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Impact of Parental History of Myopia on the Development of Myopia in Mainland China School-Aged Children

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ABSTRACT

BACKGROUND: Myopia is a very common condition and a significant public health problem in China. The objective of the study was to explore the genetic influence on myopia in Mainland China school-aged children in Beijing.

METHODS: In 2008, the data from 15,316 Chinese school students aged 6–18 years from 19 randomized schools in Beijing were analyzed to evaluate genetic influence on myopia in children. Heritability was calculated by mid-parent–offspring regression and parent–offspring regression.

RESULTS: The estimate of heritability was 0.30 (95% CI, 0.27–0.33) for refractive value (RV). The adjusted mean refractive error was −2.33D (95% CI, −2.45 to −2.21) in children with two myopic parents compared with −1.13D (95% CI, −1.78 to −1.08) in children with no parental myopia. The adjusted odds ratio (OR) was 2.83 (95% CI, 2.47–3.24) in children with two myopic parents compared with no parental myopia.

CONCLUSION: The study found a strong association between parental history of myopia and genesis of myopia in the offspring even after adjusting for environmental factors.

KEYWORDS: myopia, parental history, epidemiology

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Introduction

Myopia is a very common condition and a significant public health problem in China. The prevalence of myopia in Chinese school-aged children was one of the highest in the world according to the Report of Student Physical Health Monitoring by the Ministry of Education of China. According to the report, the prevalence of myopia in Beijing (31.10% for primary school students, 62.12% for middle school students, and 77.88% for high school students) is higher than the average of the whole country and shows an upward trend.[1] Myopia is known to be associated with a variety of ocular complications such as glaucoma, cataract, retinal detachment, optic disc changes, and maculopathy.[2,3] Therefore, preventing the occurrence of myopia is important in China.

The etiology of myopia involves genetic factors and environmental components.[4–7] Previous studies have showed that environmental risk factors for myopia include near work, intelligence quotient (IQ), education level, outdoor activity (sport and leisure activities), and light exposure.[8–12] It has been well established that genetics play an important role in refractive error. Several familial studies have shown that prevalence of myopia in children increased when there was at least one

parent affected.[7,13,14] Moreover, twin studies have highlighted the greater concordance between myopic monozygotic twins than between dizygotic twins.[15–19]

It is generally believed that a disease caused mainly by genetic factors tends to have an earlier onset, more affected family members, and more severe clinical presentations compared to the same disease caused mainly by environmental factors.[19,20] A study of the general prevalence and trend, with both parents with myopia compared to no parental myopia among 2888 Chinese children aged from 7 to 17 years and their parents conducted in Hong Kong, showed that the highest prevalence of myopia occurred when both parents were myopic and the lowest when neither parent was myopic.[7] In our study, we sought to investigate the same possible association but with a significantly larger sample size and also adjusting for possible environmental risk factors.

The aim of this report is to estimate the heritability of ocular refraction using variance component analysis and to explore the relationship between parental refractive status and the likelihood of myopia in Mainland China school-aged children.

Methods

Subjects. The sample of this study came from a multistage stratified randomized sampling, in which 18 districts in Beijing were divided into three strata namely developed region, developing region, and undeveloped region according to the economic indicator of GDP; 9 schools including 3 primary schools, 3 middle schools, and 3 high schools were randomly selected from each stratum (a total of 27 schools was drawn, but only 19 schools were consented for the study) and a total of 900 students from each school were randomly drawn in 2008. Parents and students were provided an explanation of the study and the parents gave their consent for their children's participation in the study if Beijing Municipal Commission of Education approved the study protocol. The protocol was approved by the Commission. A questionnaire designed to evaluate the genetic, environmental, and behavioral risk factors of myopia was used. It included four parts; the first part, general characteristics (gender, age, parents' education, parents' profession, and family income); the second part, near work questions (reading or writing distance, studying time per day, hours of watching TV and using computer per day, distance to TV, etc.); the third part, sports, sleeping, and nutrition questions (hours of sports per day, hours of sleeping per day, quantity of sweet foods, fruit, vegetable, and high protein foods, etc.); the fourth part, parental myopia.

Examination. An auto kerato-refractometer (model RM A7000, Topcon Ltd, Japan) was used to obtain the average of five consecutive refraction readings (all readings <0.25D apart) and the average of two corneal curvature readings in the flatter and steeper meridians was calculated.

