

Study on the impact of refractive anisometropia on strabismus, stereopsis, and amblyopia in children

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Abstract

To preliminarily explore the correlation between different types and degrees of refractive errors and strabismus, amblyopia, and stereopsis. A retrospective collection was conducted on a total of 145 patients with anisometropia who visited our hospital for strabismus and pediatric ophthalmology from January 2023 to August 2023. Based on the nature of anisometropia in both eyes, it was divided into 4 groups: Farsighted anisometropia (36 cases); myopic anisometropia (38 cases); astigmatic anisometropia (35 cases); mixed anisometropia (36 cases), and 30 children with normal vision were collected. Both groups of subjects underwent routine slit lamp and fundus examinations to exclude other organic eye diseases. The test indexes were: visual acuity, diopter, strabismus, far-stereoscopic vision, near-stereoscopic Titmus, and random static zero-order stereoscopic vision. The results of this study showed that compared with the normal control group, the incidence of strabismus was higher in the anisometropia group. When the refractive error was $\geq 1.00\text{D}$, the far stereopsis and random dot static 0-order stereopsis in the anisometropia group decreased more significantly, and the difference between the groups was statistically significant ($P < .05$). Far-sighted and mixed astigmatism were more prone to amblyopia than myopia and regular astigmatism ($P < .05$). However, there was no statistical difference in near stereopsis Titmus between the anisometropia group and the control group ($P > .05$). Children with anisometropia are more likely to have strabismus, stereopsis and amblyopia than normal children.

Abbreviation: logMAR = logarithmic minimal angle of resolution.

Keywords: amblyopia, anisometropia, stereopsis, strabismus

1. Introduction

Refractive anisometropia is a common condition in the field of ophthalmology, and according to reports, the prevalence of refractive anisometropia ($\geq 1.00\text{D}$) is between 3.79% and 21.8% domestically and internationally.^[1] The prevalence of refractive anisometropia increases with age, degree of myopia, and decrease in best corrected visual acuity.^[2] Refractive anisometropia refers to the difference in refractive power between the 2 eyes along 1 or more meridians. It is rare for both eyes to have identical refractive status, and most people show some degree of difference. The Chinese Society of Pediatrics Strabismus and Amblyopia Prevention and Treatment Group divides refractive anisometropia into physiological and pathological categories. Physiological refractive anisometropia refers to a difference in refractive power between the 2 eyes of $<1.00\text{D}$ for cylinder or $<1.50\text{D}$ for

sphere, while pathological refractive anisometropia refers to a difference of 1.00D or more for cylinder or 1.50D or more for sphere.^[3,4] Internationally, there is no unified standard for the classification of pathological refractive anisometropia. Most foreign scholars consider a difference of 1.00D or more in refractive power between the 2 eyes as refractive anisometropia and divide it into physiological and pathological categories based on the presence of binocular single vision impairment in clinical practice.

Refractive astigmatism can be divided into myopic refractive astigmatism, hyperopic refractive astigmatism, astigmatic refractive astigmatism, and mixed refractive astigmatism according to its nature. It can also be classified into simple refractive astigmatism, compound refractive astigmatism, and mixed refractive astigmatism based on whether the refractive nature and status of both eyes are identical. Additionally, based on the causes of

SQ and JC contributed to this article equally.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This paper has been reviewed by relevant departments of our hospital, such as the Science and Education Department, Medical Department and Ethics Committee of The Second Hospital of Dalian Medical University. The research content involved in this research meets the requirements of medical ethics and academic morality of our hospital, and the research content is reasonable, the risks are controllable, and there are no violations. The relevant research carried out is in line with the safe, standardized and true scientific research guiding principles, and in line with the requirements of the clinical research ethics code.

