·Clinical Research·

Relationship between higher-order aberrations and myopia progression in schoolchildren: a retrospective study

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Abstract

• **AIM: To investigate the relationship between higher-order aberration (HOA) and myopic progression in schoolchildren.**

• **METHODS: Between April 23 2011 and August 29, 2011 in the children's myopia outpatient clinic of the West China Hospital of Sichuan University, 148 eyes of 74 schoolchildren were reviewed. HOAs for a 6-mm pupil were measured with an aberrometer. Myopic progression rate was defined according to the change in spherical equivalent refraction (SER) divided by the time span (years). Subjects with myopic progression rate of ≥0.50 diopters (D) were classified as the 'fast' group and the subjects with myopic progression rate of <0.50D were classified as the 'slow' group. A retrospective study was conducted to compare HOA between the two groups, using root mean square (RMS) values and Zernike coefficients.**

• **RESULTS: The RMS values of HOA (t=2.316, P=0.02), HOA without Z_4^0(t=2.224, P=0.03),third-order aberrations (t'=2.62, P=0.01), and coma (t'=2.49, P=0.01) were significantly higher in the fast group than those in the slow group. The individual Zernike coefficients of Z_3^{-1} (t=-2.072, P=0.04) and Z_5^1 (Z=-2.627, P=0.01) displayed statistically significant differences between the two groups. Significant correlations were found between the RMS values of HOA (r=0.193, P=0.019), RMS values of HOA without Z_4^0 (r=0.23, P=0.005), RMS values of coma (r=0.235, P=0.004),RMS values of third-order aberrations (r=0.243, P=0.003), and the progression rate.**

• **CONCLUSION: Our results provide evidence of a relationship between HOA and myopic progression. In a future prospective longitudinal study, we aim to verify whether HOA is a risk factor for myopic progression.**

• **KEYWORDS:** aberration; myopic; children; disease progression; refractive errors/etiology
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INTRODUCTION

Myopia is a common refractive error in the Chinese population, especially in young people [1,2]. The etiology of myopia is multifactorial, and both genetic and environmental factors contribute to its development [3]. In recent studies, researchers have identified close work [4], poor retinal image [3], and peripheral refraction [5] as environmental factors of myopia progression. A higher-order aberration (HOA) is a visual aberration that is higher than second-order aberrations. Unlike first-order and second-order aberrations, HOAs cannot be corrected by lenses. However, HOAs can reduce the retinal image quality similarly to lower-order aberration[6,7].

Because HOAs can lead to a poor retinal image, it is possible that HOA is correlated with myopia progression. To address this issue, a number of previous studies have been conducted to investigate whether HOA in the eyes of young people with myopia is different from that in the eyes of emmetropic individuals. However, the results appear to be contradictory. Some studies found a higher level of HOA in myopic eyes compared with emmetropic eyes[8-12], whereas others found no difference between them [13-17]. Moreover, all these studies focused on the relationship between HOA and refractive state. The studies were static, and did not assess change in refractive error over time. To date, there have been no dynamic studies into the correlation between HOA and myopia progression.

With the aim of assessing the relationship between HOA and myopic progression dynamically, we carried out a retrospective study in myopic schoolchildren.

SUBJECTS AND METHODS

Subjects Participants were recruited between April 23, 2011 and August 29, 2011 from the Optometry Centre of the West China Hospital of Sichuan University. The target population comprised children aged 6-16 years old who received cycloplegic refraction annually over 1-3 years in the Centre, whose cylinder measurement was less than -2.50 diopters (D), and whose best-corrected visual acuity was not less than 20/20. Any subject with a history of ocular abnormality or systemic illness was excluded. The study was approved by the ethics committee of Sichuan University, and performed in accordance with the Declaration of Helsinki. The parents or other guardians of the participants were informed of the details of the study, before signing the informed consent documents.

Methods Before the measurements of refractive error and HOA, 1% tropicamide eyedrops were used to paralyze the accommodation of the eye and dilate the pupil sufficiently.

