

# Abnormal higher order aberrations in anisometropic amblyopia

**Lingyi Zhang**

Sichuan University West China Hospital

**Meng Liao**

Sichuan University West China Hospital

**Wenqiu Zhang**

Sichuan University West China Hospital

**Longqian Liu** (✉ [b.q15651@hotmail.com](mailto:b.q15651@hotmail.com))

West China Hospital at Sichuan University <https://orcid.org/0000-0002-2265-4625>

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## Research article

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# Abstract

## Background

The study compared ocular higher-order aberrations (HOAs) between monocular anisometropic amblyopia children and similar anisometropia children with normal best-corrected visual acuity (BCVA). The amblyopia eyes could not reach the standard BCVA level of their age even after several months' regular treatment of amblyopia. We tried to find if these intractable amblyopia eyes have abnormal HOAs.

## Methods

Fifty school-aged children (5–9 years) with hyperopic anisometropia were recruited at West China hospital clinic. Each subject shall be reexamined once every three months, four consecutive reexaminations for 12 months, of which only 25 subjects with normal BCVA after wearing glasses shall be included in the control group. The rest 25 subjects were treated by glasses and six months' patching. Their interocular difference of visual acuity was still more than or equal to LogMAR 0.2, and the eyes with poor visual acuity did not reach the normal level in the twelfth month. These subjects were included in the amblyopia group. The BCVA, HOAs (5 mm pupil diameter), and axial length were recorded for all subjects.

## Results

There were significant differences of higher order aberrations in C (3, -3) between the amblyopia eyes and the other three groups of eyes with normal BCVA (all  $p < 0.05$ ). There were significant differences of higher-order aberrations in third-order root-mean-square aberrations(RMS) between the amblyopia eyes and the low-diopter eyes from two subject groups(both  $p < 0.05$ ). Compared to high-diopter eyes in the control group, there were a significantly higher C(3,-3) in all amblyopia eyes and a significantly higher third-order RMS ( $p = 0.040$ ) in the moderate-to-severe amblyopia group. In the Pearson correlation test, the C(3,-3) and third order RMS demonstrated statistically significant correlations with BCVA ( $r = -0.19$ ,  $p = 0.04$ ;  $r = 0.37$ ,  $p < 0.01$ ).

## Conclusions

The anisometropic amblyopia eyes had different HOAs from the eyes with normal visual acuity. The third-order aberrations were the primary abnormal higher-order aberration in amblyopia eyes.

## 1. Background

Anisometropia is common in the clinic, which refers to the unequal diopter between two eyes. Among them, the eyes with higher hyperopia anisometropia have more risks of amblyopia, because the retina images of these eyes are much more blurred than that of the opposite eyes. After the hyperopia anisometropic amblyopia patients wear corrected glasses, most of the amblyopia patients' best corrected visual acuity(BCVA) could be improved, and some of them need to be supplemented by patching treatment (cover the healthy eyes)<sup>1</sup>. However, a few amblyopia eyes can not improve the corrected visual acuity to the normal level even if these patients received patching treatment. Therefore, in the treatment of children with hyperopia anisometropic amblyopia, other factors may affect the final BCVA, such as higher-order aberrations.

Aberrations refer to the deviation between the ideal image plane and the actual image plane of retinal imaging, higher order(above second order) of which can not be corrected by wearing glasses. It has also been pointed out that higher-order aberrations cause poor corrected visual acuity, but their effects gradually decrease with the increase of age from the visual development stage to the age of thirty<sup>2</sup>. However, the effect of higher-order aberrations on the BCVA of amblyopia eyes is still controversial. Previous studies have found that among children aged 38 to 161 months with refractive amblyopia, high-order aberrations played an essential role in the BCVA of amblyopia<sup>3</sup>. Vincent's study on amblyopia and higher-order aberrations proposed a significant difference in the fourth order aberrations between anisometropic amblyopia and the opposite eye<sup>4</sup>. Hoshing's study also suggested that the three order and four order aberrations had an abnormal increase in the eyes of anisometropic amblyopia<sup>5</sup>. But another research showed that there was no significant difference between the higher-order aberrations of anisometropic amblyopia and the eyes with normal visual acuity<sup>6</sup>. The

different results of these studies may be due to the large age span of the subjects in the experiment, and the different refractive states between the two eyes in comparison, which have not clarified the characters of high-order aberrations in hyperopia anisometropic amblyopia.