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refractive astigmatism, it can be classified as axial refractive astigmatism, refractive astigmatism, lenticular refractive astigmatism, and mixed refractive astigmatism.^[5,6]

Refractive error not only affects vision but also damages binocular visual function.^[7] Studies have shown significant interactions between refractive error, strabismus, amblyopia, and binocular stereoacuity.^[8] Refractive errors (such as myopia, hyperopia, or astigmatism) are associated with the development and progression of strabismic amblyopia, a condition characterized by decreased vision and eye misalignment.^[9] The refractive error in patients with strabismic amblyopia will further affect binocular vision and stereoscopic depth perception. Correction of the refractive error combined with appropriate strabismus and amblyopia treatment can improve binocular vision and stereoscopic depth perception.^[10] In school-age children and adults, refractive error is the main cause of amblyopia.^[11] Physiological refractive error usually has no symptoms. When refractive error reaches a certain degree, it can cause decreased vision, amblyopia, changes in contrast sensitivity, and decreased stereoscopic acuity.^[12] Previous studies have mainly focused on hyperopia and myopia refractive error, and there is little knowledge about the relationship between astigmatism and mixed refractive error and amblyopia or stereopsis. Furthermore, refractive error can cause binocular fusion and accommodation problems, but there are few reports on whether it affects strabismus. The specific correlation between refractive error combined with strabismus and refractive error combined with amblyopia and stereopsis has not been clarified. Generally, when the refractive error difference between the 2 eyes is 0.25D, there will be a 0.5% difference in image size formed on the retina. Most scholars at home and abroad believe that when the refractive error difference between the 2 eyes is >2.50D, which means that the difference in retinal image size between the 2 eyes exceeds 5%, it will affect binocular fusion function and lead to decreased stereoscopic acuity.^[13] Many patients in clinical practice with refractive error <2.50D also experience varying degrees of decreased stereoscopic acuity. Therefore, whether mild to moderate refractive error is a risk factor for decreased stereoscopic acuity needs further investigation.

Currently, there is still insufficient understanding of the characteristics of strabismus and amblyopia caused by different types and degrees of refractive error, as well as the degree of damage to stereoscopic vision. Therefore, this article aims to explore the relationship between refractive error and strabismic amblyopia and binocular stereoscopic vision, and the possible influencing mechanisms, in order to provide clinical evidence for early intervention and treatment of children's vision impairment.

2. Data and methods

2.1. Clinical data

A retrospective collection was conducted on a total of 145 patients with anisometropia who visited our hospital for strabismus and pediatric ophthalmology from January 2023 to August 2023. Based on the nature of anisometropia in both eyes, it was divided into 4 groups: Farsighted anisometropia (36 cases); myopic anisometropia (38 cases); astigmatic anisometropia (35 cases); mixed anisometropia (36 cases). The normal control group consisted of 30 children with normal vision in both eyes without anisometropia.

The diagnostic criteria for anisometropia were a difference of $\geq 1.00\text{D}$ in equivalent spherical refractive error (SE) between both eyes. Depending on the severity of anisometropia, it was classified into the following groups: low-degree group (difference in refractive error $\geq 1.00\text{D}$), moderate-degree group (difference in refractive error $\geq 2.00\text{D}$), and high-degree group (difference in refractive error $\geq 3.00\text{D}$). Based on the nature of anisometropia in both eyes, it was divided into 4 groups: Farsighted anisometropia, with

either 1 or both eyes being hyperopic, a difference in spherical refractive error $\geq 1.00\text{D}$, and a difference in cylindrical refractive error $< 1.00\text{D}$; myopic anisometropia, with either 1 or both eyes being myopic, a difference in spherical refractive error $\geq 1.00\text{D}$, and a difference in cylindrical refractive error $< 1.00\text{D}$; astigmatic anisometropia, with a difference in spherical refractive error $< 1.00\text{D}$ and a difference in cylindrical refractive error $\geq 1.00\text{D}$ in both eyes; and mixed anisometropia, with a difference in spherical and cylindrical refractive errors $\geq 1.00\text{D}$ in both eyes.

2.2. Criteria for inclusion

Patients with slight differences in refractive error: the visual acuity of low-degree myopia should not be lower than the minimum visual acuity of the same age group, and they should be able to understand and cooperate with various examinations.

Criteria for exclusion: patients with binocular amblyopia, opacities of the refractive media, nystagmus, ptosis, fundus abnormalities, previous history of eye trauma, history of surgery, combined with systemic diseases, and those who cannot cooperate with various examinations.

