Incidence of Myopia in High School Students with and without Red-Green Color Vision Deficiency

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Purpose. To investigate the influence of color vision on myopia development by testing refraction error and axial length of the eye for high school students with and without color vision deficiency (CVD).

Methods. A school-based cross-sectional, cluster sample study was conducted to test the color vision and refractive error of 16,539 high school students. Students were screened for CVD using a pseudoisochromatic plate. CVD was confirmed in students failing the test using a Farnsworth-Munsell 100-Hue Test which also served to classify the subtype (protan or deutan). Three classmates of each CVD subject, matched in five myopia risk factors, were chosen to form the normal color vision (CN) control group. Ophthalmic examinations were performed to determine refractive status and axial length.

Results. Of the students, 509 were found to have red-green CVD and 927 were selected as the CN control group. The prevalence of myopia in the CVD group (45.6%) was significantly lower than that of the CN group (65.8%; \( P < 0.001 \)). The CVD group was also less myopic in refraction (\( P < 0.001 \)) than CN, and protan subjects had shorter axial lengths than those in the control group (\( P = 0.007 \)).

Conclusions. Color vision deficiencies appear to influence the development of myopia. The observed lower incidence of myopia in people with CVD may be linked to the reduced functionality of the L/M chromatic mechanism. (Invest Ophthalmol Vis Sci. 2009;50:1598–1605) DOI:10.1167/iovs.07-1362

During eye development, early visual experience plays a critical role in controlling eye growth, with a predictable change in axial length to match the position of the image focal plane with the retinal plane.\(^1\)\(^2\) Placing a positive or negative lens before the eye, thus shifting the image focal plane to a position in front of or behind the retina, leads to a shorter or longer axial length and consequently a hyperopic or myopic eye.\(^3\)\(^4\) The process by which the eye grows to match its retina with the image focal plane is called emmetropization, a term originally used to describe the elimination of refractive errors in neonates during early eye development. The active emmetropization is functionally analogous to accommodation, by which the focal plane of a near visual target is brought to the retinal plane through a change in the refractive power of the lens.

The optical system is not free of chromatic aberration. Longitudinal chromatic aberration (LCA), caused by the dispersion of the ocular media, causes a single object to form multiple chromatic images within the eye, located at different distances from the retina for different color images. For example, a distant object could produce a red (long-wavelength [L]) image behind the retina, a blue (short-wavelength [S]) image in front of the retina, and green and yellow (middle-wavelength [M]) images near or at the retina. In the human eye, the long-wavelength (700 nm) and short-wavelength (450 nm) images are separated by approximately 1.7 to 2.0 D, with very small individual variations.\(^5\)\(^6\) Given that multichromatic images simultaneously stimulate the retina with different amounts of defocus, the question of how the mechanisms controlling eye growth respond is of particular interest in the study of emmetropization and myopia development.

Processing of visual information under photopic conditions is initiated by three types of photoreceptors—S-, M-, and L-sensitive cones—and subsequently mediated by a luminance and two opponent chromatic mechanisms, the red/green (or L/M) and yellow/blue (or [L+M]/S) channels. Each cone type is sensitive to a broad range of wavelengths, but has its own peak sensitivity (e.g., 440, 543, and 566 nm for the S-, M-, and L-cones, respectively).\(^7\)\(^8\) Signals of the M- and L-cones are additively fed into the luminance channel and compared in the L/M chromatic opponent channel. The (L+M)/S chromatic opponent channel compares the responses from the S-cone and the summed responses from the L- and M-cones.\(^9\)\(^10\)\(^11\) Animal studies with chicken and fish demonstrated that when illumination consisted of only a single or narrowband wavelength, the eye grew after the monochromatic image focal plane, determined by LCA.\(^12\)\(^13\) From these findings, Kroger and Wagner\(^14\) inferred that all chromatic mechanisms contribute to the emmetropization process. However, the luminance channel response to LCA alone, without participation of chromatic mechanisms, could also predict the dependency of eye growth on illuminant wavelength. Moreover, emmetropization in humans may be different from that in animals. Therefore, direct study of the human eye is needed to determine the role of chromatic mechanisms in emmetropization and myopia development.