In addition to age<sup>7</sup>, refractive status (myopia or hyperopia)<sup>8,9</sup>, the value of higher-order aberrations itself is affected by many factors, including diopter<sup>10</sup>, axial length<sup>11,12</sup>, measured diameter range<sup>13,14</sup>, cycloplegia<sup>15,16</sup>, measurement time (morning or afternoon)<sup>17</sup>.

In this study, subjects with the same anisometropia and diopter were selected to compare the higher-order aberrations between amblyopia eyes and eyes with normal BCVA. Our study tried to balance the diopter, axial length in two subjects groups. And the measured diameter range, cycloplegia and measurement time were same for each subject. It was found that the third-order and fourth-order aberrations in anisometropic amblyopia with hyperopia were abnormal and showed different performances in amblyopia with varying degrees.

## 2. Methods

### 2.1 Subjects and screening

50 children (5-9 years old) with hyperopia anisometropic amblyopia were recruited from the optometry and pediatric ophthalmology clinic of West China Hospital. The inclusion criteria are as follows: (1) the interocular difference of hyperopic spherical diopter  $\geq 1.50D$ , hyperopic spherical diopter  $\geq 2.00D$  for high-diopter eyes, and hyperopic spherical diopter  $\geq 0.50D$  for low-diopter eyes; (2) the interocular difference of cylinder diopter  $\leq 1.00D$ , and cylinder diopter  $\leq 0.50D$ . (3) Each subject shall be reexamined once every three months, four consecutive reexaminations for 12 months, of which only 25 subjects with normal BCVA after wearing glasses for six months were included in the improved group. The rest 25 subjects were treated by glasses and six months' patching. Their interocular difference of visual acuity was still more than or equal to LogMAR 0.2, and the eyes with poor visual acuity did not reach the normal level in the twelfth month. These subjects were included in the non-improved group. In the non-improved group, we divide amblyopia patients into two groups according to the difference of the BCVA between the eyes: one group was moderate-to-severe amblyopia group, the BCVA difference between the two eyes of the subjects in the group is higher than LogMAR 0.2; the other group was mild amblyopia group, the BCVA difference between the two eyes of the subjects is equal to LogMAR 0.2.

The exclusion criteria were: (1) The best-corrected visual acuity had fluctuation during the follow-up period. (2) During the follow-up period, there were other eye diseases, or other diseases affecting BCVA. (3) Patients with poor compliance with patching or wearing glasses. (4) The results of eye movement test, light reflex test, cover test and , the prism and alternate cover test had no sign of strabismus, and the strabismus degree from distance or near prism was less than  $2\Delta$ ; (5)  $4\Delta$  was used to ruled out the subjects, who with micro strabismus or macular inhibition blind spot.

The trial analysis data were collected at the fourth follow-up visit, but all subjects received routine pediatric ophthalmic examination at each follow-up visit. Routine pediatric ophthalmic examination including slit lamp test, ophthalmoscope test and examination like fundus photography was performed by the same ophthalmologist to exclude any other ocular disease.

The compliance was guaranteed by parents who monitored children's daily habits on a record list. Only children who were willing to wear glasses and eye patches according to the treatment plans were recruited because of their excellent compliance. Three subjects dropped out because they stopped wearing glasses for over three days in the ninth month. The study was approved by the West China Medical Ethics Committee, Sichuan University, and complied with the Declaration of Helsinki's guidelines. Informed consent was obtained from each patient and their guardian.

### 2.2 Main data

The optical and biometric data, including axial length and higher-order aberrations (3 to 6 orders), were measured for both eyes in 50 subjects.