Cycloplegic refraction, which included object retinoscopy and subject refraction, was measured by the same experienced optometrist. Based on the outcome of refraction, the myopic progression rate was calculated as change in spherical equivalent refraction (SER) divided by the time span (years). The group of subjects with myopic progression rate <0.50D was defined as the ‘slow’ group, and the group of subjects with myopic progression rate ≥0.50D was defined as the ‘fast’ group.

At each participant’s most recent visit, the root mean square (RMS) of the HOA and Zernike coefficients up to the fifth order were measured across a 6.0mm pupil by a single experienced optometrist using an aberrometer (Zywave II; Bausch & Lomb, Rochester, NY, USA). Three measurements were taken, and the mean was calculated and used for analysis.

Statistical Analysis Data analysis was performed using SPSS software (version 16.0; SPSS Inc., Chicago, IL, USA). The clinical characteristics of enrolled subjects including age, SER, cylinder, and pupil diameter were compared between the fast and slow groups using the paired *t*-test. Analysis of HOA was based on a 6.0mm pupil diameter. Zernike coefficients up to the fifth order were transformed into the standard form recommended by the Optical Society of America. The RMS values of the total HOA, HOA without Z_4^0, third- to fifth-order aberration, coma aberration, and trefoil aberration were calculated for analysis. Coma aberration is the square root of the sum of the squared coefficients of Z_3^{-1}, Z_3^1, Z_5^{-1}, Z_5^1; trefoil aberration is the square root of the sum of the squared coefficients of Z_3^{-3}, Z_3^{-3}, Z_5^{-3}, Z_5^3; and HOA without Z_4^0 is the higher-order aberration without spherical aberration. For comparison of the aberrations between the fast and slow groups, the one-sample Kolmogorov-Smirnov test was first used to evaluate whether the distribution of all variables was normal. Student's *t*-test was then used when the distribution was normal, and the Wilcoxon rank sum test was used when the distribution was not normal. Spearman correlation was used to analyze the relationship between the RMS values of HOA at the most recent visit and the myopic progression rate. P<0.05 was considered statistically significant.

Table 1 Clinical characteristics of the enrolled myopic children $\bar{x} \pm s$

Parameters	Fast group (n=99)	Slow group (n=49)	P
Age(a)	12.01±2.06	12.16±2.26	0.68
SER(D)	-4.23±1.58	-3.79±1.92	0.14
Cylinder(D)	-0.58±0.61	-0.48±0.52	0.37
Pupil diameter(mm)	8.71±0.63	8.58±0.57	0.23

RESULTS

Subject Characteristics In total, 74 schoolchildren (148 eyes) satisfied the study criteria. All eligible children were Chinese. Of the 148 eyes, 99 had rapidly developing myopia and were classified as the fast group, whereas the other 49 eyes had slowly developing myopia and were classified as the slow group. Table 1 lists the characteristics of the enrolled subjects. There were no significant differences in subject characteristics including age, SER, cylinder, and pupil diameter between the fast and slow groups (P>0.05).

Root Mean Square Values of Higher-Order Aberrations in the Fast and Slow Groups The RMS values of fourth- and fifth-order aberrations were not normally distributed, and thus were compared using the Wilcoxon rank sum test. The RMS values of third-order aberration, coma, and trefoil were analyzed by separate variance estimation t-test because the variances of the fast group and the slow group were not equal. The other RMS values of HOA were analyzed by Student's t-test. As shown in Table 2, the RMS values of the total HOA (t=2.32, P=0.02), HOA without Z_4^0 (t=2.22, P=0.03), third-order aberration (t'=2.62, P=0.01), and coma (t'=2.49, P=0.01) were significantly different between the slow and fast myopic progression groups.

Zernike Coefficients of Higher-Order Aberrations in the Fast and Slow Groups Zernike coefficients of HOA (third- to fifth-order aberrations) are presented in Table 3. The Zernike coefficients values were normally distributed except for Z_5^{-5}, Z_5^1, Z_5^3, and Z_5^5. There was a statistically significant difference in vertical coma (Z_3^{-1}) (t=-2.07, P=

