

# Association Between Color Vision Deficiency and Myopia in Chinese Children Over a Five-Year Period

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**PURPOSE.** To explore the relationship of color vision deficiency with myopia progression and axial elongation in Chinese primary school children during a five-year cohort study.

**METHODS.** A total of 2849 grade 1 students (aged  $7.1 \pm 0.4$  years) from 11 primary schools were enrolled and followed up for five years. Cycloplegic autorefractometry and axial length were measured annually. Color vision testing was performed using Ishihara's test and the City University color vision test.

**RESULTS.** The prevalence of color vision deficiency was 1.68%, with 2.81% in boys and 0.16% in girls. Color-deficient cases consisted of 91.6% deutan and 8.3% protan. Over the five years, the cumulative incidence of myopia was 35.4% (17/48) in the color-vision deficiency group, which was lower than the 56.7% (1017/1794) in the color normal group ( $P = 0.004$ ). Over the five-year study period, the change in spherical equivalent refraction in the color vision-deficiency group ( $-1.81$  D) was also significantly lower than that in the color normal group ( $-2.41$  D) ( $P = 0.002$ ).

**CONCLUSIONS.** The lower incidence and slower progression of myopia in children with color-vision deficiency over the five-year follow-up period suggest that color-deficient individuals are less susceptible to myopia onset and development.

**Keywords:** color vision, myopia, color vision deficiency, children

Myopia has emerged as a serious public health issue, with the prevalence increasing rapidly worldwide,<sup>1,2</sup> especially in East Asia.<sup>3</sup> Myopia in Chinese adolescents reached 53.6% in 2018.<sup>4</sup> Increasingly early onset of myopia leads to a higher risk of pathological myopia with complications (e.g., secondary cataracts, glaucoma, and retinal detachment) that cannot be treated by wearing spectacles.<sup>5,6</sup> Thus understanding the cause of myopia is essential to address the myopia epidemic.

During normal eye growth, the eye grows to match its retinal position with the image focal plane, a process termed *emmetropization*.<sup>7</sup> Mismatches cause the images to fall either in front of the retina, resulting in myopia, or behind it, resulting in hyperopia. Visual experience plays an essential role in the process of emmetropization.<sup>8</sup> Other evidence suggests that the spectral composition of ambient light may affect emmetropization and ocular growth.<sup>9-11</sup> For example, exposure to lights with longer wavelengths

increases eye growth and induces myopic development in chicks<sup>10</sup> and guinea pigs<sup>12</sup> but induces hyperopia in tree shrews and monkeys.<sup>13-15</sup>

Natural light has a wide range of wavelengths. Even under the same lighting conditions, there are differences between people with normal color vision (CN) and people with color vision deficiencies (CVD) regarding the relative activations of long (L-), medium (M-), and short (S-) wavelength sensitive cones.<sup>16</sup> Normal color vision in humans is trichromatic, depending on L-, M-, and S- cone types.<sup>17</sup> The absence, shift in spectral sensitivity, or deterioration of any cone type may lead to a CVD.<sup>18</sup> Congenital red-green CVDs are the most common deficiencies in human populations and comprise two broad types: protan and deutan deficiencies.<sup>19</sup> Protanopia is characterized by the presence of M- and S- cones only and protanomaly by L-cones being replaced by a hybrid cone with a spectral sensitivity intermediate between L- and M- cones. Similarly, deuteranopia is



characterized by the presence of L- and S- cones and deuteranomaly by M- cones being replaced by a hybrid cone with a spectral sensitivity intermediate between L- and M- cones.<sup>16</sup> Therefore relative to CN and given that a growing body of literature shows that emmetropization is sensitive to chromatic cues,<sup>9,11,20,21</sup> it is reasonable to predict that refractive status may differ between people with CVD and CN.

Previous cross-sectional studies have reported conflicting results regarding the relationship between color vision and myopia. Qian et al.<sup>22</sup> reported that among Chinese high school students aged 15 to 18 years old, the prevalence of myopia in a red-green CVD group was significantly lower than that in a CN group. Ostadimoghaddam et al.<sup>23</sup> also reported a lower prevalence of myopia in a red-green CVD group than in a CN group in Iranian primary school students aged 7 to 12 years. However, another study demonstrated no relationship between red-green CVD and refractive error among Iranian primary school children aged 7 to 12.<sup>24</sup>

Given the conflicting findings of the above studies, longitudinal studies on the effects of color vision on myopia onset and progression are necessary. Therefore we conducted a large-sample cohort study among Chinese students over five years to explore whether the type of color vision was predictive of changes in refractive error and axial length.

## METHOD

### Study Population

The Anyang Childhood Eye Study is a school-based cohort study designed to observe annually the development of myopia and its risk factors among Chinese students in urban areas of Anyang City, Henan Province, Central China.<sup>25,26</sup> Details of the methodology have been reported elsewhere.<sup>27</sup> At baseline, 2893 grade 1 students from 11 primary schools were examined between February and May 2012 and were followed up for five years. Each child provided verbal assent, and informed written consent was obtained from at least one parent. The study was approved by the Institutional Review Board of Beijing Tongren Hospital, Capital Medical University, and adhered to the tenets of the Declaration of Helsinki.

