-Refractometer, a trial box and frame, and finally corroborating the refraction by retinoscopy.

Finally, biomicroscopic examination of the anterior segment and indirect ophthalmoscopy were performed to assess the optic disc, the retinal vessels and the macula, and rule out any ocular alteration that may affect visual acuity.

Seven days after the first visit, BCVA was verified with the Snellen chart and converted into logMAR according to the visual acuity conversion chart, and patients with a visual acuity of 20/30 or less (0.18 logMAR) in one or both eyes were selected.

The aforementioned process was carried out in each patient who participated in the study, in order to obtain the refractive defect at the time of entry in the database, to classify it and define the type of amblyopia.

With the refractive defect corrected, the study of stereopsis and fusion was carried out.

After collecting primary data, they were organized in Microsoft Excel to later be exported to the SPSS version 22 program. The variables that were measured in a nominal and ordinal way were expressed in absolute and relative frequency, while for the

Table 1. Distribution of the eyes according to the depth and type of amblyopia

Depth of amblyopia	Anisometropic amblyopia (n = 12)		Isoametropic amblyopia (n = 15)	
	OD (%)	OS (%)	OD (%)	OS (%)
Mild	1 (8.3%)	5 (41.7%)	11 (73.3%)	11 (73.3%)
Moderate	2 (16.7%)	4 (33.3%)	4 (26.7%)	4 (26.7%)
Severe	2 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Total	5 (41.7%)	9 (75.0%)	15 (100%)	15 (100%)

OD: right eye; OS: left eye.

metrics the mean, standard deviation and the minimum and maximum values were determined. Spearman's rank correlation coefficient (ρ) and contingency coefficient (C) were applied, and a confidence level of 95% was defined ($p = 0.05$).

The bioethical principles were met (in accordance with the provisions of the National Health System and provided for in Law No. 41 on Public Health) and the study was approved by the scientific and ethics committees of the Instituto Cubano de Oftalmología Ramón Pando Ferrer, in accordance with the principles of the Declaration of Helsinki. For the development of the study, we obtained the informed consent of the guardians of the children who participated in the research, a document in which the principles of benefit of the procedure and legality of the work are exposed, as well as the autonomy of the patients to decide to participate or withdraw from the study.

Results

Of the 27 children with amblyopia included in the study, AI was found in 15 (55.6%) and AA in 12 (44.4%).

Table 1 shows the distribution of the eyes according to the depth and type of amblyopia. In AA, a predominance of left amblyopic eyes is observed (nine for 75%), of which five showed mild amblyopia and four moderate, for 41.7% and 33.3%, respectively. In the five amblyopic right eyes, a similar distribution of moderate and severe amblyopia was observed, in two eyes each, for 16.7%; only one eye (8.3%) had mild amblyopia.

In AI, mild amblyopia prevailed in 11 right eyes and 11 left eyes, with 73.3%, followed by moderate in four right and left eyes, for 26.7%.

Table 2 shows the distribution of right and left eyes according to anisometropia magnitude and

Table 2. Distribution according to the magnitude of anisometropia and depth of amblyopia

Depth of amblyopia	Magnitude of anisometropia							
	Mild		High		Very high		Total	
	OD	OS	OD	OS	OD	OS	OD	OS
Mild								
n	1	5	0	0	0	0	1	5
% (n ₃)	20	55.5	0.0	0.0	0.0	0.0	20	55.5
% (n ₁)	8.3	41.7	0.0	0.0	0.0	0.0	8.3	41.7
Moderate								
n	1	2	1	2	0	0	2	4
% (n ₃)	20	22.2	20	22.2	0.0	0.0	40	44.4
% (n ₁)	8.3	16.7	8.3	16.7	0.0	0.0	16.7	33.3
Severe								
n	1	0	0	0	1	0	2	0
% (n ₃)	20	0.0	0.0	0.0	20	0.0	40	0.0
% (n ₁)	8.3	0.0	0.0	0.0	8.3	0.0	16.7	0.0
Total								
n	3	7	1	2	1	0	5	9
% (n ₃)	60	77.8	20	22.2	20	0.0	100	100
% (n ₁)	25	58.3	8.3	16.7	8.3	0.0	41.7	75

OD: right eye; OS: left eye.

n1: total number of patients with anisometropic amblyopia (12); n3: total number of eyes with anisometropic amblyopia (5 for right eye and 9 for left eye).

