• Investigation •

Prevalence of heterophoria in a population of school children in central China: the Anyang Childhood Eye Study

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Abstract

• **AIM**: To investigate the prevalence of heterophoria and the relationship between heterophoria and refractive error in a school-based study conducted in central China.

• **METHODS:** A total of 2363 7th-grade children were recruited into the cross-sectional school-based Anyang Childhood Eye Study (ACES) by cluster sampling method. Heterophoria was examined using alternate cover and cover-uncover testing. The Maddox rod and prism test were conducted at 33 cm and 6 m distance fixation. Uncorrected viual acuity (UCVA) and best-corrected viual acuity (BCVA) were recorded as logarithm of the minimum angle of resolution (logMAR) with cycloplegic autorefraction by administrating of Mydrin-P and 1.0% cyclopentolate. Hyperopia was defined as the spherical equivalent (SE) refraction of +0.50 D or greater, and higher hyperopia was defined as the SE refraction in the range of -0.49 to +0.49 D, and myopia was in the SE refraction range from -0.50 D to less.

• **RESULTS**: Totally 2260 students in grade 7 were examined. Response rate among eligible children was 95.64%. Totally 486 children, 22.66% of the population, were diagnosed with heterophoria in which 479 were diagnosed with exophoria at near distance, and 6 with esophoria. Totally 89 (4.15%) children were diagnosed with heterophoria in which 82 had exophoria, and 7 had esophoria at far distance. Exophoria was common at near fixation (22.33%). Myopia was examined to be related to exophoria at near distance (OR 3.03, 95%Cl 2.33-3.95) and far distance fixation (OR 1.90, 95%Cl 1.09-3.32).

• **CONCLUSION:** Exophoria is a predominant heterophoria for 7th-grade junior school in central China. Significant

associations are discovered between heterophoria and refractive error. Hyperopia is associated with esophoria, and myopia is associated with exophoria.

• **KEYWORDS:** heterophoria; exophoria; esophoria; refractive errors; epidemiology; children

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INTRODUCTION

H eterophoria is a tendency of both eyes to deviate from the parallel when fusional vergence is broken^[1]. Esophoria and exophoria are the turning of the eye inward and outward respectively from active position when fusion is suspended. Heterophoria may have no symptoms, but poorly controlled heterophoria may cause diplopia, eye pain, blurred vision, dizziness, fatigability and headache, even with the tendency of intermittent heterotropia.

The prevalence of heterophoria has been study in many studies, and it varied greatly in different regions^[2-6]. However, most studies are in agreement that orthophoria is the most common state at distance fixation^[5,7-8], with a tight distribution^[5]. Recently, many clinic-based and school studies have reported the prevalence of strabismus and amblyopia^[5,7,9-11]. But, few researches of refractive error for children in East Asia have been focused on heterophoria. Some studies have showed that factors such as age^[8,12-13], gender^[14], and ethnicity^[12] were associated with heterophoria. Although researches often reported that heterophoria was associated with refractive error; disagreement often occurs^[4-5,14]. Some studies showed that there was no association, nor no direct correlation^[4,14-16]. Another study reported that refractive error was related to heterophoria mostly^[5]. In our study, we aim to report the prevalence of heterophoria in Chinese school-aged children and to examine its relationship to refractive errors.

SUBJECTS AND METHODS

Ethical Approval The study adhered to the Declaration of Helsinki and was approved by the Beijing Tongren Hospital Ethical Committee. The informed consent was signed by parents or legal guardians of all participating students.

Populations The Anyang Childhood Eye Study (ACES) was a cross sectional, school-based, survey of eye health and refraction in Anyang urban areas, Henan Province, China. Detailed study methods have been described^[17-18]. Out of the 2363 eligible 7th-grade students, 2260 (95.64%) finished the screening between October 2011 to December 2011.

Procedures

Distant visual acuity The presenting visual acuity of all students (distant visual acuity with own spectacles) were measured at a distance of 4 m using Logarithmic Visual Acuity Chart (Precision Vision, LaSalle, IL, USA). All students were measured monocularly, and the detailed procedure has been reported elsewhere. Subjective refraction was performed for these students with distant visual acuity worse than logMAR 0.0 (20/20) to get the best corrected visual acuity.