#### 2.2.1 Refraction

After total cycloplegia (1% Tropicamide eyedrop), the refraction dioptre of all participants was done randomly by anyone of the two optometrists at each visit. The subjective refraction was measured by phoropter. The objective refraction was measured by retinoscopy and autorefractometry, which could help measure subjective refraction. The spherical equivalent refractive error (SER) is the sum of

spherical diopter and half-cylindrical diopter. The EDTRS chart was used to measure the participants' best-corrected visual acuity with their corrected glasses<sup>18</sup>. The visual acuity (VA) was recorded as a log MAR. The subjective refraction of the twelfth month was used as the results.

### 2.2.2 Axial length (AL)

The data were measured by non-contact instrument IOL Master (Carl Zeiss Meditec, Germany) for all the subjects<sup>19</sup>. The Signal to Noise Ratio of each subject was more than 3 ( $3.2 \pm 0.3$ ).

### 2.2.3 Higher-order aberrations

As the measurement diameter affects the change of higher-order aberrations of the eyes, each subject should recheck the pupil diameter before measurement to ensure that the pupil diameter is not less than the required diameter during measurement.

All higher-order aberrations were collected in the data collection stage of this experiment, because no statistical difference was found in the fifth or above order aberrations, and their contribution to visual effect was weak<sup>26</sup>, so they were not listed in the results. The data was measured by the i-Trace (Carl Zeiss Meditec, Germany). I-Trace uses laser ray tracing technology and describes aberrations by the Zernike coefficient. Zernike polynomials of the irregularities aberrations were computed over a circular pupil of 5mm diameter, associating to the America National Standards Institute<sup>20</sup>. Compared with other instruments. i-Trace showed good repeatability performance<sup>21</sup>. All the subjects were tested between 10:00 AM and 2:00 PM to reduce the daily variation<sup>17</sup>. In view of enantiomorphism (mirror symmetry between fellow eyes of an individual), the appropriate coefficient of left eyes was changed so that all eyes could be considered as right eyes<sup>22</sup>.

The RMS is an acronym for the root mean square of each order aberrations. It is a mathematical expression of the effective value of higher-order aberration that affects the light wave in each order.

## 2.3 Data analysis

Four eye groups' data was included in the analysis, including the high-diopter (amblyopia) eyes and the low-diopter eyes in the amblyopia group, the high-diopter eyes, and the low-diopter eyes in the control group. Each dataset of higher-order aberrations, visual acuity, and axial length showed normal distributions in these four eye groups (by Kolmogorov-Smirnov test). Firstly, the comparison between the four groups' eyes was analyzed by one-way ANOVA. These normal distribution datasets all showed homogeneity of variance except the visual acuity. Then the multiple comparisons after ANOVA among normal datasets were tested by Bonferroni Test (the LSD-t Test with Bonferroni correction). Dunnett's T3 Test was used to test the visual acuity. Secondly, the Paired Sample T-test was used to find the interocular differences between the high-diopter and low-diopter eyes. The Paired Sample T-test is much more effective than the LSD-t Test because the dataset of each subject for interocular comparison is paired.

All data of two amblyopia subgroups, and the refractive data (sphere, cylinder and SER) were non-normally distributed. The analyses were performed by Kruskal-Wallis H Test firstly. Furthermore, Nemenyi Test (with correction) was used to analyze the results of the pairwise comparison between groups. All the statistical analyses were performed by IBM SPSS version 19.0 software, SPSS (Chicago, IL, USA).

## 3. Results

### 3.1 The comparison of refractive power among four groups

There was no significant difference in gender, age, and the proportion of left and right low-diopter eyes in the amblyopia group and the control group (Table 1). The results of anisometropia and diopter comparison between the control group and the amblyopia group were shown in Table 2. There was no statistical difference in the amount of anisometropia between the two groups (sphere, cylinder, SER, AL), indicating that the two groups were the same amount of hyperopia anisometropia. The difference of corrected visual acuity between the two groups was statistically significant ( $P < 0.001$ ) because the amblyopia group was monocular amblyopia.