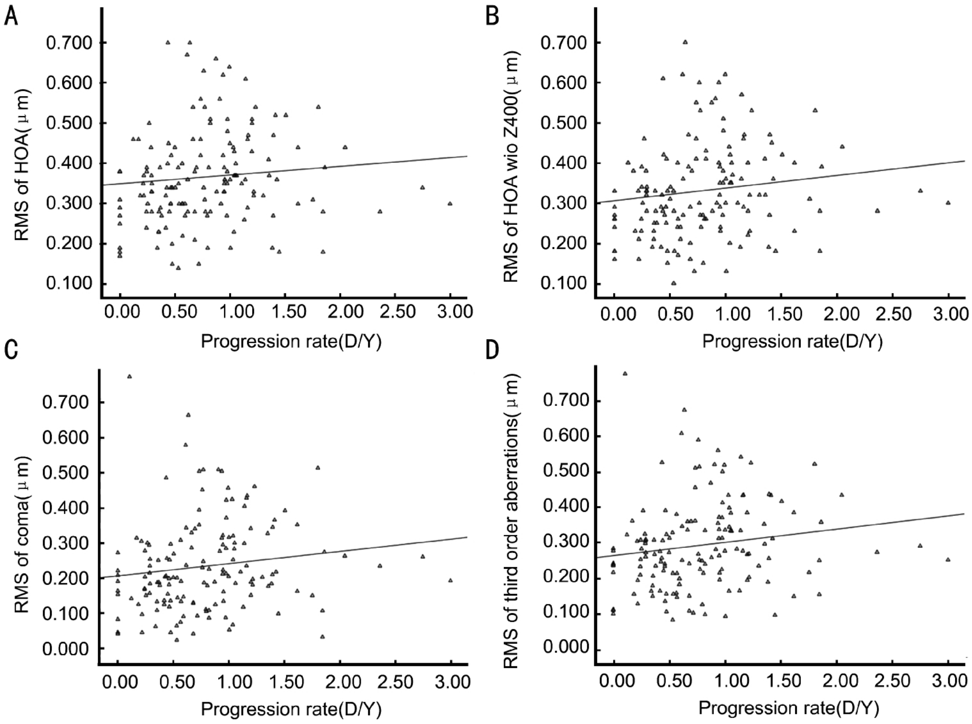

Figure 1 Relationship between RMS and myopia progression Significant correlation was found A: between the root mean square (RMS) value of total higher-order aberrations (HOAs) and the myopic progression rate (r=0.19, P=0.019); B: between the RMS value of HOA without Z_4^0 and the myopic progression rate (r=0.23, P=0.005); C: between the RMS value of coma and the myopic progression rate (r=0.235, P=0.004); and D: between the RMS value of third-order aberrations and the myopic progression rate (r= 0.24, P=0.003).

Table 2 Root mean square values of higher-order aberrations (HOAs) in the two groups $\bar{x}\pm s$

RMS	Fast group	Slow group	P
Total HOA	0.38±0.12	0.33±0.12	0.02
HOA without Z_4^0	0.35±0.13	0.30±0.11	0.03
Third order	0.31±0.13	0.26±0.02	0.01
Fourth order	0.18±0.10	0.19±0.08	0.61
Fifth order	0.07±0.03	0.07±0.03	0.82
Trefoil	0.17±0.08	0.16±0.06	0.26
Coma	0.25±0.13	0.20±0.12	0.01

0.04) and horizontal secondary coma (Z_5^1) (Z= -2.63, P=0.01) between the fast group and the slow group.

Relationship Between Root Mean Square Values and Myopia Progression The RMS values of total HOA, HOA without Z_4^0, coma, and third-order aberrations increased with the myopic progression rate (Figure 1, P<0.05), but the r value was less than 0.3 and the correlation was weak.

DISCUSSION

This retrospective study of 148 myopic eyes in schoolchildren suggests that HOA in myopic eyes is correlated with myopia progression and that eyes with fast-developing myopia have higher levels of HOA.