Refraction was analyzed using spherical equivalent (SE) = sphere + half negative cylinder power. Myopia was defined as at least −0.75D in both the horizontal and vertical

meridians on cycloplegic autorefraction. Cyclopentolate 1% drops were used for cycloplegia and measurements were taken 30 minutes after drop instillation. Only the children were refracted. Data (SE) from the right and left eye were similar (Pearson correlation coefficient = 0.88) and thus, results from the left eye were presented.

Statistical analyses. In classical quantitative genetics,[21,22] the correlation between relatives is taken into account by the relationship matrix, where the correlation between any two individuals is twice their coefficient of co-ancestry.[22] This relationship matrix, inferred from the pedigree, is then used to estimate the heritability via a mixed linear model using maximum likelihood or Bayesian methods.[22] Heritability was calculated by mid-parent–offspring regression and parent–offspring regression. Multiple line regression models with refractive value (RV) as the dependent variable and parental myopia as the main covariate were constructed adjusting for age, gender, parental education, reading or writing distance, hours of sports and outdoor activities, hours spent watching TV or using the computer, and hours of sleeping. The linear trend tests were performed by parental myopia status (neither, one, both) to count the adjusted means of the refractive error and the odds ratio (OR) for children with no, one, or two myopic parents by multiple linear regression models after adjusting for the same risk factors. Data analysis was conducted using a commercially available software (Stata, Ver.9.0; Stata, College Station, TX, USA).

Results

In all, 15,316 school-aged students (response rate of 94.5%) from grade 1 in primary school to grade 3 in high school located in different districts in Beijing were invited to participate in the survey [primary school students, 5643 (36.8%); middle school students, 4378 (28.6%); and high school students, 5295 (34.6%); male students, 7434 (48.5%) and female students, 7882 (51.5%); urban areas, 6230 (40.7%) and suburban areas, 9086 (59.3%)]. Regions were classified as urban or suburban according to their population density. The number of boys was 7434 while the number of girls was 7882. According to our analysis, there was no significant difference between boys and girls on heritability of myopia.

Heritability of refractive value. The mean refractive error was −1.45D (SD 2.50; range −14.78 to 14.37) and the prevalence rate of myopia was 8178/15,316 (53.40%; 95% CI, 52.60–54.19%).

Our estimates of heritability show that the additive effect is responsible for about 24% ($P < 0.001$) by mother–offspring line regression and 25% ($P < 0.001$) by father–offspring line regression without adjusting for gender, age, parental education, reading distance, hours of studying, hours of TV, hours of sports and outdoor activities, and hours of sleeping. The proportions were 31% and 34%, respectively, by the same way after adjusting for environmental factors. Moreover, the proportion of heritability was 22% by mid-parent–offspring line

regression without adjusting for the environmental factors; it increased to 30% ($P < 0.001$) after adjusting for the environmental factors (Table 1).

Association between parental myopia and myopia in their children. Unadjusted means of the refractive error for children with no, one, and two myopic parents were −1.18D, −1.87D, and −2.14D, respectively (trend test, $P < 0.001$, Table 2). The results were −1.13D, −1.93D, and −2.33D, respectively (trend test, $P < 0.001$), after adjusting for factors such as age, gender, parental education, reading or writing distance, hours of sports and outdoor activities, hours spent watching TV or using the computer, and hours of sleeping.

The prevalence rate of myopia in the parents is generally lower than their children in this study (prevalence rate of myopia in fathers is 14.93% and in mothers is 17.8%). The prevalence rates of myopia for children with no, one, and both parents with myopia were 49.77%, 59.62%, and 64.42% respectively (trend test, $P < 0.001$, Table 3). From univariate analyses, myopia was associated with both parents with myopia compared to no parental myopia (OR = 1.88; 95% CI, 1.69–2.10; Table 3), and also associated with one parent with myopia (OR = 1.53; 95% CI, 1.42–1.65). A final multivariate model was constructed with myopia as the outcome variable and age, gender, parental education, reading or writing distance, hours of sports and leisure activities per day, hours of watching TV or using computer per day, hours of studying per day, and hours of sleeping as explanatory variables. Myopia was associated with two parents with myopia compared to no parental myopia (OR = 2.83; 95% CI, 2.47–3.24; Table 3), and also associated with one parent with myopia (OR = 1.91; 95% CI, 1.75–2.10).