Table 1  
The overview of subjects.

Amblyopia group	Control group	p	
Age(years)	7.43 ± 2.15	7.51 ± 2.06	0.887
Male/Female	9/17	13/13	0.270
Left /right eye with higher diopter	11/15	8/18	0.398

Table 2  
The comparison of anisometropia and diopter between the two groups.

	Amblyopia group			Control group				The p of interocular difference	
	Amblyopia eyes	Contralateral eyes	p	The interocular difference	Non-dominant eyes	Dominant eyes	p		The interocular difference
Sphere(D)	1.96 ± 1.92	4.38 ± 2.05	0.00	2.49 ± 1.78	1.65 ± 1.73	4.03 ± 1.66	0.00	2.32 ± 1.28	0.898
Cylinder(D)	0.31 ± 0.57	0.72 ± 0.62	0.17	0.38 ± 0.053	0.45 ± 0.51	0.70 ± 0.59	0.37	0.24 ± 0.064	0.350
SER(D)	2.46 ± 1.92	4.88 ± 2.05	0.00	2.68 ± 1.85	2.15 ± 1.73	4.53 ± 1.66	0.00	2.44 ± 1.33	0.672
AL(mm)	22.11 ± 0.71	21.65 ± 0.69	0.00	0.457 ± 0.473	22.15 ± 0.85	21.83 ± 0.84	0.00	0.328 ± 0.450	0.320
BCVA(LogMAR)	0.07 ± 0.08	0.41 ± 0.21	0.00	0.346 ± 0.185	0.04 ± 0.08	0.05 ± 0.08	0.083	0.012 ± 0.032	0.00

*Abbreviations:* SER spherical equivalent refractive error, AL axial length, BCVA best corrected visual acuity.

There were statistically significant differences between the two groups ( $p < 0.001$ ). The contrast of the best-corrected visual acuity between two eyes only existed in the amblyopia group. There was no statistical difference in the diopter of two eyes between the two groups.

### 3.2 The multiple comparisons of all standard data among four groups

The analysis showed substantial differences in the visual acuity, the C (3, -3) ( $F = 3.416$ ,  $p = 0.020$ ) and third-order RMS ( $F = 3.356$ ,  $p = 0.022$ ) among four eye groups. The results of the Bonferroni Test and Dunnett's T3 Test showed multiple comparisons after ANOVA among the full sets of all standard data (Table 3). The amblyopia eyes had significantly lower visual acuity than the other three groups of eyes (all  $p < 0.001$ ). There were significant differences in C (3, -3) ( $P = 0.015$ ) and third-order RMS ( $P = 0.040$ ) between the high-diopter eyes in the non-improved group and in the improved group. And There was also a significant difference in C (3, -3) ( $p = 0.037$ ) between the high-diopter eyes in the non-improved group and the low-diopter eyes in the improved group. There was no statistical difference in the higher-order aberrations between the low-diopter and high-diopter eyes in the control group.

Table 3  
The significant results of multiple comparison among four groups of eyes .