In a series of studies which controlled the effects of LCA and changes in luminance contrast,\(^16\)\(^17\)\(^18\)\(^19\)\(^20\)\(^21\) chromatic mechanisms were proven to play an important role in controlling...
methods

study population and sampling

A school-based cross-sectional randomized stratified cluster-sampling study was conducted in the Xuhui district, Shanghai, and three cities (Urumqi, Turfan Basin, and Hetan) of the Xinjiang Province. In China, students graduating from junior high school are placed in different high school tracks based on final year grades. If the child performs well in final examinations, he or she may enter into a key senior high school. Otherwise, the student can choose a general or vocational high school. There are 25 high schools in Shanghai and Xinjiang. Informed consent was obtained from each student from the 24 schools were invited. The research adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of the Xinhua Hospital of Fudan University. Permission to conduct the study was obtained from the Ministry of Education of Shanghai and Xinjiang. Informal consent was obtained from each parent after explaining the nature and possible consequences of the study.

The presence of congenital CVD was determined using the Yuzip refractive error correction; cycloplegic autorefraction (KR-8100; Topcon, Tokyo, Japan) and subjective validation based on the autorefraction results to obtain the best corrected visual acuity (BCVA); noncontact tonometry (CT-60; Topcon); slit-lamp biomicroscopy (model BQ900; Haag-Streit, Bern, Switzerland); axial length of the globe (ultrasound biomicroscopy; Compuscan; Storz Ophthalmic, Inc., St. Louis, MO). Cycloplegia was achieved with 1 drop of combined

control sampling

Students with a diagnosis of CVD and their classmates were required to finish a structured questionnaire that included demographic data, parental history of myopia (whether one or two of the parents wore nearsighted eye glasses, and if so, whether their refractions were less than −5 D), and behavioral factors (amount of time spent on reading, writing, video games, computer work, and sports each day outside of school, as well as reading distance). Answers to the questionnaire were used to select matched controls for the CVD cases. Three classmates with normal color vision were chosen as control subjects for each CVD student. The matching factors included: identical sex, similar age (±1 year), similar parental history (the same number of parents with myopia less than or higher than −5 D), closest dipter-hour (a weighted measure that takes into account viewing distance and the duration of various activities; ±2 dipter-hours), and the amount of time spent outdoors (±1 hour). If more than three matched the condition, a random-number table was used to select three classmates whose student identification numbers were close to that of the CVD student. Analysis of the questionnaire and selection of the controls were performed by a separate specialized technical staff.

ophthalmic examination

The following factors were analyzed: visual acuity, with the logMAR chart without refractive error correction; cycloplegic autorefraction (KR-8100; Topcon, Tokyo, Japan) and subjective validation based on the autorefraction results to obtain the best corrected visual acuity (BCVA); noncontact tonometry (CT-60; Topcon); slit-lamp biomicroscopy (model BQ900; Haag-Streit, Bern, Switzerland); axial length of the globe (ultrasound biomicroscopy; Compuscan; Storz Ophthalmic, Inc., St. Louis, MO). Cycloplegia was achieved with 1 drop of combined

Table 1. Sex-Specific Prevalence of Red-Green CVD

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td></td>
<td>Participants</td>
<td>n (%)</td>
</tr>
<tr>
<td>SH</td>
<td>5207</td>
<td>186 (3.57)</td>
</tr>
<tr>
<td>XJJ</td>
<td>1597</td>
<td>59 (3.69)</td>
</tr>
<tr>
<td>XJIH</td>
<td>981</td>
<td>42 (4.28)</td>
</tr>
<tr>
<td>Total</td>
<td>7785</td>
<td>287 (3.69)</td>
</tr>
</tbody>
</table>
the relative risk of having myopia or hyperopia for the CVD groups in comparison to the corresponding CN groups. A random-effects GLS regression test34 was performed to assess the effect of CVD on refractive error and axial length (Stata, version 7.0; Stata Corporation, College Station, TX). Graphs were made with another program (SPSS, ver. 11.5; SPSS Sciences, Chicago, IL).