Discussion

Our results correlate with previous studies, which showed that RVs are influenced by genetic factors.[7,13] Our estimates of heritability showed that the additive effect is responsible for 22% ($P < 0.001$) without adjusting for other environmental factors, but this proportion increased to 30% ($P < 0.001$) after adjusting for environmental factors. These results are consistent with previously reported estimates derived from parent–offspring correlations. For instance, Biino et al.[23] reported an estimate of 27% in a heritability analysis of biometric ocular traits in a Sardinian population.

Moreover, higher heritability estimates have been reported in twin and sibling studies. Guggenheim et al.[24] investigated correlations in refractive errors between siblings in a Singaporean cohort study and found a correlation in refractive error of 44.7% after adjusting for age and sex. A twin study undertaken by Dirani et al.[18] showed that the effects of additive genes explained 58% and 47% of the variance for refractive error in the men and women, respectively. A similar study by Hammond et al reported an additive effect for refractive error of 85% in British women.

In order to allow an accurate comparison between heritability estimates, two points have to be considered. First, analysis of twins provides an upper estimate of heritability, which may not accurately measure the degree of genetic influence in the non-twin population.[6,25] Second, heritability is a population-specific parameter and it might be different among populations because of different environmental factors or different genetic backgrounds.[21] Our study estimates the heritability in a Mainland Chinese population in Beijing, and some reported risk factors of myopia were taken into account.

Several previous studies reported the impact of family history on the development of myopia. With myopia defined as at least −0.75D, Mutti et al.[12] studied the possible association between juvenile myopia and parental myopia in 366 eighth grade students in the US. They reported an OR of 6.4 for two myopic parents compared with no parental myopia. Jones et al.[5] reported an OR of 5.40 for children with two myopic parents compared to children with no myopic parents, which is also higher than our adjusted OR of 2.83. Their findings are based on a study population of 514 children from US high schools between school grade 1 and 8. Our adjusted OR correlates with Saw et al.[26] who reported an OR of 3.1 in young Singaporean men based on a cross-sectional study of national servicemen aged between 18 and 23 years, enlisted in the Singapore Armed Forces. Their sample population was representative of the entire young male Singapore population. The wide range of ORs among these studies may be due to sample variation, recruitment schemes, recall bias, definition of myopia, and various risk factors among different populations.[27] However, all these studies suggested that parental myopic status is an important risk factor.

Several other studies have explored the genetic influence on myopia in Chinese children. In terms of sample size,

Table 1. Heritability (h^2) estimates for refractive values (RVs).

VARIABLE	n	UNADJUSTED		ADJUSTED	
		REGRESS COEFFICIENT (95% CI)	h^2 (SD)	REGRESS COEFFICIENT (95% CI)	h^2 (SD)
RV					
Mother	15316	0.121 (0.098–0.143)	0.24 (0.01)	0.157 (0.137–0.178)	0.31 (0.01)
Father	15316	0.128 (0.103–0.154)	0.25 (0.01)	0.171 (0.147–0.195)	0.34 (0.01)
Parental mean	15316	0.222 (0.189–0.253)	0.22 (0.02)	0.296 (0.266–0.326)	0.30 (0.02)

Table 2. Unadjusted and adjusted means of refraction by parental myopia.

| PARENTAL MYOPIA | N | REFRACTIVE ERROR (D) | | | |
		UNADJUSTED MEAN (SD)	95% CI	ADJUSTED MEAN (SD)	95% CI
Neither	9893	−1.18 (0.02)	−1.23, −1.14	−1.13 (0.02)	−1.78, −1.08
One	3883	−1.87 (0.04)	−1.94, −1.79	−1.93 (0.04)	−2.01, −1.85
Both	1540	−2.14 (0.07)	−2.27, −2.01	−2.33 (0.06)	−2.45, −2.21
P for trends		<0.001		<0.001	

our study is comparable to the Beijing Pediatric Eye Study,[28] which was a population-based cross-sectional study of 16,771 students aged 7–18 years. In multivariate analysis, the prevalence of myopia (defined as ≤−1.00 diopters) was associated with parental myopia with an OR of 1.35. In contrast, our OR of 2.83 is higher with myopia defined as ≤−0.75 diopters.

Guo et al.[29] conducted a school-based cross-sectional study of 382 grade 1 and 299 grade 4 children in Greater Beijing. Other than maternal myopia, myopia in school-aged children was also associated with less outdoor activity, more indoor studying, older age, and urban region of habitation. The authors suggested that outdoor activity could help reduce the high prevalence of myopia in the young generation in Beijing.