The RMS values of HOA (t=2.32, P=0.02), HOA without Z_4^0 (t=2.22, P=0.03), third-order aberrations (t'=2.62, P=0.01), and coma (t'=2.49, P=0.01) were significantly higher in the fast group than in the slow group. The individual Zernike coefficients of Z_3^{-1} (t=-2.07, P=0.04) and Z_5^1 (Z=-2.63, P= 0.01) displayed a statistically significant difference between the two groups. A statistically significant correlation was found between the RMS values of HOA and myopia progression rate (r=0.19, P=0.02), the RMS values of HOA without Z_4^0 and progression rate (r=0.23, P=0.005), the RMS values of coma and progression rate (r=0.235, P=0.004), and the RMS values of third-order aberrations and progression rate (r=0.243, P=0.003). These results showed that the fast-developing myopic eyes had higher levels of

Table 3 Zernike coefficients of higher-order aberrations in the two groups $\bar{x}\pm s$

Zernike coefficients	Fast group	Slow group	P
Third order			
Z_3^{-3}	0.05±0.13	0.03±0.12	0.64
Z_3^{-1}	-0.16±0.20	-0.09±0.18	0.04
Z_3^{1}	-0.03±0.11	-0.00±0.11	0.24
Z_3^{3}	0.01±0.12	0.03±0.11	0.35
Fourth order			
Z_4^{-4}	-0.01±0.06	-0.01±0.05	0.75
Z_4^{-2}	-0.00±0.05	-0.01±0.05	0.46
Z_4^{0}	-0.10±0.12	-0.09±0.13	0.56
Z_4^{2}	0.01±0.07	0.01±0.08	0.83
Z_4^{4}	-0.03±0.06	-0.03±0.07	0.85
Fifth order			
Z_5^{-5}	0.01±0.03	0.01±0.03	0.51
Z_5^{-3}	-0.00±0.03	0.01±0.03	0.09
Z_5^{-1}	-0.01±0.04	-0.01±0.04	0.49
Z_5^{1}	-0.01±0.02	-0.00±0.02	0.01
Z_5^{3}	0.00±0.02	0.00±0.02	0.98
Z_5^{5}	0.00±0.03	0.00±0.04	0.52

HOA compared with the slow-developing myopic eyes.

It has been found that abnormal visual experiences can lead to myopia by extending axial length [18,19]. These abnormal visual experiences included form deprivation [20], peripheral retinal image [5], lens-induced defocus [21,22], retinal abnormalities [32324], insufficient accommodation in close work[4], and poor retinal image [3].

HOA is known to be one of the primary causes of poor retinal image. The question is whether there is any direct relationship between HOA and myopia. In response to this issue, Collins *et al* [25] compared the level of HOA in progressing myopia with that in emmetropia, and found that individuals with progressing myopia had higher HOA. Paquin *et al* [26] found that HOA increased with the refractive error in myopic and emmetropic eyes. Coletta *et al* [27] showed in a study of marmosets that the form-deprived myopic eyes of the animals with monocular deprivation had greater HOA than their fellow untreated eyes. However, these results may simply indicate that there is a difference in HOA between myopia and emmetropia, as all used emmetropia as the control condition. Moreover, this difference in HOA might be caused by a difference in refractive error, rather than by progression of myopia. Karimian *et al*[28],who studied aberrations in 162 eyes, found that SER correlated with spherical aberration and horizontal coma. A similar result was reported by Kwan *et al* [29], who found that fourth-order aberrations and spherical aberration correlated with SER. All these authors considered that HOA played a role as an accompaniment instead of a precursor to myopia. In our study, we used slow-developing myopia as the control condition, with fast-developing myopia as the experimental condition, and the influence of SER was excluded by balancing the SER between them; our results showed that there was a relationship between higher HOA and fast progression of myopia.

Some previous studies suggested that there was no difference in HOA between myopia and emmetropia[15], but results have been contradictory. The reason for this discrepancy may be that higher HOA is present only in certain stages of myopia development, and that these HOAs have been masked in previous studies by including data from people with stable myopia [30]. Another possible reason is that there may be a different relationship between myopia and HOA in subjects with different ethnic backgrounds [31]. In our study, subjects with fast-developing myopia had higher HOA than subjects with slow-developing myopia.

It has been reported previously that HOA changes with age [28,32-37] and pupil diameter [35,38,39]. In our study comparing HOA, we ensured that there was no difference in age or pupil diameter between the fast group and the slow group. Other studies have found that coma correlated with astigmatism[40], and that astigmatic eyes tended to have larger HOA [16,28]. In our study, the levels of astigmatism were also equal between the two groups and the influence of astigmatism was excluded.

