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Evaluation of Stereoacuity and Binocular Functions in Patients with Anisometropic Amblyopia Through Titmus, TNO, and Synoptophore

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Abstract

Introduction: The aim of the study was to evaluate the effect of amblyopia on binocular functions in patients with anisometropic amblyopia.

Methods: This prospective study was conducted on 45 patients with anisometropic amblyopia. The difference between the best-corrected visual acuities of the two eyes (DVA) for the depth of amblyopia, the spherical equivalent difference between two eyes (D-SE) and root-mean-square spherical equivalent (RMS-SE) for the degree of anisometropia, the Titmus and the TNO tests for the stereoacuity and synoptophore for the fusion capabilities was used.

Results: The mean age was 21.44±7.45 years. Twenty-three patients had moderate-severe amblyopia and 22 had mild amblyopia. There was a correlation between D-SE and TNO and RMS-SE and TNO in the mild group; DVA and Titmus, DVA and TNO, and RMS-SE and Titmus in the moderate-severe group; DVA and RMS-SE, DVA and Titmus, DVA and TNO, and D-SE and TNO in all patients without grouping. The stereoacuity levels were subnormal and decreased in relation to the depth of amblyopia. About 31.1% of patients with the Titmus and 17.8% with the TNO had good stereoacuity. None of the patients could reach the best threshold value with the TNO test. Three patients were able to achieve the best threshold value with the Titmus. All patients had first-degree fusion. About 95% of mild amblyopia and 75% of moderate-severe amblyopia had second and third-degree fusion.

Discussion and Conclusion: This study shows a relationship between the depth of amblyopia and the stereoacuity levels and the amount of anisometropia. The RMS-SE as an anisometropia index and the Titmus or the TNO test as a stereoacuity test may be used to predict the depth of amblyopia in patients with anisometropic amblyopia.

Keywords: Amblyopia; anisometropia; synoptophore; titmus; TNO

Amblyopia is clinically defined as decreasing of visual acuity in one or both eyes, caused by inadequate visual stimulation, causing pattern visual deprivation or abnormal binocular interaction in the critical period of visual development, without detectable organic cause, and can be partially or completely reversible by therapeutic methods where possible. Amblyopia results in reduced visual acuity, binocularity, stereopsis, and contrast sensitivity of high spatial frequencies[1-3]. Amblyopia is the most common cause of monocular vision loss in the population un-

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der 40 years and its prevalence varies among countries and according to the population studied but is approximately 1.2–4%[3-5].

Amblyopia is classified as strabismic amblyopia, anisometropic amblyopia, mixed amblyopia, and stimulus deprivation amblyopia[1-3]. Anisometropia is a difference in the refractive error between the two eyes of an individual and is a well-known cause of amblyopia. There is an active inhibition of fovea in anisometropic amblyopia to eliminate sensory interference by the superimposition of a focused and a defocused image from the fixation point[1,2,6]. It may occur together with strabismus amblyopia, but it is difficult to determine whether the amblyopia is primary (due to anisometropia), secondary (strabismus), or a combination of both[2-7]. The prevalence of anisometropic amblyopia is about 4.7% in children[7]. Strabismic amblyopia results from active inhibition within the retinocortical pathways of visual input originating in the fovea of the deviating eye. Stimulus deprivation amblyopia occurs as a result of an obstruction to the passage of light secondary to a condition such as congenital cataract, blepharoptosis, and aphakia[1,2,8].

Binocular vision is obtained from two retinal images fused through the motor and sensory processes culminating in the perception of a single image and stereoscopic depth. It has been classified into three levels by Claud Worth: Simultaneous perception (first-degree fusion), flat fusion (second-degree fusion), and stereopsis (third-degree fusion). The measurement of stereoacuity is an important tool in the assessment of binocular functions and is widely used for the diagnosis and management of amblyopia[9-13].

This study aimed to evaluate stereoacuity with the Titmus and the TNO Stereotests and binocular functions with the synoptophore in patients with anisometropic amblyopia.

Materials and Methods

This prospective study was conducted on a total of 45 patients with anisometropic amblyopia at the Department of Ophthalmology, Atatürk University, Erzurum, Türkiye. The study protocol was approved by Institutional Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients.

The exclusion criteria were as follows: (1) Age ≤7 years (because the development of binocular vision is not completed until the age of 5) or ≥40 years; (2) patients with ocular pathologic characteristics (including strabismus) except for refractive errors; and (3) patients with a history of ocular surgery or trauma. All patients underwent a complete ophthalmologic examination, including subjective and objective refraction, uncorrected (UCVA), and best-corrected distant visual acuity (BCVA) with the Snellen chart at 6 m, biomicroscopy, biomicroscopy-assisted fundoscopy, direct ophthalmoscopy, Hirschberg test, cover test, cover-uncover test, alternate cover tests, and Maddox rod test.