Our outcomes also agree with the findings from studies on Chinese children in different countries. For instance, Ip et al.[30] looked at the influence of parental myopia on spherical equivalent refraction (SER) in a population-based sample of 12-year-old Australian children. The prevalence of myopia in the children increased with the number of myopic parents (7.6%, 14.9%, and 43.6% for no, one, or two myopic parents, respectively). Furthermore, interactions between parental myopia and ethnicity were also significant for SER, reflecting greater decreases in SER with the number of myopic parents in the children of East Asian ethnicity than in the children of European–Caucasian ethnicity.

Our study did not investigate the direct association between parental history of myopia and age of onset of myopia in children. However, a cross-sectional study of 887 participants between ages of 17 and 45 years, conducted by Liang et al.,[27] has found a strong genetic influence on the onset of myopia even after adjusting for environmental factors. Of note, children with highly myopic parents tended to have an earlier onset of myopia (≤11 years) with an OR of 2.61. In addition, another cross-sectional study of 716 school children aged 6–14 years, undertaken by Zadnik et al.,[13] suggested that the premyopic eye in children with a family history of myopia already resembles the elongated eye present in myopia. Because of the cross-sectional design of these studies, the pattern of growth of these eyes and the subsequent occurrence of myopia could not be ascertained. The possible association between parental history of myopia and onset of myopia in offsprings requires further investigations as it may have an implication in the refractive correction of school-aged children.

There are some limitations in this study. As for any retrospective epidemiologic study, our analysis may be subject to recall bias. Moreover, the questionnaire may not be the most accurate tool to assess the amount of near work or other activities associated with myopia.

Conclusion

To date, this is the largest retrospective study for myopia in Mainland China school-aged children. It showed a significant association between parental myopia and genesis of myopia in the offspring. Moreover, children with two myopic parents are at higher risk of developing higher degree of myopia than those with only one myopic parent. The latter, in turn, are more likely to develop myopia compared to those with no parental myopia.

Author Contributions

LL and SY had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. LL, YG, EA, GX, XZ, and SY developed the study concept and design, and were involved in acquisition of data, analysis and interpretation of data, statistical analysis, drafting of the manuscript, and critical

Table 3. Prevalence rates of myopia and odds ratio (OR) by parental myopia.

PARENTAL MYOPIA	n	PREVALENCE RATES OF MYOPIA	UNADJUSTED OR (95% CI)	ADJUSTED OR (95% CI)
Neither	9893	49.77%	1.00 (referent)	1.00 (referent)
One	3883	59.62%	1.53 (1.42, 1.65)	1.91 (1.75, 2.10)
Both	1540	64.42%	1.88 (1.69, 2.10)	2.83 (2.47, 3.24)
P for trends		<0.001	<0.001	<0.001

revision of the manuscript for important intellectual content, and provided administrative, technical, or material support. SY did study supervision. All authors reviewed and approved of the final manuscript.