Because spherical aberration makes up so large a proportion of HOAs [12], we used HOA without Z_4^0 to investigate, in particular, the relationship between myopia progression and HOA, with spherical aberration excluded. Consequently, we found that HOA without Z_4^0 was correlated with myopia progression.

In conclusion, our findings showed that HOA was correlated with myopia progression. However, it remains unclear whether HOA is a cause or a presentation of myopia progression. Our future prospective, longitudinal study will aim to verify whether HOA is a risk factor for myopia progression.

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REFERENCES

1 Sun J, Zhou JB, Zhao PQ, Lian JC, Zhu H, Zhou YX, Sun Y, Wang YF, Zhao LQ, Wei Y, Wang LN, Cun BY ,Ge SF, Fan XQ. High prevalence of myopia and high myopia in 5060 Chinese university students in Shanghai. *Invest Ophthalmol Vis Sci* 2012;53(12):7504-7509

2 He MG, Zheng YF, Xiang F. Prevalence of myopia in urban and rural children in mainland China. *Optom Vis Sci* 2009;86(1):40-44

3 Flitcroft DI. The complex interactions of retinal, optical and environmental factors in myopia aetiology. *Prog Retin Eye Res* 2012;31(6): 622-660

4 Gwiazda J, Thorn F, Bauer J, Held R. Myopic children show insufficient accommodative response to blur. *Invest Ophthalmol Vis Sci* 1993;34 (3): 690-694

5 Charman WN, Radhakrishnan H. Peripheral refraction and the development of refractive error: a review. *Ophthalmic Physiol Opt* 2010;30 (4):321-338

6 Li S, Xiong Y, Li J, Wang N, Dai Y, Xue L, Zhao H, Jiang W, Zhang Y, He JC. Effects of monochromatic aberration on visual acuity using adaptive optics. *Optom Vis Sci* 2009;86(7): 868-874

7 Feizi S, Karimian F. Effect of higher order aberrations on contrast sensitivity function in myopic eyes. *Jpn J Ophthalmol* 2009;53(4): 414-419

8 He JC, Sun P, Held R, Thorn F, Sun X, Gwiazda JE. Wavefront aberrations in eyes of emmetropic and moderately myopic school children and young adults. *Vision Res* 2002;42(8):1063-1070

9 Buehren T, Collins MJ, Carney LG: Near work induced wavefront aberrations in myopia. *Vision Res* 2005;45(10):1297-1312

10 Kirwan C, O'keefe M, Soeldner H. Higher-order aberrations in children. *Am J Ophthalmol* 2006;141(1):67-70

11 Philip K, Martinez A, Ho A, Conrad F, Ale J, Mitchell P, Sankaridurg P: Total ocular, anterior corneal and lenticular higher order aberrations in hyperopic, myopic and emmetropic eyes. *Vision Res* 2012;52(1):31-37

12 Hartwig A, Atchison DA. Analysis of higher-order aberrations in a large

clinical population. *Invest Ophthalmol Vis Sci* 2012;53(12):7862-7870

13 Hartwig A, Atchison DA, Radhakrishnan H. Higher-order aberrations and anisometropia. *Curr Eye Res* 2013;38(1):215-219

14 Llorente L, Barbero S, Cano D, Dorronsoro C, Marcos S. Myopic versus hyperopic eyes: axial length, corneal shape and optical aberrations. *J Vis* 2004;4(4):288-298

15 Li T, Zhou X, Chen Z, Chu R, Hoffman MR. Relationship between ocular wavefront aberrations and refractive error in Chinese school children. *Clin Exp Optom* 2012;95(4):399-403

16 Cheng X, Bradley A, Hong X, Thibos LN. Relationship between refractive error and monochromatic aberrations of the eye. *Optom Vis Sci* 2003;80(1):43-49

17 Leenheer RS, Niemeyer M, Koning J, Bowen A, Dunbar JA. Higher order aberrations: Normative data in the pediatric population. *J AAPOS* 2010;14(1):e21

18 Meng W, Butterworth J, Malecaze F, Calvas P. Axial length of myopia: a review of current research. *Ophthalmologica* 2011;225(3):127-134