2.3. Examination methods

All subjects completed visual acuity, slit-lamp, fundus, ocular alignment, fixation nature, extraocular muscle paralysis refraction, and stereopsis examinations. Each examination was repeated 3 times. Visual acuity was assessed using a standard logarithmic visual acuity chart, measuring both uncorrected visual acuity and best corrected visual acuity. Refraction status was determined by an experienced optometrist after ocular muscle paralysis using keratometry and prism neutralization methods to determine the nature and degree of strabismus. Atropine eye ointment at a concentration of 10 g/L was used for cycloplegia. Refractive power was assessed by the same optometrist once the pupils returned to normal. The optometrist also evaluated the best corrected distance and near visual acuity, recorded in decimal form. After refractive correction, Titmus stereoacuity was measured. Participants wore corrective lenses and polarized glasses, and the examination was conducted at a distance of 40cm under natural indoor lighting. Normal stereopsis was defined as ≤ 60 seconds of arc, while abnormal stereopsis was defined as > 60 seconds of arc or inability to identify stereoscopic fly. For statistical purposes, individuals who could only identify the stereoscopic fly or could not see it at all were recorded as 3000 seconds of arc in the stereopsis analysis. To avoid monocular cues, an additional method involving rotating the images by 180 degrees was used for differentiation. Amblyopia was defined as a visual acuity difference of 2 lines or more between the eyes according to Snellen or logMAR (logarithmic minimal angle of resolution) charts.^[14]

2.4. Statistical methods

Data analysis was conducted using SPSS 26.0 statistical software (IBM SPSS, SPSS Inc., Chicago, IL). The chi-square test was used for categorical data, and experimental data for quantitative variables were expressed as mean $\pm$ standard deviation (mean $\pm$ SD). The *t*-test was used, with *P* < .05 indicating statistical significance.

3. Results

Comparison of amblyopia, strabismus characteristics, and stereo vision examination results among different types of refractive error children

3.1. Baseline characteristics of refractive error group and normal control group

There are 145 patients with astigmatism, aged from 6 to 15 years old, with an average age of 7.5 ± 3.0 years. Among them, there are 74 boys and 71 girls. Among them, there were 36 cases of farsighted anisometropia group, 38 cases of myopic anisometropia group, 35 cases of astigmatic anisometropia group, and 36 cases of mixed anisometropia group. The normal control group consisted of 30 children with normal vision in both eyes, aged 6 to 15 years with a mean age of 8.2 ± 2.5 years, including 18 males and 12 females. The Diopter difference between the groups of hyperopic anisometropia, myopic anisometropia, astigmatic anisometropia, and mixed anisometropia were 2.513 ± 1.203 , 2.142 ± 0.471 , 1.152 ± 0.683 , and 4.581 ± 2.586 , respectively; whereas the value in the normal control group was 0.278 ± 0.263 , as shown in Table 1.

3.2. Astigmatism and amblyopia

Comparison between the normal control group and the astigmatism group revealed that the astigmatism group was more likely to develop amblyopia, and the differences were statistically significant ($P < .05$), as shown in Table 1.

3.3. Refractive anisometropia and strabismus

When comparing the normal control group with the refractive anisometropia group, there was no statistically significant difference between the normal control group and the group with

astigmatic anisometropia ($\chi^2 = 0.569$, $P > .05$). However, there was a statistically significant difference between the normal control group and the other groups ($P < .05$). The occurrence rate of exotropia, esotropia, and mixed strabismus was higher in all refractive anisometropia groups compared to the normal control group, as shown in Table 2.

3.4. Uneven refraction and stereoscopic vision

(a) Results of distant stereoscopic vision observation
When comparing the normal control group and the group with uneven refraction, it is evident that the group with uneven refraction has significantly poorer distant stereoscopic vision compared to the normal control group. There is a statistical difference in both groups ($P < .05$), as shown in Table 3.

(b) Near stereopsis Titmus observation results
There was no statistical difference between the normal control group and the group with myopic anisometropia ($t = 1.964$, $P > .05$) or the group with astigmatic anisometropia ($t = 1.862$, $P > .05$) when compared pairwise. However, there was a significant statistical difference between the normal control group and the group with Farsighted anisometropia ($t = 4.306$, $P < .05$) as well as the group with mixed anisometropia ($t = 5.160$, $P < .05$). The near stereopsis was significantly worse in the hyperopic and mixed anisometropia groups compared to the normal control group, as shown in Table 4.