	Group 1 - Group 2	Mean difference	Stangard error	Bonferroni Test (adjusted p)
C (3,-3)	LA - AA	0.108	0.057	0.362
	LA - LC	-0.067	0.057	1.000
	LA - HC	-0.043	0.057	1.000
	<b>AA - LC</b>	<b>-0.176</b>	<b>0.057</b>	<b>0.015</b>
	<b>AA - HC</b>	<b>-0.151</b>	<b>0.057</b>	<b>0.037</b>
	LC - HC	0.024	0.057	1.000
3rd order RMS	<b>LA - AA</b>	<b>-0.211</b>	<b>0.088</b>	<b>0.019</b>
	LA - LC	-0.034	0.088	0.615
	LA - HC	-0.027	0.088	0.759
	AA - LC	0.166	0.088	0.063
	<b>AA - HC</b>	<b>0.184</b>	<b>0.088</b>	<b>0.040</b>
	LC - HC	0.017	0.088	0.844
	Group 1 - Group 2	Mean difference	Stangard error	Dunnett's T3 Test (p)
Visual acuity	<b>LA - AA</b>	<b>-0.342</b>	<b>0.045</b>	<b>0.000</b>
	LA - LC	0.023	0.024	0.905
	LA - HC	0.012	0.024	0.997
	<b>AA - LC</b>	<b>0.365</b>	<b>0.045</b>	<b>0.000</b>
	<b>AA - HC</b>	<b>0.354</b>	<b>0.045</b>	<b>0.000</b>
	LC - HC	-0.012	0.024	0.997
<i>Abbreviations: RMS</i> root mean square, <i>LA</i> indicates the eyes with low diopter in the amblyopia group, <i>AA</i> indicates the amblyopia eyes in the amblyopia group, <i>LC</i> indicates the eyes with low diopter in the control group, <i>HC</i> indicates the eyes with high diopter in the control group.				

There was also a significant difference in third-order RMS between the high-diopter eyes and the fellow eyes in the non-improved group ( $p = 0.019$ ). However, the Paired Sample T-test is much more effective than the LSD-t Test when comparing paired data. Table 4 showed the difference of HOA between low-diopter and high-diopter eyes in each group analyzed by the Paired Sample T-test. In the non-improved group, the third-order aberration C (3,-3) and third-order RMS, with a statistically significant difference, were higher in the high-diopter eye (amblyopia) ( $p = 0.019$  and  $p = 0.005$ , respectively).

Table 4  
The interocular difference of HOAs, visual acuity and axial length in the two groups.

Amblyopia group		Control group				
Overview	Dominant eye (N = 25)	Non-dominant eye (N = 25)	Paired t-test (p)	Dominant eye (N = 25)	Non-dominant eye (N = 25)	Paired t-test (p)
<b>C(3, -3)</b>	-0.058 ± 0.126	-0.166 ± 0.183	<b>0.019</b>	0.009 ± 0.274	-0.015 ± 0.210	0.088
C(3, -1)	-0.001 ± 0.133	-0.030 ± 0.323	0.584	-0.022 ± 0.317	0.047 ± 0.167	0.649
C(3,1)	0.026 ± 0.134	0.09 ± 0.320	0.355	0.023 ± 0.267	-0.002 ± 0.130	0.712
C(3,3)	0.042 ± 0.152	-0.071 ± 0.226	0.106	0.027 ± 0.139	-0.013 ± 0.257	0.475
C(4, -4)	0.018 ± 0.057	0.011 ± 0.111	0.770	-0.011 ± 0.045	0.016 ± 0.056	0.662
C(4, -2)	-0.013 ± 0.102	0.012 ± 0.077	0.684	-0.009 ± 0.071	-0.002 ± 0.062	0.699
C(4,0)	-0.012 ± 0.077	-0.045 ± 0.387	0.682	0.039 ± 0.105	0.003 ± 0.086	0.110
C(4,2)	0.010 ± 0.078	0.043 ± 0.108	0.170	0.014 ± 0.104	-0.015 ± 0.063	0.245
C(4,4)	0.027 ± 0.066	0.036 ± 0.129	0.716	-0.009 ± 0.098	0.031 ± 0.080	0.087
<b>3rd order RMS</b>	0.247 ± 0.132	0.458 ± 0.342	<b>0.005</b>	0.281 ± 0.214	0.274 ± 0.436	0.843
4th order RMS	0.144 ± 0.101	0.258 ± 0.364	0.130	0.121 ± 0.160	0.124 ± 0.102	0.933
VA(LogMAR)	0.07 ± 0.08	0.41 ± 0.21	<b>&lt;0.001</b>	0.04 ± 0.08	0.05 ± 0.08	0.083
AL (mm)	22.11 ± 0.71	21.65 ± 0.69	<b>&lt;0.001</b>	22.15 ± 0.85	21.83 ± 0.84	<b>0.001</b>

*Abbreviations: RMS* root mean square.