REFERENCES

1. Beijing student fitness and health survey; 2005. Available at http://tmc.bjedu.gov.cn/tiyu/ty_xxlt/2012-06-20/1103.html.
2. Saw SM, Gazzard G, Shih-Yen EC, Chua WH. Myopia and associated pathological complications. *Ophthalmic Physiol Opt*. 2005;25(5):381–91.
3. Tong L, Saw SM, Chua WH, et al. Optic disk and retinal characteristics in myopic children. *Am J Ophthalmol*. 2004;138(1):160–2.
4. Loman J, Quinn GE, Kamoun L, et al. Darkness and near work: myopia and its progression in third-year law students. *Ophthalmology*. 2002;109(5):1032–8.
5. Jones LA, Sinnott LT, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci*. 2007;48(8):3524–32.
6. Morgan I, Rose K. How genetic is school myopia? *Prog Retin Eye Res*. 2005;24(1):1–38.
7. Yap M, Wu M, Liu ZM, Lee FL, Wang SH. Role of heredity in the genesis of myopia. *Ophthalmic Physiol Opt*. 1993;13(3):316–9.
8. Tay MT, Au Eong KG, Ng CY, Lim MK. Myopia and educational attainment in 421,116 young Singaporean males. *Ann Acad Med Singapore*. 1992;21(6):785–91.
9. Wu HM, Seet B, Yap EP, Saw SM, Lim TH, Chia KS. Does education explain ethnic differences in myopia prevalence? A population-based study of young adult males in Singapore. *Optom Vis Sci*. 2001;78(4):234–9.
10. Czepita D, Goslawski W, Mojsa A, Muszynska-Lachota I. Role of light emitted by incandescent or fluorescent lamps in the development of myopia and astigmatism. *Med Sci Monit*. 2004;10(4):168–71.
11. Rose KA, Ip JM, Robaei D, et al. Near-work and outdoor activities and the prevalence of myopia in Australian school students aged 12–3 years: the Sydney Myopia Study. *Invest Ophthalmol Vis Sci*. 2006;47:5453.
12. Mutti DO, Mitchell GL, Moeschberger ML, Jones LA, Zadnik K. Parental myopia, near work, school achievement, and children's refractive error. *Invest Ophthalmol Vis Sci*. 2002;43(12):3633–40.
13. Zadnik K, Satariano WA, Mutti DO, Sholtz RI, Adams AJ. The effect of parental history of myopia on children's eye size. *JAMA*. 1994;271(17):1323–7.
14. Farbrother JE, Kirov G, Owen MJ, Guggenheim JA. Family aggregation of high myopia: estimation of the sibling recurrence risk ratio. *Invest Ophthalmol Vis Sci*. 2004;45(9):2873–8.
15. Sorsby A, Fraser GR. Statistical note on the components of ocular refraction in twins. *J Med Genet*. 1964;1(1):47–9.
16. Chen CJ, Cohen BH, Diamond EL. Genetic and environmental effects on the development of myopia in Chinese twin children. *Ophthalmic Paediatr Genet*. 1985;6(1–2):353–9.
17. Hammond CJ, Snieder H, Gilbert CE, Spector TD. Genes and environment in refractive error: the twin eye study. *Invest Ophthalmol Vis Sci*. 2001;42(6):1232–6.
18. Dirani M, Chamberlain M, Shekar SN, et al. Heritability of refractive error and ocular biometrics: the Genes in Myopia (GEM) twin study. *Invest Ophthalmol Vis Sci*. 2006;47(11):4756–61.
19. Ford D, Easton DF, Stratton M, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. *Am J Hum Genet*. 1998;62(3):676–89.
20. Rebbeck TR. Inherited genetic predisposition in breast cancer. A population-based perspective. *Cancer*. 1999;86(11 suppl):2493–501.
21. Falconer DS, MacKay TFC. *Introduction to Quantitative Genetics*. 4th ed. Harlow, Essex, UK: Longmans Green; 1996.
22. Lynch M, Walsh B. *Genetics and Analysis of Quantitative Traits*. Sunderland, MA: Sinauer; 1998.
23. Biino G, Palmas MA, Corona C, et al. Ocular refraction: heritability and genome-wide search for eye morphometry traits in an isolated Sardinian population. *Hum Genet*. 2005;116(3):152–9.
24. Guggenheim JA, Pong-Wong R, Haley CS, Gazzard G, Saw SM. Correlations in refractive errors between siblings in the Singapore Cohort Study of Risk-factors for Myopia. *Br J Ophthalmol*. 2007;91(6):781–4.
25. Khoury MJ, Beaty TH, Cohen BH. *Fundamentals of Genetics Epidemiology*. New York: Oxford University Press; 1993.
26. Saw SM, Wu HM, Seet B, et al. Academic achievement, close up work parameters, and myopia in Singapore military conscripts. *Br J Ophthalmol*. 2001;85(7):855–60.
27. Liang CL, Yen E, Su JY, et al. Impact of family history of high myopia on level and onset of myopia. *Invest Ophthalmol Vis Sci*. 2004;45(10):3446–52.
28. You QS, Wu LJ, Duan JL, et al. Factors associated with myopia in school children in China: the Beijing childhood eye study. *PLoS One*. 2012;7(12):e52668.
29. Guo Y, Liu LJ, Xu L, et al. Outdoor activity and myopia among primary students in rural and urban regions of Beijing. *Ophthalmology*. 2013;120(2):277–83.
30. Ip JM, Huynh SC, Robaei D, et al. Ethnic differences in the impact of parental myopia: findings from a population-based study of 12-year-old Australian children. *Invest Ophthalmol Vis Sci*. 2007;48(6):2520–8.