**RESULTS**

There were 309 CVD subjects in the final statistics, including 287 males (3.69% of males tested) and 22 females (0.26% of females tested). Table 1 summarizes the prevalence of CVD in different regional and ethnic groups. The prevalence of CVD in the Han Chinese (from both Shanghai and Xinjiang) was 3.68% in the males and 0.11% in the females. For the Uygur Chinese, the prevalences were 3.69% and 0.69%, respectively. There was no significant difference between the Han and Uygur nationalities in the prevalence of CVD in males ($\chi^2 = 0.00, P = 0.985$), whereas the Uygur females had a higher rate of CVD than did the Han ($\chi^2 = 21.35, P < 0.001$). Among the 309 students with CVD confirmed by FM 100, 142 (45.95%) were protan subjects (SH: 89, XJU: 31, and XJH: 22) and 167 (54.05%) were deutan subjects (SH: 103, XJU: 43, and XJH: 21). The mean $\sqrt{\text{TES}}$ for CN, protan, and deutan subjects were 4.59, 10.31, and 10.71, respectively (Fig. 1). Of the 927 students selected to be control subjects (CVD: CN at 1:3, Table 2), 426 were matched for protan subjects (CN-P) and 501 were matched for deutan subjects (CN-D).

The median uncorrected logMAR visual acuity was 0.3 (range, $-0.1$ to +0.8) in the CN group and 0.1 (range, $-0.1$ to +0.8) in the CVD group. The median BCVA was 0 (range, 0–0.3 to +0.1) for both the CN and CVD groups. Mean intraocular pressure (IOP) was 16.20 ± 2.93 mm Hg (range, 8–24) in the CN group and 16.53 ± 3.15 mm Hg in the CVD group (range, 9–24). All students with an IOP higher than 20 mm Hg received a second IOP measurement with the Goldmann application tonometer, and all measurements fell within the normal range. No significant difference was found in IOP between CVD and CN (random-effects GLS regression test: $P = 0.079$).

The mean refraction and axial length were $-1.80 \pm 2.47$ D (range, $-10.0$ to $+5.5$) and $24.44 \pm 1.34$ mm (range, $20.5$–$28.0$) in the right eye and $-1.66 \pm 2.50$ D (range, $-13.5$ to $+6.0$) and $24.35 \pm 1.35$ mm (range, $20.6$–$29.9$) in the left eye of all students. The correlation coefficients of refraction and axial length between the right and left eyes were 0.93 (Spearman’s correlation: $P < 0.001$) and 0.91 (Pearson correlation: $P < 0.001$), respectively. To standardize statistical analyses, only refraction and axial length of the right eye were used.

**Analysis of Refractive Error Prevalence by Color Vision Groups.** Myopia was present in 45.6% of the CVD subjects and 65.8% of the CN subjects. This difference in myopia

<table>
<thead>
<tr>
<th>Table 2. Results of the Questionnaire</th>
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<tbody>
<tr>
<td><strong>SH CVD</strong></td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
</tr>
<tr>
<td>Parental myopia (%)</td>
</tr>
<tr>
<td>Parental high myopia (%)*</td>
</tr>
<tr>
<td>Parental high myopia (%)**</td>
</tr>
<tr>
<td>Diopter-hours/week (mean ± SD)†</td>
</tr>
<tr>
<td>Sports (mean ± SD)</td>
</tr>
</tbody>
</table>

* High myopia: $<-5$ D.
† Diopter-hours = 3 × (hours spent reading) + 2 × (hours spent playing video games or working on the computer at home) + 1 × (hours spent watching television).
Incidence of Myopia with and without CVD

Mean refractive error for the CVD group was $-1.31 \pm 2.31$ D, which was significantly less myopic than the refractive error level of $-1.97 \pm 2.50$ D for the CN group (random-effects GLS regression test: $P < 0.001$).

Figure 3 and Table 4 show the mean refractive error for the two CVD subtypes and their corresponding CN groups, analyzed as a whole and also by region and ethnicity. The mean refractive errors for both the protan (Fig. 3a) and the deutan (Fig. 3b) groups were significantly less myopic than for the corresponding CN groups (random-effects GLS regression test: $P < 0.001$ for the protan group; $P < 0.001$ for the deutan group).

When the random-effects GLS regression test was performed according to region and ethnicity, the difference in mean refractive error was significant for some groups but not for all (Fig. 3). In SH, the mean refractive error of the CN-P subjects was significantly more myopic than that for the protan subjects ($P = 0.002$) and the mean refractive error of the CN-D subjects was significantly more myopic than that for the deutan subjects ($P = 0.007$). No significant difference in mean refractive error was found either between the protan and CN-P subjects or between the deutan and CN-D subjects for XJU ($P = 0.507$ for protan subjects; $P = 0.074$ for deutan subjects). For XJH, the differences in mean refractive error between both types of CVD and the corresponding CN groups were not significant, but the probability approached the significance level for the protan group ($P = 0.054$ for protan subjects; $P = 0.110$ for deutan subjects).