(c) Random dot static 0 order stereoscopic visual observation results

When compared pairwise between the normal control group and the group with refractive astigmatism, the normal control

Table 1

The incidence of amblyopia in different types of anisometropia group and normal control group was compared [n (%)].

Index		Amblyopia [n (%)]	χ^2	P
Study Group (n = 145)	Farsighted anisometropia group (n = 36)	15 (41.67)	16.177	<.05
	Myopic anisometropia group (n = 38)	8 (21.05)	5.274	<.05
	Astigmatic anisometropia group (n = 35)	7 (20.00)	4.804	<.05
	Mixed anisometropia group (n = 36)	18 (50.00)	20.625	<.05
Control group (n = 30)		0 (0.00)		

P: compared to the control group.

Table 2

The incidence of strabismus in different types of anisometropia group and normal control group was compared [n (%)].

Index		Strabismus [n (%)]	χ^2	P
Study Group (n = 145)	Farsighted anisometropia group (n = 36)	13 (36.11)	10.520	<.05
	Myopic anisometropia group (n = 38)	25 (65.79)	27.691	<.05
	Astigmatic anisometropia group (n = 35)	4 (11.43)	0.569	>.05
	Mixed anisometropia group (n = 36)	13 (36.11)	10.520	<.05
Control group (n = 30)		1 (3.33)		

P: compared to the control group.

Table 3

The incidence of dissotropia between different types of anisometropia group and normal control group was compared [n (%)].

Index		Positive distal stereopsis [n (%)]	χ^2	P
Study Group (n = 145)	Farsighted anisometropia group (n = 36)	18 (50.00)	20.625	<.05
	Myopic anisometropia group (n = 38)	25 (65.79)	12.689	<.05
	Astigmatic anisometropia group (n = 35)	27 (77.14)	5.845	<.05
	Mixed anisometropia group (n = 36)	14 (38.89)	10.520	<.05
Control group (n = 30)		30 (100.00)		

P: compared to the control group.

group showed a better performance in random dot static 0 order stereoscopic visual observation than the group with refractive astigmatism, and there was a statistically significant difference ($P < .05$) as shown in Table 5.

The relationship between the degree of refractive amblyopia and the characteristics of strabismus, and the results of stereo vision examination.

3.5. Proportions of amblyopia in each group

When comparing the normal control group and the group with refractive amblyopia, there was no statistically significant difference in the mild group ($\chi^2 = 2.770, P > .05$). However, there was a statistically significant difference between the normal control group and the other groups ($P < .05$). The proportion of amblyopia significantly increased when the refractive amblyopia in both eyes was $\geq 2.00D$. The higher the refractive amblyopia, the higher the occurrence rate of amblyopia (Table 6).

3.6. Proportions of strabismus in each group

When comparing the normal control group and the group with refractive amblyopia, the group with refractive amblyopia was more likely to have strabismus, and the difference was statistically significant ($P < .05$). The occurrence rate of strabismus was significantly higher in the group with refractive amblyopia when the refractive amblyopia in both eyes was $\geq 1.00D$ compared to the normal control group (Table 6).

3.7. Results of distance stereo vision in each group

When comparing the normal control group and the group with refractive amblyopia, there was a statistically significant difference ($P < .05$) in distance stereo vision. The distance stereo vision decreased as the degree of refractive amblyopia increased (Table 6).

3.8. Comparison of random dot stereogram 0-order stereo vision results

When comparing the normal control group and the group with refractive amblyopia, there was a statistically significant

difference ($P < .05$) among the groups in the normal control group. When the refractive amblyopia in both eyes was $\geq 1.00D$, there was impaired random dot stereogram 0-order stereo vision, and the degree of impairment increased as the degree of refractive amblyopia increased. When the refractive amblyopia in both eyes was $\geq 3.00D$, the normal rate of random dot stereogram 0-order stereo vision was 0 (Table 6).

3.9. Near stereo vision Titmus results

When comparing the normal control group and the group with refractive amblyopia, there was no statistically significant difference between the normal control group and the low group ($t = 1.408, P > .05$). However, there was a statistically significant difference between the normal control group and the other groups ($P < .05$). When the refractive amblyopia in both eyes was $\geq 2.00D$, the near stereo vision decreased significantly compared to the normal control group. The higher the refractive amblyopia, the more significant the decrease (Table 6).