19 Wallman J, Turkel J, Trachtman J. Extreme myopia produced by modest change in early visual experience. *Science* 1978;201(4362):1249-1251

20 Huo LJ, Cui DM, Yang X, Wan WJ, Liao RD, Trier K, Zeng JW. A retrospective study: form-deprivation myopia in unilateral congenital ptosis. *Clin Exp Optom* 2012;95(4):404-409

21 Sivak JG. The role of the lens in refractive development of the eye: animal models of ametropia. *Exp Eye Res* 2008;87(1):3-8

22 Zhu X, McBrien NA, Smith EL, 3rd, Troilo D, Wallman J. Eyes in various species can shorten to compensate for myopic defocus. *Invest Ophthalmol Vis Sci* 2013;54(4):2634-2644

23 Wallman J. Retinal influences on sclera underlie visual deprivation myopia. *Ciba Found Symp* 1990;155:126-134

24 Tarabishy AB, Alexandrou TJ, Traboulsi EI. Syndrome of myelinated retinal nerve fibers, myopia, and amblyopia: a review. *Surv Ophthalmol* 2007;52(6):588-596

25 Collins MJ, Buehren T, Iskander DR. Retinal image quality, reading and myopia. *Vision Res* 2006;46(1-2):196-215

26 Paquin M-P, Hamam H, Simonet P. Objective measurement of optical aberrations in myopic eyes. *Optom Vis Sci* 2002;79(5):285-291

27 Coletta NJ, Marcos S, Troilo D. Ocular wavefront aberrations in the common marmoset Callithrix jacchus: Effects of age and refractive error. *Vision Res* 2010;50(23):2515-2529

28 Karimian F, Feizi S, Doozande A. Higher-order aberrations in myopic eyes. *J Ophthalmic Vis Res* 2010;5(1):3-9

29 Kwan WC, Yip SP, Yap MK. Monochromatic aberrations of the human eye and myopia. *Clin Exp Optom* 2009;92(3):304-312

30 Charman WN. Aberrations and myopia. *Ophthalmic Physiol Opt* 2005; 25(4): 285-301

31 Cervino A, Hosking SL, Ferrer-Blasco T, Montes-Mico R, Gonzalez-Meijome JM. A pilot study on the differences in wavefront aberrations between two ethnic groups of young generally myopic subjects. *Ophthalmic Physiol Opt* 2008;28(6):532-537

32 Athaide HV, Campos M, Costa C. Study of ocular aberrations with age. *Arq Bras Oftalmol* 2009;72(5):617-621

33 Plainis S, Pallikaris IG. Ocular monochromatic aberration statistics in a large emmetropic population. *J Modern Optics* 2008;55(4/5):759-772

34 Zhang FJ, Zhou Z, Yu FL, Lu ZL, Li T, Wang MM. Comparison of age-related changes between corneal and ocular aberration in young and mid-age myopic patients. *Int J Ophthalmol* 2011;4(3): 286-292

35 Applegate RA. Three-dimensional relationship between high-order root-mean-square wavefront error, pupil diameter, and aging. *Journal Of The Optical Society Of America A, Optics, Image Science, And Vision* 2007;24(3):578-587

36 Atchison DA, Markwell EL. Aberrations of emmetropic subjects at different ages. *Vision Res* 2008;48(21):2224-2231

37 Nemeth G, Hassan Z, Szalai E, Berta A, Modis L Jr. Analysis of age-dependence of the anterior and posterior cornea with scheimpflug imaging. *J Refract Surg* 2013;29(5):326-331

38 Wu WJ, Zhang ZP, Qian YY, Li XM, Yu QR, Bai L, Yang X. Changes in monochromatic higher-order aberrations in different pupil sizes with accommodation in young emmetropes. *Zhonghua Yanke Zazhi* 2008;44(7): 603-608

39 Bisneto OS, Temporini ER, Arieta CEL, Moreira H. Relationship between high-order aberrations and age and between high-order aberrations and refraction errors. *Arq Bras Oftalmol* 2007;70(2):290-297

40 Hu JR, Yan ZH, Liu CF, Huang LN. Higher-order aberrations in myopic and astigmatism eyes. *Zhonghua Yanke Zazhi* 2004;40(1):13-16