Figure 4 shows the regression curves of the mean refractive errors for each CVD subtype and its corresponding CN group, with the estimated marginal means ($\hat{y}$-axis) plotted against the color vision groups ($x$-axis). The estimated marginal mean took into account each mean in proportion to its sample size. An interaction analysis in a univariate general linear model indicated that no significant difference in the regression coefficients existed between these two slopes ($F = 0.018$, $P = 0.892$).

Analysis of Axial Length by Color Vision Group. Mean axial length was significantly shorter for the CVD group ($24.30 \pm 1.33$ mm) than the CN group ($24.49 \pm 1.34$ mm; random-effects GLS regression test: $P = 0.007$).

When CVD subjects were analyzed according to subtype, a significant difference in axial length was found between the...
protan (24.25 ± 1.26 mm) and CN-P (24.48 ± 1.32 mm; random-effects GLS regression test: \( P = 0.023 \)) subjects, but not between the deutan (24.36 ± 1.40 mm) and CN-D (24.50 ± 1.35 mm; random-effects GLS regression test: \( P = 0.117 \)) subjects. Figure 5 and Table 4 show the mean axial length for the two CVD subtypes and their corresponding CN groups, analyzed as a whole and also by region and ethnicity.

As shown in Figure 5, no significant difference in axial length was found between the protan and CN-P subjects or the deutan and CN-D subjects for the SH (random-effects GLS regression test: \( P = 0.210 \) for protan subjects; \( P = 0.258 \) for deutan subjects) and XJU (\( P = 0.481 \) for protan subjects; \( P = 0.606 \) for deutan subjects) groups. In the XJH group, the axial length of the CN-P group was significantly longer than that in the protan group (random-effects GLS regression test: \( P = 0.016 \) for protan subjects; \( P = 0.293 \) for deutan subjects).

Color vision, refractive error, and axial length were evaluated for 309 high school students with red-green CVD and 927 students with CN. A lower prevalence of myopia was found for the CVD group than the CN group. The CVD group also had less myopic refraction (\( -0.66 \) D) and shorter axial length (\( -0.19 \) mm) than the CN group had. Matching each CVD subject with three CN controls ensured any difference found could not be attributed to behavioral or genetic risk factors. The findings suggest that color vision influences the refractive development of the human eye with the tendency of red-green color-defective eyes to be less myopic.

In comparison to CN subjects, protan subjects had a lower prevalence and milder degree of myopia as well as a shorter axial length. This difference could be explained by responses of the luminance channel under the influence of LCA. The luminance channel for protan eyes is dominated by M-cones and is thus more sensitive to light of shorter wavelength, whereas the luminance channel of eyes with normal color vision is dominated by both L- and M-cones. Therefore, protan eyes are more sensitive to images focused at a position in front of that of CN eyes, since the focal plane of a shorter wavelength is located in front of that of a longer wavelength due to the LCA. This could result in a shorter axial length and lower degree of myopia for the protan eyes.

In comparison to CN subjects, deutan subjects also showed a lower prevalence of myopia and less myopic refractive error. However, the axial length of the deutan subjects showed no difference to that of CN eyes. The shorter axial length for protan eyes, but not for deutan eyes, when compared to CN eyes, suggests that the eye may be able to detect a difference in the plane of maximum luminance contrast between the two