• 3.3 The correlation analysis between higher-order aberrations and best corrected visual acuity

We hypothesized that the higher-order aberrations might cause the poor corrected visual acuity of amblyopia eyes. The correlation analysis of 100 eyes was shown in Table 5 to demonstrate the hypothesis. We did not involve the refraction data (sphere, cylinder and SER) because these lower-order aberrations had been corrected for all subjects. The C (3,-3) (r=-0.19, p = 0.04) were weakly correlated with the best-corrected visual acuity. The third order RMS was significantly correlated with the best-corrected visual acuity (r = 0.37, p < 0.01). There were no significant differences in the correlation analysis of all low-diopter eyes.

Table 5  
The bivariate correlation analysis of 100 eyes' visual acuity and other factors.

		C(3,-3)	C(3,-1)	C(3,1)	C(3,3)	3rd RMS
BCVA	Pearson test	-0.07	-0.17	0.12	<b>-0.19</b>	<b>-0.37</b>
	(r)					
	p	0.49	0.08	0.24	<b>0.04</b>	<b>0.00</b>
		C(4,-4)	C(4,-2)	C(4,0)	C(4,2)	C(4,4)
	Pearson test	-0.15	0.06	-0.05	0.17	-0.06
	(r)					
	p	0.13	0.55	0.61	0.08	0.56
						4rd RMS
						0.18
						0.05

*Abbreviations: BCVA* best corrected visual acuity

3.4 The multiple comparisons between the high-diopter eyes in the control group and amblyopia eyes in two amblyopia sub-groups.

To further investigate the relationship between the severity of amblyopia and the higher-order aberrations, the twenty-five subjects with amblyopia were divided into the mild amblyopia group (n = 11) and the moderate-to-severe group (n = 14). For the comparison of low-diopter eyes, there was no statistical difference between the two amblyopia groups with different degree and the improved group. For the comparison of high-diopter eyes, there were statistically significant differences in visual acuity (Hc = 40.643, p < 0.001) and third-order RMS (Hc = 7.549, p = 0.023) among the three groups. Then the two factors were multiply compared by Nemenyi Test. The best-corrected visual acuity of two amblyopia groups was lower than that in the improved group (both p < 0.001). There was only a statistically significant difference of third-order RMS between the moderate-to-severe amblyopia eyes and the high-diopter eyes in the improved group (p = 0.04) (Table 6).

Table 6

The significant results of multiple comparison between the non-dominant eyes in the control group and amblyopia eyes from two sub-group .

	H	Nemenyi Test (adjusted p)
<b>Visual acuity</b>		
HC – mild amblyopia eyes	10.64	<b>0.00</b>
HC – moderate-to-severe amblyopia eyes	39.03	<b>0.00</b>
mild amblyopia eyes – moderate-to-severe amblyopia eyes	5.62	0.06
<b>3rd order RMS</b>		
HC* – mild amblyopia eyes	3.56	0.17
HC* – moderate-to-severe amblyopia eyes	6.31	<b>0.04</b>
mild amblyopia eyes – moderate-to-severe amblyopia eyes	0.410	0.82
<i>Abbreviations: HC the eyes with high diopter in the control group. RMS the root mean square. H is the coefficient of Nemenyi Test.</i>		

## 4. Discussion

Subjective blur increased more quickly for the higher-order aberrations than for lower-order aberrations,<sup>23,24</sup> whose influence was considered a possible factor of amblyopia' poor visual acuity<sup>25</sup>. If amblyopia eyes still cannot improve the best-corrected visual acuity, we should consider the possibility that there are abnormal higher-order aberrations in these eyes. Our study showed the third-order RMS was an important factor of abnormal higher-order aberrations. And the abnormal C (3,-3) we found in other tables could be considered as an assistant factor.