In this study, the criteria for amblyopia were BCVA of ≤0.8 in the affected eye or ≥2 rows of difference in visual acuity on Snellen between two eyes. A difference of ≥1.00 diopter (D) between spherical or cylindrical refractive errors of the two eyes was accepted as inclusion criteria for anisometropia. The patients were evaluated both without grouping and as to the severity of amblyopia, divided into two subgroups as mild and moderate-severe amblyopia. Eyes with BCVA of ≤0.5 were classified as moderate-severe amblyopia and >0.5 better eyes as mild amblyopia. Two different methods were used to determine the degree of anisometropia as an anisometropia index.

1. Refractive errors of each eye were converted to spherical equivalent (SE). The SE was calculated by adding the sum of the sphere power with half of the cylinder power. Then, the difference between the spherical equivalents (D-SE) of both eyes was calculated[14].
2. Root-mean-square spherical equivalent (RMS-SE) values developed by Safir and Kulikowski[15] were used for the amount of anisometropia as follows:

S1: First eye spherical power, S2: Fellow eye spherical power

C1: First eye cylindrical power, C2: Fellow eye cylindrical power

A1: First eye axis value, A2: Fellow eye axis value

The binocular functions were evaluated with the synoptophore. Quantitative stereopsis (stereoacuity) was measured with the Titmus Stereo Fly-Wirt Circles (Stereo Fly Tests, Sbisa Industriale SPA Italy) and the TNO (Test for Stereoscopic Vision, Eleventh Edition, Lameris Ootech BV, Netherlands) stereotests. The Titmus and the TNO tests were performed at a distance of 40 cm while wearing polarized glasses for Titmus, red/green glasses for TNO.

Statistical Analysis

Statistical analysis was performed using SPSS Version 24 (IBM Corp., Chicago, IL, USA). Results were expressed as mean±standard deviation (SD), range, and percentage. The Shapiro–Wilk test was used for the normality of data distribution. According to the normality distribution, correlation analysis was performed with the Pearson's correlation coefficient test or Spearman's correlation coefficient test. The Wilcoxon test was used to determine whether there was a difference between the TNO and the Titmus tests or D-SE and RMSE-SE values. p<0.05 was considered statistically significant.

Results

A total of 45 patients with anisometropic amblyopia (31 females and 14 males) were evaluated. The mean age was 21.44±7.45 years (9–38 years). Twenty-three (51.1%) had moderate-severe and 22 (48.9%) had mild amblyopia. Thirty (66.67%) of amblyopic eyes were right and 15 (33.33%) were left eyes. The mean±SD and the range of the D-SE, RMS-SE, difference visual acuity (DVA), Titmus stereoacuity, and TNO stereoacuity in patients with subgroups and without grouping are shown in Table 1. A significant positive correlation was found between D-SE and RMS-SE values in subgroups and all patients without grouping as seen in Table 1. RMS-SE values were higher than D-SE values in 21 patients in the mild group, 17 patients in the moderate-severe group, and 38 patients in total, and the difference between both indexes was statistically significant (Wilcoxon; for the mild group: z=−3.783, p=0.000; for the moderate-severe group: z=−2.920, p=0.003; for all patients: z=−4.583, p=0.000). There was a statistically significant correlation between the depth of amblyopia (DVA) and Titmus and TNO values in the moderate-severe group and in all patients with grouping, but no correlation in the mild group. As the depth of amblyopia increased, stereo acuity decreased.

The Titmus and the TNO measurements of patients are shown in Table 2. In all patients without grouping, the TNO values were higher (worse stereoacuity) than the Titmus values in 44 cases (n (total)=45, z=−5.819 and p=0.000); in the mild group, the TNO values were higher than the Titmus values in 21 cases (n (total)=22, z=−4.028 and p=0.000); in the moderate group, the TNO values were higher the Titmus values in 23 cases (n (total)=23, z=−4.205 and p=0.000) with the Wilcoxon test. No patients reached 30 s of arc (″) and 15″ threshold values, the most sensitive levels with the TNO test. Only three patients were able to reach the most sensitive level (40″) with the Titmus test.