4. Discussion

Anisometropia is a condition in which the refractive power of the 2 eyes is different. The refractive power of the eyes is measured using the equivalent spherical diopters (spherical diopters + 1/2 cylindrical diopters) as the measurement standard. Based on current domestic and foreign literature, this study uses a difference of $\geq 1.00D$ in equivalent spherical diopters (SE) between the 2 eyes as a diagnostic criterion.^[15] A 3-year study conducted in New Zealand found that the incidence of exotropia increases with myopia, and the degree of esotropia corresponds to hyperopia, with a higher degree of hyperopia associated with a higher probability of esotropia. However, the relationship between anisometropia and strabismus is still unclear.^[16] Anisometropia is an important factor that causes amblyopia and decreased stereoscopic vision function, with the severity of amblyopia having a more pronounced impact on stereopsis compared to the magnitude of anisometropia.^[17]

The impact of different types and degrees of anisometropia on the development of visual function varies.^[18] In this study of 145 children with anisometropia, 51 children were found to have concomitant strabismus, resulting in a strabismus incidence rate

Table 4				
The incidence of nearstereoscopic Titmus was compared between different types of anisometropia group and normal control group ($\bar{x} \pm s$).				
Index		Near stereopia Titmus ($\bar{x} \pm s$)	t	P
Study Group (n = 145)	Farsighted anisometropia group (n = 36)	566.86 $\pm$ 659.25	4.306	<.05
	Myopic anisometropia group (n = 38)	210.53 $\pm$ 453.18	1.964	>.05
	Astigmatic anisometropia group (n = 35)	188.73 $\pm$ 414.03	1.862	>.05
	Mixed anisometropia group (n = 36)	709.54 $\pm$ 701.29	5.160	<.05
Control group (n = 30)		47.53 $\pm$ 28.82		

P: compared to the control group.

Table 5				
The incidence of static 0th-order stereoscopic vision at random points was compared between the refractive anisometry group and the control group [n (%)].				
Index		Random points are static and order 0 stereoscopic vision is normal [n (%)]	χ^2	P
Study Group (n = 145)	Farsighted anisometropia group (n = 36)	7 (19.44)	29.578	<.05
	Myopic anisometropia group (n = 38)	22 (57.89)	6.685	<.05
	Astigmatic anisometropia group (n = 35)	21 (60.00)	5.737	<.05
	Mixed anisometropia group (n = 36)	9 (25.00)	24.983	<.05
Control group (n = 30)		26 (86.67)		

P: compared to the control group.

Table 6
Results of different degrees of anisometropia and control groups.

Index	Study group (n = 145)			Control group (n = 30)
	≥1.00D (low group, n = 62)	≥2.00D (moderate group, n = 41)	≥3.00D (height group, n = 42)	
Refractive anisome (D, $\bar{x} \pm s$)	1.256 ± 0.214	2.648 ± 0.269	4.863 ± 2.073	0.269 ± 0.251
Amblyopia [n (%)]	8 (12.90)	12 (29.27)	26 (61.90)	0 (0.00)
χ^2	2.770	10.566	29.068	
P	>.05	<.05	<.05	
Strabismus [n (%)]	15 (24.19)	18 (43.90)	18 (42.86)	1 (3.33)
χ^2	6.124	14.548	14.073	
P	<.05	<.05	<.05	
Positive distal stereopsis [n (%)]	52 (83.87)	20 (48.78)	6 (14.29)	30 (100.00)
χ^2	3.892	21.820	51.429	
P	<.05	<.05	<.05	
Random points are static and order 0 stereoscopic vision is normal [n (%)]	34 (54.84)	8 (87.80)	0 (0.0)	26 (86.67)
χ^2	9.029	31.306	56.974	
P	<.05	<.05	<.05	
Near stereopsis Titmus ($\bar{x} \pm s$)	133.11 ± 331.39	358.17 ± 486.31	962.60 ± 676.23	47.53 ± 28.82
T	1.408	3.488	7.392	
P	>.05	<.05	<.05	

P: compared to the control group.

of 35.2%, significantly higher than the normal control group (3.33%). Due to the lack or reduced use of accommodation when nearsighted patients look at near objects, the weakened accommodative convergence and reduced horizontal divergence force, combined with the unequal retinal image clarity and size caused by anisometropia, can lead to binocular fusion disorder and an increased likelihood of exotropia. Another study conducted abroad suggests that strabismus and anisometropia can also influence each other.^[19] Strabismus alters the abnormal visual experience and can affect the process of emmetropization in the dominant eye and the deviating eye, thereby exacerbating the formation of anisometropia.