Cycloplegic autorefraction The refractive status of the students was examined by using an auto-refractor (HUVITZ, HRK-7000A, South Korea)^[19] before and after cycloplegia. Both eyes were administered a drop of topical anesthetic Alcaine (AlconPharmaceuticals, Puurs, Belgium) to relieve discomfort, following by 2 drops of 1.0% cyclopentolate (Cyclogyl, AlconPharmaceuticals) and a drop of Mydrin-P (SantenPharmaceuticals, Osaka, Japan) at 5min interval. Thirty minutes later, a third drop of cyclopentolate was administered for the eyes with pupil size less than 6.0 mm or pupillary light reflex still existed. Three consecutive values of sphero-cylindrical auto-refraction were averaged^[18]. Spherical equivalent (SE) was calculated as the sum of the spherical plus a half of the cylindrical error. Hyperopia was defined as the SE refraction of +0.50 D or greater, and higher hyperopia was defined as +2.00 D or greater. Emmetropia was defined as the SE refraction from -0.49 to +0.49 D, and myopia included the SE refraction from -0.50 D to less.

Ocular alignment and movement Ocular alignment and movement were measured by using Hirschberg light reflex, cover test, and prism cover-uncover test. Fixation targets at both near (33 cm) and far distance (6 m) were used to perform cover test^[17]. If glasses were broken, measurements were performed both with and without refractive correction. Monocular and binocular movements were measured at nine diagnostic positions with a stationary head position. The presence of strabismus, the type (esotropia, exotropia, hyper/ hypotropia, or dissociated vertical deviation), characteristics (intermittent or constant), and size (prism diopter, PD) were also recorded^[20].

Definition of heterophoria All the ocular alignment measurements were performed by ophthalmologists. If children had manifest heterotropia, their data were excluded from analysis. Using cover and uncover test and alternate cover test to determine the heterophoria and its' type. The degree of heterophoria was measured using the Maddox rod and prism test^[21]. The red Maddox rod was placed in front of one eye. The children were asked to report the relative position of the Maddox rod streak with respect to the torchlight, which was shown at a distance of 33 cm. The distance between the Maddox rod streak and the torchlight was neutralized with the help of prisms and the values were recorded. Orthophoria was defined that the degree of heterophoria was between -2 PD and +2 PD.

Other ocular examinations A comprehensive eye examination was also performed to all students, which include slit lamp examination, fundus examination, ocular biometry, color vision assessment, and stereopsis screening. To exclude retinal pathologies, digital retinal photographs were taken for all students. The questionnaires were completed by the parents of students. Sociodemographic information including parental occupation, parental education, city of birth, nationality, and parental age were recorded. The students' information including medical history, birth, maternal obstetric history *etc.*

Statistical Analysis Prevalence was defined as the ratio of the number of students with any type of heterophoria to the total number of examined students. All the data were independently double entered into database (Epidata 3.1). All statistical analyses were performed using Statistical Analysis System Software [SAS version 9.3 software (SAS Institute, Inc, Cary, NC, USA)]. The odds ratio of having heterophoria among children with different refractive error subgroups were compared using Polytomous logistic regression with a generalized logit link.

RESULTS

A total of 2260 students in grade 7 were examined, and the response rates among eligible children were 95.64%. After excluding those who met the exclusion criteria or had missing data, eventually there were 2145 subjects available for this analysis. The mean age range of the all students was $12.35\pm0.61y$. Totally 50.40% of the students were male, and 49.60% were female.

Totally 486 (22.66%) children were diagnosed with heterophoria, in which 479 had exophoria, 6 had esophoria, 1 had vertical dissociated heterophoria at near distance. At distance fixation, 89 (4.15%) children from all the included children were diagnosed with heterotropia of whom 82 had exophoria, and 7 had esophoria.

Prevalence of Heterophoria Table 1 displays prevalence of heterophoria among students at distance and near fixation. Exophoria presents in 22.33% at near and 3.82% at distance fixation of the students. Orthophoria presents in 91.10% of the children at distance fixation. Esophoria was rare at near (0.28%) and at far fixation (0.33%).

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Table 1 Prevalence of heterophoria							
Parameters	Orthophoria	Esophoria	Exophoria	Vertical heterophoria	Strabismus		
Near	1554 (72.45)	6 (0.28)	479 (22.33)	1 (0.05)	105 (4.90)		
Distance	1954 (91.10)	7 (0.33)	82 (3.82)	0	101 (4.71)		

Table	2 Distribi	ition of	heterophoria	a degree a	at near a	nd dis	tance fixatio	n
			merer opinor it					

Parameters	≤-15 PD	>-15 PD, ≤-10 PD	>-10 PD, ≤-5 PD	>-5 PD, ≤2 PD	>2 PD, ≤5 PD	>5 PD, ≤10 PD	>10 PD, ≤15 PD
Near	69	110	107	44	1	3	2
Distance	0	3	19	32	4	1	0

Table 3 Number, proporti	ion and odds ratios f	for heterophoria	(without glasses)	at near fixation	among children	with different r	efractive
status by myopia and hyp	eropia						

Donomotoro	Orthophoria	Eso	phoria	Exo	phoria
Parameters	n (%)	n (%)	OR (95%CI)	n (%)	OR (95%CI)
Emmetropia	570 (87.96)	0	1.00	78 (12.04)	1.00
Myopia	937 (70.40)	5 (0.38)	-	389 (29.23)	3.03 (2.33-3.95)
Hyperopia	19 (82.61)	1 (4.35)		3 (13.04)	1.15 (0.33-3.98)

Hyperopia was defined as SE refraction of +2.00 D or greater. Emmetropia included SE refraction from -0.49 to +1.99 D, and myopia was defined as SE refraction of -0.50 D or less. Overall χ^2 =88.48, *P*<0.001.