The mean stereoacuity of 21 mild amblyopic patients with third-degree fusion (third-degree fusion) was 134.762±102.5″ (40–400″) for the Titmus and 345.71±404.68″ (60–1980″) for the TNO test. The mean stereoacuity of 17 the moderate-severe amblyopic pa-

Table 1. The mean, SD, range, and correlations of the variables in patients with anisometropic amblyopia

Group	Mean±SD	Range	p values for the correlations					Significant correlations
			DVA	D-SE	RMS-SE	Titmus	TNO	
Mild (n=22)								
DVA	0.30±0.06	0.20–0.40		0.808	0.794	0.626	0.839	D-SE and RMS-SE
D-SE	1.59±0.876	0.25–3.00	0.808		0.000	0.063	0.005	D-SE and TNO
RMS-SE	1.92±0.71	0.93–3.12	0.794	0.000		0.051	0.003	RMS-SE and TNO
Titmus	135±100.04	40–400	0.626	0.063	0.051		0.000	Titmus and TNO
TNO	340.91±395.57	60–1980	0.839	0.005	0.003	0.000		
Moderate-severe (n=23)								
DVA	0.69±0.12	0.50–0.90		0.603	0.078	0.003	0.007	DVA and Titmus
D-SE	1.728±1.28	0.00–4.50	0.603		0.006	0.363	0.461	DVA and TNO
RMS-SE	2.40±0.93	0.75–4.07	0.078	0.006		0.037	0.180	D-SE and RMS-SE
Titmus	271.74±263.69	400–800	0.003	0.363	0.037		0.000	RMS-SE and Titmus
TNO	751.304±756.76	120–1980	0.007	0.461	0.180	0.000		Titmus and TNO
All patients without grouping (n=45)								
DVA	0.50±0.22	0.2–0.9		0.702	0.042	0.007	0.005	DVA and RMS-SE
D-SE	1.661±1.092	0.00–4.50	0.702		0.000	0.087	0.037	DVA and Titmus
RMS-SE	2.17±0.86	0.75–4.07	0.042	0.00		0.002	0.003	DVA and TNO
Titmus	204.8±210.53	40–800	0.007	0.087	0.002		0.00	D-SE and RMS-SE
TNO	550.67±635.66	120–1980	0.005	0.005	0.003	0.000		D-SE and TNO

SD: Standard deviation; DVA: Best-corrected visual acuity difference between two eyes; D-SE: Spherical equivalent difference; RMS-SE: Root-mean-square spherical equivalent.

Table 2. Titmus and TNO results in the anisometropic amblyopes

TITMUS	TNO									
Arc of seconds	**15**	**30**	**60**	**120**	**240**	**480**	**1980**	**Total (n)**	**Percent (%)**	**Cumulative Percent (%)**
40		1	1	1			3	6.7	6.7	
50		1	2	1			4	8.9	15.6	
60			2				2	4.4	20.0	
80			2	3			5	11.1	31.1	
100					2	1		3	6.7	37.8
140				1	7	4		12	26.7	64.4
200					1	6	1	8	17.8	82.2
400						2	2	4	8.9	91.1
800							4	4	8.9	100
Total (n)	0	0	2	8	15	13	7	45	100	
Percent (%)	0	0	4.4	17.8	33.3	28.9	15.6	100		
Cumulative Percent (%)	0	0	4.4	22.2	55.6	84.4	100			

tients with third fusion was 221.765±233.57″ (40–800″) with the Titmus test, 522.353±567.14″ (120–1980″) with the TNO test. The mean stereoacuity of six moderate-severe amblyopic patients with suppression was 413.33±314.37″ (140–800″) with the Titmus test and 1400±898.53″ (240–1980″) for the TNO test.

Foveal fixation was detected in all patients with a direct ophthalmoscope. First-degree fusion was found in all patients with or without grouping, although it was poor in five patients on synoptophore. Patients with second-degree fusion also had third-degree fusion. There were second and third-degree fusions in 84.44% of 45 patients and poor fusion in 11 of 38 patients. Seven patients had suppression. The results of the synoptophore examination are shown in Table 3.

Mixed astigmatism was the most common refractive error in eyes with amblyopia. The distribution of refractive errors by groups and eyes is presented in Table 4.