Refractive amblyopia is the most common type of amblyopia, accounting for more than 30%.^[20] The American Academy of Ophthalmology proposed clinical diagnosis and treatment guidelines for amblyopia in 1997, stating that myopic refractive amblyopia is >3.00D, hyperopic refractive amblyopia is >1.50D, and astigmatic refractive amblyopia is >1.50D, which require close observation or treatment. Research has shown that the probability of amblyopia significantly increases when hyperopic refractive amblyopia is >1.00D and myopic refractive amblyopia is >2.00D.^[21] Domestic studies have also found a significant increase in the proportion of amblyopia when hyperopic refractive amblyopia is >1.00D, astigmatic refractive amblyopia is >1.00D, and myopic refractive amblyopia is >3.00D. This indicates that amblyopia is more likely to occur in hyperopic and astigmatic refractive amblyopia, while myopic refractive amblyopia only leads to amblyopia to a certain degree. In the results of this study, the proportion of amblyopia caused by hyperopic and mixed astigmatic refractive amblyopia is also significantly higher than that of myopic refractive amblyopia. We analyze the reasons as follows: Low myopic refractive amblyopia can form alternating visual acuity, that is, clear imaging can be achieved on the retina by using the high myopic eye for near vision and the emmetropic or low myopic eye for distance vision, thus slowing down the formation of amblyopia. Hyperopic refractive amblyopia occurs at a younger age, but patients often identify and receive treatment later, leading to the lack of clear image stimulation on the macula of the retina during the sensitive period of visual development, resulting in amblyopia formation. On the other hand, myopic refractive amblyopia affects older patients who have undergone physiological myopia, emmetropization, and myopia progression, and the retina has received normal light stimulation and the visual acuity has

experienced normal development stages, resulting in a smaller proportion of amblyopia.^[22] Hyperopic refractive amblyopia has poorer near vision than myopic refractive amblyopia, and during the sensitive period of visual development, near-vision impairment is more likely to lead to amblyopia formation than distance vision impairment.

Stereovision can be divided into coarse and fine stereovision. Fine stereovision refers to the static 0-order fine disparity representation of high spatial frequency in the macular area. Coarse stereovision, on the other hand, refers to the dynamic second-order coarse disparity representation of low spatial frequency in the peripheral visual field. Many scholars have reported changes in stereovision before and after treatment for anisometropic amblyopia during the critical period of sensitivity. As visual acuity improves in the amblyopic eye, the gradually clearer external stimuli stimulate the brain cortex to generate fusion of the stimuli. Fusion function and stereovision can be significantly improved. However, it is relatively difficult to reconstruct the functional activity of higher-level central vision related to stereovision. Therefore, although anisometropic amblyopia can be corrected to achieve normal visual acuity, the impaired stereovision function is difficult to fully reach the level of normal children. The impact of different degrees and types of anisometropic amblyopia on stereovision development varies. This study evaluates the stereovision of children with anisometropic amblyopia from 3 different aspects: distant stereovision of the synoptophore, near stereovision (Titmus), and static zero-order stereovision with random dots. When the anisometropic amblyopia is ≥ 1.00D, both distant stereovision and static 0-order stereovision tend to decrease. When the anisometropic amblyopia is ≥ 2.00, near stereovision (Titmus) also decreases compared to the normal control group. As the degree of anisometropic amblyopia increases, stereovision gradually declines, which is consistent with previous studies.

5. Limitation

There are certain limitations in this study. Firstly, the sample size of the study is relatively small and there is also little variability, which may result in significant sampling errors. Secondly, the results of this study are compared to a normal control group. Subsequent research needs to further analyze the relationship between different degrees of refractive error and binocular

disparity, and strengthen the comprehensiveness of the results. It is hoped that future studies can include a larger number of participants to obtain more convincing and detailed conclusions.

6. Conclusion

In summary, children with anisometropia are more likely to have strabismus, stereopsis and amblyopia than normal children.

Author contributions

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