Table 4 Number	r, proportion	and odds	ratios for	heterophoria	(without	glasses) a	t distance	fixation	among	children	with	different
refractive status	by myopia ar	nd hyperop	ia									

Davamatara	Orthophoria	Es	ophoria	Exophoria		
Parameters	n (%)	n (%)	OR (95%CI)	n (%)	OR (95%CI)	
Emmetropia	632 (97.38)	1 (0.15)	1.00	16 (2.47)	1.00	
Myopia	1267 (95.03)	5 (0.37)	2.49 (0.29-21.39)	62 (4.65)	1.90 (1.09-3.32)	
Hyperopia	22 (95.65)	1 (4.35)	28.6 (1.73-472.93)	0	-	

Hyperopia was defined as SE refraction of +2.00 D or greater. Emmetropia included SE refraction from -0.49 to +1.99 D, and myopia was defined as SE refraction of -0.50 D or less. Overall χ^2 =17.43, *P*<0.001.

Degree of Heterophoria Table 2 shows the distribution of heterophoria degree at distance and near fixation. The magnitude of horizontal heterophoria at both near and distance were not normal distribution (P<0.0001). The distribution of near and distance heterophoria were shifted towards exophoria. The average degree of heterophoria was 10.65 PD (exophoria) and 5.95 PD (esophoria) at near fixation. The average degree of heterophoria was 3.67 PD (exophoria) and 4.02 PD (esophoria) at distance fixation.

Large Heterophoria Totally 486 children were diagnosed with heterophoria at near fixation, in which 335 were measured using Maddox rod and prism test. Totally 181 children had large heterophoria (≥10 PD), maximum 30 PD.

Association Between Refractive Error and Heterophoria Tables 3 and 4 show the association between refractive error and heterophoria of the students with the definition of SE refraction $\geq +2.00$ D for hyperopia. Significant association was found between heterophoria (measured without glasses) and cycloplegic refractive error, for both distance (*P*<0.0001) and near fixation (*P*<0.0001). Students with hyperopia were more likely to be esophoric at distance than those without refractive error. Students with myopia were more likely to have exophoria at distance and near fixation.

Tables 5 and 6 show the association between refractive error and heterophoria of the students. Refractive error was defined as SE refraction \leq -0.50 D and \geq +0.50 D. Significant associations were found between heterophoria (measured without glasses) and cycloplegic refractive error, for near fixation (*P*<0.0001). Students with myopia were significantly more likely to have exophoria both at distance and near fixation than those without refractive error.

There are 278 children with heterophoria worn glasses habitually. Significant relationship was found between heterophoria and corrected refractive error for both distance (P<0.01) and near fixation (P<0.0001). The heterophoria degree with glasses was much lower than that without glasses (Tables 7 and 8).

DISCUSSION

The results from our study showed that orthophoria was the most common eye position for 7th-grade students at distance

Donomotors	Orthophoria	Eso	phoria	Exophoria		
Parameters	Orthophoria Esophoria n (%) n (%) OR (95%CI) 295 (87.54) 0 1.00 937 (70.40) 5 (0.38) - 294 (88.02) 1 (0.30) -	OR (95%CI)	n (%)	OR (95%CI)		
Emmetropia	295 (87.54)	0	1.00	42 (12.46)	1.00	
Myopia	937 (70.40)	5 (0.38)	-	389 (29.23)	2.91 (2.06-4.11)	
Hyperopia	294 (88.02)	1 (0.30)	-	39 (11.68)	0.93 (0.58-1.48)	

Table 5 Number, proportion and odds ratios for heterophoria (without glasses) at near fixation among children with different refractive status by myopia and hyperopia

Hyperopia was defined as SE refraction of +0.50 D or greater. Emmetropia included SE refraction from -0.49 to +0.49 D, and myopia was defined as SE refraction of -0.50 D or less. Overall χ^2 =74.95, *P*<0.001.