Table 3. Results of the synoptophore examinations in the anisometropic amblyopes

	First-degree fusion		Second-degree fusion		Third-degree fusion	
Group	**Positive**	**Negative**	**Positive**	**Negative**	**Positive**	**Negative**
Mild	22 (poor:1)	0	21 (poor:2)	1	21 (poor:2)	1
Moderate-severe	23 (poor:4)	0	17 (poor:9)	6	17 (poor:9)	6
Total	45 (poor:5)	0	38 (poor:11)	7	38 (poor:11)	7

Table 4. Refractive errors in patients with anisometropic amblyopia

	Mild group		Moderate-severe group		
Refractive Errors	**Right**	**Left**	**Right**	**Left**	**Total**
Hyperopia	0	3	0	0	3
Myopia	0	0	0	1	1
Simple myopic astigmatism	0	0	1	0	1
Simple hyperopic astigmatism	0	1	0	0	1
Compound myopic astigmatism	3	2	1	1	7
Compound hyperopic astigmatism	4	3	7	1	15
Mixed astigmatism	5	1	9	2	17
Total	12	10	18	5	45

Discussion

Copps,[16] in 1944, was the first to try confirming the relationship between anisometropia and amblyopia in absence of strabismus[17]. Anisometropia may cause amblyopia by causing a loss of foveal resolution in the less focused eye, by localized mechanisms of foveal inhibition (development of a suppression scotoma), or by loss of stereo acuity and binocular function (perhaps caused by loss of resolution or by a suppression scotoma)[1-4,9,18,19]. It is still controversial how large a refractive error difference between both eyes will cause amblyopia and how many or which children with significant anisometropia will develop amblyopia. It is controversial whether there is a relationship between the parameters used as the anisometropia index and the depth of amblyopia[3,20-23]. Bhatia et al.[18] found no relationship between the degree of anisometropia and the depth of amblyopia in 61 unilateral anisometropic amblyopes with anisometropia of 0.50 D or more between two eyes, either being sphere or cylinder. Kutschke et al.[6] reported no direct correlation between the degree of anisometropia and the depth of amblyopia in 124 amblyopic patients with anisometropia of 1.00 D or more. Helveston[24] found no relationship between the degree of anisometropia and the depth of amblyopia in 37 non-strabismic anisometropic with anisometropia of 0.50 D or more in the sphere or cylindrical spherical equivalent. Malik et al.[25] found no direct correlation between the degree of anisometropia and the depth of amblyopia in 118 amblyopic patients with anisometropia of 0.50 D or more, those also had central fixation. Abrahamsson et al.[26,27] followed 310 children with astigmatism ≥1.00 D in at least one eye during a period of 3 years but found no relationship between the amount of anisometropia and amblyopia. Tomaç et al.[28] found no statistically significant positive correlation between the amount of anisometropia and the depth of amblyopia in 25 anisometropic adults, three of whom were not amblyopic.

In contrast, Toker et al.[29] reported a significant relationship between D-SE and RMS-SE values and the depth of amblyopia in 64 pure anisometropic patients (age range: 5–60 years). Townshend et al.[14] also reported a positive correlation between the amount of anisometropia and the depth of amblyopia in 35 untreated pure anisometropic amblyopes (age range:7–70 years) with anisometropia of 0.75 D in either spheric or cylindric values. D-SE, RMS-SE, and a modified formula, called the Townshend index, were used for anisometropic indexes. Sen[19] evaluated a total of 172 anisometropic amblyopes (167 anisohyperopic and five anisomyopic), of whom only five were under age seven, and reported that higher anisometropic difference was associated with more severe amblyopia. Weakley[17] found a positive correlation between the type or degree of anisometropia and the incidence and severity of amblyopia in 411 patients with various levels of anisometropia. Zaka-Ur-Rab[30] reported that the depth of amblyopia correlated with the degree of anisometropia in 85 cases of untreated anisometropic amblyopia. In another study by Duman et al.,[7] a positive correlation between depth of amblyopia and amount of anisometropia was reported in 38 anisometropic patients.

In our study, the two most common refractive errors in amblyopic eyes were mixed astigmatism and compound hyperopic astigmatism. A spherical or cylindrical difference of at least 1.00 D between the two eyes was taken as inclusion criteria for anisometropia. To determine the degree of anisometropia, D-SE and RMS-SE values were used as anisometropia indexes, as did Townshend et al.[14] and Toker et al.[29] In contrast to Townshend et al.[14] and Toker et al.,[29] no significant correlation was found between the depth of amblyopia (DVA) and D-SE or RMS-SE in subgroups ($p>0.05$). However, in all patients without subgrouping, no significant correlation between D-SE and the depth of amblyopia ($p=0.702$) was found, while there was a statistically significant positive correlation between RMS-SE and the depth of amblyopia ($p=0.042$). Based on this result, it can be said that using RMS-SE as an anisometropia index may be a better option for estimating the depth of amblyopia. This result was similar to Toker et al.[29]