Table 3. Distribution of patients according to the magnitude of anisometropia and fusion

Fusión	Magnitud de la anisometropía			Total
	Mild	High	Very high	n (%)
	n (%)	n (%)	n (%)	
Sensory fusion	8 (66.7%)	2(16.7%)	1 (8.3%)	11(91.7%)
Supression	0 (0%)	1(8.3%)	0 (0%)	1(8.3%)
Total (n ₁ = 12)	8 (66.7%)	3(25.0%)	1(8.3%)	12(100%)

n₁: total number of patients with anisometropic amblyopia (12 for right eye and left eye).

amblyopia type. Of the five amblyopic right eyes, three had a magnitude of mild anisometropia <3.00 D, one moderate and the other one severe (20% each). One eye with a high magnitude of anisometropia had moderate amblyopia, and the eye with a very high magnitude (> 6.00 D) had severe amblyopia (20%). Of the seven left eyes, five (55.5%) had a mild magnitude of anisometropia and two (22.2%) moderate. However, the two eyes with high magnitude had moderate amblyopia. No statistically significant correlation was observed between the depth of amblyopia and the magnitude of anisometropia in right eye ($\rho = 0.249$; $p = 0.217$), nor in the left eye ($\rho = 0.344$; $p = -0.130$).

The binocular function evaluated in these patients included fusion and stereopsis. Tables 3 and 4 show

that there was fusion in all patients except in one 9-year-old with high anisometropia, who had subnormal stereopsis (between 40" and 100"); however, the patient with very high anisometropia had fusion and abnormal stereopsis. In these patients, no statistically significant correlation was observed between the magnitude of AA and fusion with the contingency coefficient test ($C = 0.463$; $p = 0.195$), or between the magnitude of AA and the level of stereopsis with the Spearman's correlation test ($\rho = 0.206$; $p = 0.260$).

Table 5 shows that, of the 15 patients with AI, eight (53.3%) had a subnormal stereopsis >100". Of them, five had a high refractive error, two moderate and one mild; the latter was a patient with mild astigmatism who had an elevated spherical equivalent of 8.13.

Table 4. Distribution of patients according to the magnitude of anisometropia and stereopsis

Estereopsis	Magnitude of anisometropia			Total n (%)
	Mild	High	Very high	
	n (%)	n (%)	n (%)	
Normal < 40"	2 (16.7%)	0 (0%)	0 (0%)	2 (16.7%)
Subnormal 40-100"	1 (8.3%)	1 (8.3%)	0 (0%)	2 (16.7%)
Anormal > 100"	5 (41.7%)	2 (16.7%)	1 (8.3%)	8 (66.7%)
Total (n ₁ = 12)	8 (66.7%)	3 (25.0%)	1 (8.3%)	12 (100%)

n₁: total number of patients with anisometropic amblyopia (12 for right eye and left eye).

Table 5. Fusion and stereopsis in isoametropic amblyopia

	Isoametropic amblyopia (n = 15) n (%)
Fusion	
Sensory fusion	15 (100%)
Suppression	0 (0%)
Total	15 (100%)
Stereopsis	
Normal < 40"	1 (6.67%)
Subnormal 40-100"	6 (40%)
Abnormal > 100"	8 (53.33%)
Total	15 (100%)

Discussion

In this study, we observed that the mean age at the first consultation was 8 years for AA and 6.73 years for AI, which is considered a late age, since it is almost at the end of the period of sensitivity, which is up to 8 years. This is due to a carelessness of the parents, since the country has an ophthalmological examination system from birth that includes a complete ophthalmological examination at birth, at 6 months, and at 1, 3 and 5 years before starting the school year, which is repeated every 2 years and varies according to the criteria of the ophthalmologist who does the examination.

Regarding the prevalence of amblyopia according to the degree of depth, Istek¹⁴ found moderate amblyopia (59.4%) more frequently, followed by severe (31.2%) and mild (9.4%). Sapkota¹⁶ found a predominance of severe amblyopia (46%), followed by moderate (41%), without finding a statistically significant association between the depth of amblyopia and the type of refractive error. This is not consistent with what we found in our study, where mild and moderate amblyopia predominated in AA, and mild amblyopia was predominant in AI.