Table 6 Number, proportion and odds ratios for heterophoria (without glasses) at distance fixation among children with different refractive status by myopia and hyperopia

Doromotora	Orthophoria	Ese	ophoria	Exophoria		
Farameters	n (%)	n (%)	OR (95%CI)	n (%)	OR (95%CI)	
Emmetropia	326 (97.60)	1 (0.30)	1.00	7 (2.10)	1.00	
Myopia	1267 (94.98)	5 (0.37)	1.29 (0.15-11.08)	62 (4.65)	1.75 (0.86-3.56)	
Hyperopia	328 (97.04)	1 (0.30)	1.00 (0.06-16.05)	9 (2.67)	0.78 (0.28-2.11)	

Hyperopia was defined as SE refraction of +0.50 D or greater. Emmetropia included SE refraction from -0.49 to +0.49 D, and myopia was defined as SE refraction of -0.50 D or less. Overall χ^2 =6.07, *P*>0.05.

Table 7 The comparison of the heterophoria degree with or without glasses at near fixation

Parameters	Mean	SD	Min	Max
Without glass	-9.96	5.90	-26	14
With glass	-7.32	5.39	-22	15
(12 (7 D <0.0001	270			

t=-12.67, *P*<0.0001, *n*=278.

 Table 8 The comparison of the heterophoria degree with or without glasses at distance fixation

Parameters	Mean	SD	Min	Max
Without glass	-2.33	3.41	-13	25
With glass	-2.64	3.48	-15	26
0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0				

t=2.70, *P*<0.01, *n*=278.

fixation. The distribution of heterophoria was skewed towards exophoria. Many other studies indicated similar results^[5,8,22]. While many researches have indicated that orthophoria was also the main status at near fixation^[8], our results showed exophoria is a frequent status, consistent with Leone et $al's^{[5]}$ and Hashemi *et al*'s^[13] studies. Leone *et al*^[5] reported a prevalence of 52.2% exophoria in the 12-year-old children. Hashemi *et al*^[13] reported a prevalence of 10.19% for</sup>exophoria in 6-20y. Leone *et al*^[5] reported that this finding was more significant in East Asian populations and was in line with the high prevalence of mainly intermittent exotropia^[11]. In this study, the average degree of exophoria at near fixation was higher than in the report by Leone *et al*^[5] from Australia</sup>(exophoria: 3.9 PD). As reported by Babinsky et $al^{[16]}$, heterophoria was not influenced by age, uncorrected refractive error, the AC/A ratio, or the CA/C ratio. One of the possible explanations for this difference was the different measurements for heterophoria. The degree of heterophoria was measured by

using alternate cover test and standardized detailed targets in Leone *et al*'s^[5] study, while by Maddox rod in our study.

Heterophoria examined without glasses was related to ametropia. Esophoria was related to hyperopia, and this paralleled the relationship between hyperopia and esotropia. In our study, different definitions of refractive error were used. When the definition of hyperopia was used as \geq +2.00 D^[5], the result showed that students with hyperopia were more likely to have esophoria than students without ametropia. When used the definition of hyperopia as \geq +0.50 D, there was no significant difference between the hyperopia and esophoria. Clinically, it is generally believed that esotropia was significant associated with high hyperopia^[23]. Then, it is believed the definition of refractive error with \geq +2.00 D is more reasonable.

Exophoria was related to myopia apparently. This correlation may cause by decreased demand for accommodation. Reduced demand for accommodation may let both eyes present a physiological rest position^[5,24]. In this study, the prevalence of exophoria was higher than that of Caucasian populations^[6,25]. This was in line with the high prevalence of mainly intermittent exotropia in East Asian children. It may be associated with more myopia or the different race of East Asian population^[7,18]. There were another possible factors contributing to high prevalence of exophoria among East Asian population. Clinical experience suggests that intermittent exotropia may be preceded by the poorly control of exophoria^[5]. The incidence of myopia in China was increased recently, and this was in line with the high prevalence of intermittent exotropia. Chinese government devoted much attention to myopia prevention and control recently. In order to determine if the reduction of myopia will cause the decreased prevalence in exophoria and intermittent exotropia in further, longitudinal studies in children will be needed to clarify the association. Totally 181 students had a large heterophoria (\geq 10 PD) at near fixation. Large heterophoria may cause symptoms such as blurred vision, headache, and diplopia. Decompensation of heterophoria may lead to heterotropia. This result suggested that we should pay attention to these students, especially those with complains. On the other hand, only 6 students had a large heterophoria at distance fixation. It may be also attributed to the reduced demand for accommodation^[7] or poor convergence^[26]. Most of these children have myopia^[10]. Wearing glasses reduced the degree of the heterophoria.

In conclusion, this study of 7th-grade junior high school in central China showed the prevalence of heterophoria of Chinese children, in which the prevalence of exophoria was much higher than Caucasian children. At the same time, a strong association was found between heterophoria and refractive errors. Hyperopia was associated with esophoria, and myopia was associated with exophoria.

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