The relationship between the stereoacuity and the type or amount of anisometropia is another controversial issue[3]. Many factors such as visual acuity, foveal suppression, contrast, and the fusional details play a role in stereoacuity. It has been shown that stereoacuity is better preserved than visual acuity in amblyopia. The main problem in this matter is that there are no standard stereoacuity tests compared to visual acuity tests. Therefore, results regarding stereoacuity depend on the tests used[3,9,31-33]. In the previous studies, the mean stereoacuity was reported in young normal adults (over 5 years old) as 63″ for the TNO by Reinecke et al.;[34] 40.5″ by Simons;[33] 122.5″ for the Titmus; and 40″ for the TNO by Romano et al.[35] The severity of amblyopia is related to the degree of anisometropia and stereoacuity may also be disrupted by anisometropia[16,17,34]. In our study, a statistically significant positive correlation was found between the depth of amblyopia and the stereoacuity of the Titmus and the TNO tests in patients with moderate-severe anisometropic and in all amblyopes (Table 1). As the depth of amblyopia increased, the numerical values of stereoacuity increased (decreased stereoacuity). This result was important to demonstrate the usability of stereoacuity tests in moderate-to-severe amblyopia. However, no significant relationship was found in the mild group. When evaluated for the degree of anisometropia, the relationship between the TNO and both anisometropia indexes in the mild group, between the Titmus and only RMS-SE in the moderate group, and between anisometropia indexes and the Titmus or the TNO values in all patients, except for the relationship between D-SE and the Titmus, was significant. This result showed that as the amount of anisometropia increased, stereoacuity levels decreased. In our study, while none of the anisometric patients did not perform stereopsis better than 60″ (30″ and 15″) with the TNO test, 3 cases (6.67%) passed 40″, the best threshold level with the Titmus test. Two of three cases had mild amblyopia (one with myopic astigmatism, the other with mixed astigmatism); the third had moderate-severe amblyopia with myopia. As seen in Table 2, on the Titmus test, 9 (20%) patients had 60″ and better and 14 (31.1%) had 80″ and better. However, on the TNO test, only 2 (4.4%) patients had 60″ and 8 (17.8%) had 120″ and better. According to our results, most patients had subnormal stereoacuity levels and the TNO test' results were worse than the Titmus test. Moreover, there was a significant difference between the Titmus and TNO values both in the main group and in the two subgroups. Titmus values were worse than TNO values in only one patient with mild amblyopia. Similar to our study, Weakley[17] found subnormal stereoacuity with Titmus test in 411 anisometropic patients with/without amblyopia. Tomaç et al.[28] reported that the depth of amblyopia was more related to a deterioration in binocularity than to the amount of anisometropia. In that study, stereoacuity levels were reduced or absent in 76% of patients on the TNO test. As in our study, almost all patients with anisometropia had bifoveal fusion. Levi et al.[32] measured stereoacuity with Titmus test and reported that the majority of pure anisometropic with interocular differences <4D retain some stereopsis, and the degree was correlated with the acuity of the poor eye. In that study, 42% of patients showed stereoacuity of 50″ or better.

We evaluated the degrees of binocular functions with the synoptophore. Although it was poor 5 (11%) patients, one with mild amblyopia and four with moderate-severe amblyopia, there was first-degree fusion in all patients. Second-degree fusion and third-degree fusion (stereopsis) were found in 95.45% of patients with mild amblyopia, 73.9% of patients with moderate-severe amblyopia, and 84.4% of all patients. Only one patient with mild amblyopia and six patients with moderate-severe amblyopia had no second and third-degree fusion as seen in Table 3. Results from the synoptophore showed that fusion and stereopsis were protected at a high level in mild amblyopia. However, second-degree fusion and stereopsis decreased as the depth of amblyopia increased; it showed that the results were not so bad.

The limitation of this study was the relatively small sample size of subgroups. The strength of the study was using of two different stereoacuity tests and synoptophore for binocular vision and stereopsis.

Conclusion

The study shows that there is a relationship between the depth of amblyopia and the amount of anisometropia and stereoacuity and that the binocular fusion abilities of the patients are well preserved despite the low stereoacuity levels obtained from the stereotests. Therefore, in anisometropic amblyopes, the RMS-SE as an anisometropia index, the Titmus test, or the TNO test as a stereoacuity test may be used to predict the depth of amblyopia.

Ethics Committee Approval: Study was approved by the Atatürk University Faculty of Medicine Ethical Committee (date: 05.11.1999, decision number:12-5).

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