**DISCUSSION**

**TABLE 3.** Comparison of Prevalence of Myopia and Hyperopia

<table>
<thead>
<tr>
<th>Groups</th>
<th>Myopia</th>
<th>Hyperopia</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Crude OR 95% CI</td>
<td>Crude OR 95% CI</td>
</tr>
<tr>
<td></td>
<td>( P^* )</td>
<td>( P^* )</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protan vs. CN-P</td>
<td>0.300 0.184–0.491</td>
<td>1.666 0.893–3.106</td>
</tr>
<tr>
<td>Deutan vs. CN-D</td>
<td>0.329 0.216–0.503</td>
<td>1.517 0.844–2.725</td>
</tr>
<tr>
<td>SH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protan vs. CN-P</td>
<td>0.341 0.192–0.606</td>
<td>2.005 0.698–5.760</td>
</tr>
<tr>
<td>Deutan vs. CN-D</td>
<td>0.355 0.212–0.595</td>
<td>4.586 1.277–15.067</td>
</tr>
<tr>
<td>XJU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protan vs. CN-P</td>
<td>0.196 0.024–1.623</td>
<td>1.087 0.408–2.896</td>
</tr>
<tr>
<td>Deutan vs. CN-D</td>
<td>0.126 0.029–0.548</td>
<td>0.964 0.457–2.035</td>
</tr>
<tr>
<td>XJH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protan vs. CN-P</td>
<td>0.214 0.077–0.596</td>
<td>2.941 0.799–10.827</td>
</tr>
<tr>
<td>Deutan vs. CN-D</td>
<td>0.354 0.128–0.980</td>
<td>1.953 0.420–8.892</td>
</tr>
</tbody>
</table>

Data were analyzed as a whole and also according to regional and ethnic groups. ORs and 95% CIs indicate the relative risk of having myopia or hyperopia for the CVD groups in comparison to the CN groups.

\* Based on random-effects logistic test.

Figure 6 shows regression curves of the mean axial length for each CVD subtype and its corresponding CN group. No significant difference in the regression coefficients between the two slopes was found (\( F = 0.236, P = 0.628 \)).
CVD groups. However, the similarity of the refractive data for the two CVD groups seems to challenge the above conclusion. Regardless of this disparity, the less myopic refractions for both of the CVD groups cannot be explained by a simple model that only detects the plane of maximum luminance contrast. Our observations, therefore, could suggest an involvement of the chromatic opponent mechanisms in the development of myopia. For the eye with either protan or deutan CVD, the L/M chromatic opponent mechanism has lost or reduced function in the middle- to long-wavelength range, but the (L+M)/S chromatic opponent mechanism, functioning in the short- to middle-wavelength range, is not significantly affected. Although we found that CVD subjects were less susceptible to myopia than CN subjects, they can still be affected by it. A high prevalence of myopia among Chinese students (namely, the Han students in this study) has been reported recently, and its educational system is much more intensive than that in Xinjiang. This difference may explain why Han students of Shanghai had a higher rate of myopia than did Han students from Xinjiang (Fig. 2). Of note, The Uygur students had a much lower rate of myopia and a higher rate of hyperopia than their Han classmates had. This result may have an ethnic explanation, because Uygur people have both yellow and Caucasoid race lineages as well as unique habits and customs. However, the prevalence of CVD in the Uygur students was close to that of the Han students.

Myopia is a complex trait influenced by as yet unidentified genetic factors. Previous studies have reported the impact of family history on the development of myopia. CVD is unquestionably a genetic disease. It could be interesting to study the association between genetic factors for both CVD and myopia in future research.

### Table 4. Mean Refractive Error and Axial Length

<table>
<thead>
<tr>
<th>Refractive Error (D)</th>
<th>Axial Length (mm)</th>
</tr>
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<tbody>
<tr>
<td><strong>Protan</strong></td>
<td><strong>CN-P</strong></td>
</tr>
<tr>
<td>All</td>
<td></td>
</tr>
<tr>
<td>SH</td>
<td></td>
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<tr>
<td>XJU</td>
<td></td>
</tr>
<tr>
<td>XJH</td>
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</tr>
</tbody>
</table>

The mean axial length for the (a) protan and (b) deutan groups and their corresponding CN groups analyzed as a whole and also by region and ethnicity. Overall, a significant difference in axial length was found between the protan and CN-P subjects, but not between the deutan and CN-D subjects. As for the three regional and ethnic groups, the only significant difference was between the protan and CN-P subjects in XJH (random-effects GLS regression, \(P < 0.05\)). Error bar, \(\pm SE\).
The prevalence of color vision deficiency is relatively low in our group (~2%) compared with the Caucasian population. The low prevalence of CVD in Asian populations has been reported before, with an incidence of approximately 2.98% for Chinese. In this study, the presence of CVD was determined with a pseudoisochromatic plate color vision test and then was confirmed with an FM-100 test, but not by anomaloscopy. Thus, some anomalous color vision defects may have been undetected.

In this study, we investigated the association between color vision deficiency and refractive state in human eyes. Students with abnormal color vision presented with a significantly lower vision deficiency and refractive state in human eyes. Students with abnormal color vision defects may have been undetected.

Acknowledgments

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References

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