In this study, the hyperopia anisometropia between the two groups was similar, and the subjects in the two groups had the same degree of anisometropia (spherical mirror, cylindrical mirror, equivalent spherical mirror and eye axis). However, in comparison with the contralateral eye, only the amblyopia group showed the difference of higher-order aberrations between the two eyes, and the main difference was in the third order. Previous studies have also explored the higher-order aberrations of amblyopia. Vincent's study showed that refractive amblyopes displayed higher levels of 4th order aberrations C(4,0), C(4,2) and C(4,-2) in the amblyopic eye compared to non-amblyopic eyes,<sup>3</sup> while Prakash' s study showed there was no significant difference in comparison with higher order aberrations between the normal eyes and the amblyopic eyes<sup>4</sup>. Their conclusion is different from ours, probably because in the previous experiments, only amblyopia is considered, but the numerical influence of anisometropia and diopter itself on higher-order aberrations is not considered. Different refractive states have various higher-order aberrations. Some studies have found that myopia generally has higher fourth-order aberrations<sup>27</sup>, while hyperopia mostly shows in the third-order aberrations<sup>28</sup>.

Zhao's study showed that the C(3,-1) in the intractable amblyopic group was higher than that in the metropic group<sup>29</sup>. Lee's study collected follow-up data about amblyopia and non-amblyopia children, and they found that ocular aberrations in the amblyopic eyes were significantly higher than those in the non-amblyopia group at every point of follow-up<sup>30</sup>. There are similar results between Zhao's and Lee's research and ours. The age span of Zhao's research was relatively large. Although some studies<sup>2,7</sup> have shown that the effect of higher-order aberrations on corrected visual acuity decreases with the increase of age, our similar results showed that the abnormal

difference of higher-order images was less affected by age. Only the comparison of the root mean square of higher-order aberration is found in Lee's results, and we listed every aberration in detail in our analysis and found the difference in C (3,-3).

In these 100 eyes, C (3,3) and third order RMS were related to BCVA. Because low-order aberrations had been corrected by glasses, the possible strong-correlated parameters such as spherical lens, cylindrical lens and eye axis were not included in the correlation analysis. But the significance of correlation coefficient was strong, which indicating that these correlation should not be ignored. We did not found the significant difference in C (3,3) in other results, which may be effected by the small simple size.

Besides, the sample size in the study was too small to give a certain threshold of danger. If the threshold of danger of higher-order aberrations can be confirmed in the future, the children who have abnormal higher-order aberrations should be treated by different methods. RGP (Hard Contact Lens)<sup>31</sup> or vision training after correction of high-order aberrations<sup>32</sup> can be considered, which may be beneficial for amblyopia to improve visual acuity.

## 5. Conclusions

- If amblyopia caused by hyperopia anisometropia has been corrected by glasses, and after a period of covering therapy, the best corrected visual acuity of amblyopia eyes still can not be improved. On the basis of excluding any other diseases affecting BCVA, the abnormality of high-order aberrations is also the cause of poor corrected visual acuity.
- The abnormal higher-order aberrations of amblyopia eyes are mainly the third-order aberrations, which have connection with the BCVA of amblyopia.

## Abbreviations

HOAs higher order aberrations.

BCVA best corrected visual acuity.

AL, axial length.

RMS, root mean square.

## Declarations

### Ethics approval and consent to participate

- The study was approved by the West China Medical Ethics Committee, Sichuan University, and complied with the Declaration of Helsinki's guidelines. (2018(196))
- Informed consent was obtained from each patient and their guardian in written format.

### Consent for publication

All authors agree to publish this article.

### Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files. We are willing to provide the original data and materials, but we hope that the data and materials in the supplementary information files will not be disclosed because we have have unfinished follow-up research.

### Competing interests

Not applicable

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### Authors' contributions

Lingyi Zhang designed this experiment, collected the information of patients and finished the original manuscript. Meng Liao made efforts to the data collection and explaining the results. Wenqiu Zhang provided the funding and gave some suggestions on writing. Longqian Liu guided the completion of the experimental design and revised the manuscript. All authors have read and approved the manuscript.

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