Some studies have not found an association between the magnitude of anisometropia and the depth of amblyopia¹⁷⁻¹⁹, which coincides with our study, in which when comparing the depth of amblyopia with the magnitude of anisometropia in patients with AA in the right and left eyes, no significant correlation was found ($p = 0.217$ and $p = 0.344$, respectively).

Sapkota¹⁶ and Rutstein and Corliss²⁰ found that the depth of amblyopia was related to the magnitude of anisometropia: the greater the magnitude of the anisometropia, the greater the risk of severe amblyopia.

Istek¹⁴ found that a difference in refractive error of 0.75 for astigmatism between both eyes or 1.50 for spherical defect was enough to develop amblyopia.

Binocular vision is important in the visual perception of the environment. Stereopsis occurs when images with horizontal disparity are placed in corresponding retinal areas in each eye simultaneously, and the fusion of those images results in stereoscopic acuity with depth perception.

Normal visual neurodevelopment is not established if there is a condition that interferes with binocular sensory fusion, such as a refractive error that causes blurring of the retinal image and if this condition occurs early.

Decreased binocular sensory fusion presents clinically as suppression or reduced stereoacuity²¹.

Chen, et al.¹⁵ suggest that binocular function, including fusion and stereopsis, decreases markedly as the magnitude of anisometropia increases. This may be associated with aniseiconia, which interferes with binocular vision. A degree of anisometropia >3.00 D resulted in suppression and subnormal stereopsis >40-100. With an anisometropia >6.00 D, only 16.67% had fusion and 8.33% stereopsis, being the latter more severely affected.

Jeon and Choi²² point out that stereopsis was significantly worse in the group with anisometropic amblyopia

(AA) than with anisometropia without amblyopia (NA) and in the control group; only 57.2% had a normal stereopsis in the AA group. They found a significant relationship between the degree of anisometropia and the level of stereopsis in amblyopic and non-amblyopic anisometropic patients ($p = 0.028$); however, the group with amblyopia did not show a significant correlation between the degree of anisometropia and the level of stereopsis ($p = 0.692$).

Tomac and Birdal²³ demonstrated the relationship between stereoacuity and the strength of fusion, and they state that, if fusion is weak, stereopsis decreases in proportion to the amblyopia; only 14.3% of the group with amblyopia had sensory fusion.

Rutstein and Corliss²⁰, and Jeon and Choi²² found that AA patients have better binocular function than that reported by experimental studies such as that of Brooks, et al.²⁴.

Levi, et al.²⁵ found that binocular function develops normally in anisometropies <3.00 D, but in >3 D, and mainly in >6.00 D, fusion and stereopsis are seriously affected.

This is consistent with experimental studies that indicate that 1 D anisometropia reduces stereoscopic visual acuity from 40 "to 85", and 3 D anisometropia produces a marked reduction in stereopsis in all subjects.

Yang, et al.²⁶ found that hyperopia or a spherical equivalent $>+3.00$ D is associated with a reduction in stereoacuity in the Titmus test, but this is not the case with spherical or astigmatic anisometropia.

In another study in preschool children, it was shown that a large percentage of patients with anisometropia had worse stereoacuity^{18,27}; however, in a more recent study, Lee, et al.²⁸ found an almost normal level of stereopsis in patients with anisometropia without amblyopia using their optical correction, suggesting that optical correction is the best treatment option to ensure optimal visual development in these children.

In this study, it was observed that in AA, binocular function does not develop normally in anisometropia <3.00 D, since from the eight (66.77%) patients who were in the mild group, five (41.7%) had an abnormal stereopsis $>100''$. Of the three patients with high magnitude AA, two had an abnormal stereopsis and one a subnormal stereopsis between 40" and 100". The only patient with high magnitude AA had a stereopsis $>100''$. There was no significant correlation between the magnitude of AA and fusion ($p = 0.195$), nor between the magnitude of AA and stereopsis ($p = 0.260$).

In the AI group, despite not having fusion alterations in any patient, eight had an abnormal stereopsis $<100''$.

Differences in results with other studies may be related to the small number of patients and the short time for participants selection. In this study, no association was found between the magnitude of AA and the depth of amblyopia, fusion, and stereopsis, and in most patients with refractive amblyopia, stereopsis was deteriorated and binocular function was affected.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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