### Procedures

At baseline and each annual visit, cycloplegia was induced with one drop of a 0.5% topical anesthetic (Alcaine; Alcon, Fort Worth, TX, USA), followed by two drops of 1% cyclopentolate (Alcon) and one drop of 1% tropicamide (Mydrin P; Santen, Osaka, Japan) with five-minute intervals between each drop.<sup>28</sup> Thirty minutes after the last drop, measurements were taken with an autorefractor (HRK7000 A; Huvitz, Gunpo, South Korea) and the average of three reliable measurements was used for analysis. A Lenstar LS900 instrument (Haag-Streit, Koeniz, Switzerland) was used to measure axial length three times, with average data used for analysis. Information about the number of myopic parents and time spent outdoors and on near work activities (hours per day) by the child after school hours was collected by an interviewer-administered questionnaire for parents.<sup>29</sup>

### Color Vision Testing

Students were asked to wear their current spectacles while undergoing color vision tests under artificial daylight illumination (True Daylight illuminator; 6280K; Richmond Prod-

ucts, Inc., Boca Raton, FL, USA). The presence of CVD was determined using the Ishihara test (38 Plate Edition, Tokyo, Japan). If a student was able to identify 13 or more of the first 21 plates correctly, each within three seconds, he or she was considered to have normal color vision. Otherwise, he or she was considered to have a CVD.<sup>28,30</sup> Children who failed the Ishihara test were tested with the City University color vision test (TCU test, third edition; Keeler Ltd, Windsor, UK), with the results of this test giving the type and approximate severity of color vision deficiency.<sup>27</sup> Although the Ishihara test has four diagnostic plates, these do not have high reliability (deutan/protan diagnosis can be incorrect or no diagnosis may be possible),<sup>31,32</sup> and thus the diagnosis of the City University test was accepted if the deutan/protan diagnosis was different between the two tests.

## Definitions

Myopia was defined as a spherical equivalent refraction (SER) (sphere + cylinder/2) less than  $-0.50$  diopters (D). The cumulative incidence of myopia was defined as the proportion of subjects who were not myopic at baseline but who developed myopia at any time during the follow-up period. Persistently nonmyopic students were children who were not myopic at baseline or at all follow-up visits. Only students with refractive data at the last follow-up examination were included in the analysis of the cumulative incidence of myopia. The progression of myopia was calculated as the change in SER between baseline and the follow-up visit(s). Similarly, axial elongation was calculated as the change in axial length between baseline and follow-up visit.

## Statistical Analysis

Statistical analysis was performed using SAS V.9.4 (SAS Institute Inc, Cary, NC, USA). Data from right eyes only were analyzed because refraction and ocular biometry in right and left eyes were correlated strongly (SER,  $r = 0.85$ ; axial length,  $r = 0.82$ ). Continuous variables are presented as the means  $\pm$  standard deviations if the data were normally distributed and categorical variables are presented as percentages. In the descriptive analyses of baseline characteristics, differences between the CN and CVD groups were assessed with standard parametric tests (*t*-tests) if the data were normally distributed and nonparametric tests (Mann-Whitney tests) if the data were not normally distributed. The  $\chi^2$  tests were used to analyze the five-year cumulative incidence of myopia between the CN and CVD groups. Changes in SER and axial length were compared between the CN and CVD groups using linear mixed-effects models. Age, gender, parental myopia, time outdoors, and time spent on near work were included as fixed effects in each model. The data were reanalyzed for boys alone, as they represented 95.8% of the CVD group. A *P* value  $< 0.05$  was considered statistically significant.

## RESULTS

At baseline in 2012, 2893 grade 1 students with a mean age of  $7.1 \pm 0.4$  years (range, 5.7–9.3 years) were assessed, and 2048 of these 2893 subjects (response 70.8%) provided data from the five-year visit. Color vision test data were available for 2825 children at baseline, including 48 students (1.69%) who were confirmed to have abnormal color vision (46 boys

**TABLE 1.** Baseline Characteristics of the Children

Variable	All	Normal Color Vision	Color Vision Deficiency	P Value
Age (years)	7.09 ± 0.41	7.09 ± 0.41	7.21 ± 0.38	0.02
Gender, no. of males (%)	1635 (57.6%)	1589 (57.2%)	46 (95.8%)	<0.01
SE (D)	0.98 ± 0.95	0.94 ± 1.03	1.13 ± 1.11	0.21
Axial length (mm)	22.71 ± 0.75	22.71 ± 0.76	22.69 ± 0.72	0.85
Parental myopia, n (%)				0.26
None	1619 (62.2%)	1592 (62.1%)	27 (61.4%)	
One	770 (29.6%)	754 (29.4%)	16 (36.4%)	
Both	216 (8.3%)	215 (8.4%)	1 (2.3%)	
Time outdoors (h/d)	1.03 ± 0.79	1.01 ± 0.82	1.04 ± 0.72	0.58
Time on near work (h/d)	1.79 ± 0.92	1.79 ± 0.89	1.79 ± 0.73	0.54

**TABLE 2.** Refractive Error Profile and Axial Lengths of CN and CVD Groups at the Five-year Follow-up Time Point (Mean ± SD)

Variable	n	SE (D)	Axial Length (mm)	Incident Myopia, n (%)
Normal color vision	2000	-1.38 ± 2.10	24.21 ± 1.09	1107 (55.4%)
Color vision deficiency	48	-0.51 ± 1.91*	23.85 ± 1.08*	17 (35.4%)*
Protan	4	-0.38 ± 2.11	23.90 ± 1.01	1 (25%)
Deutan	44	-0.52 ± 1.87	23.84 ± 1.11	16 (36.3%)

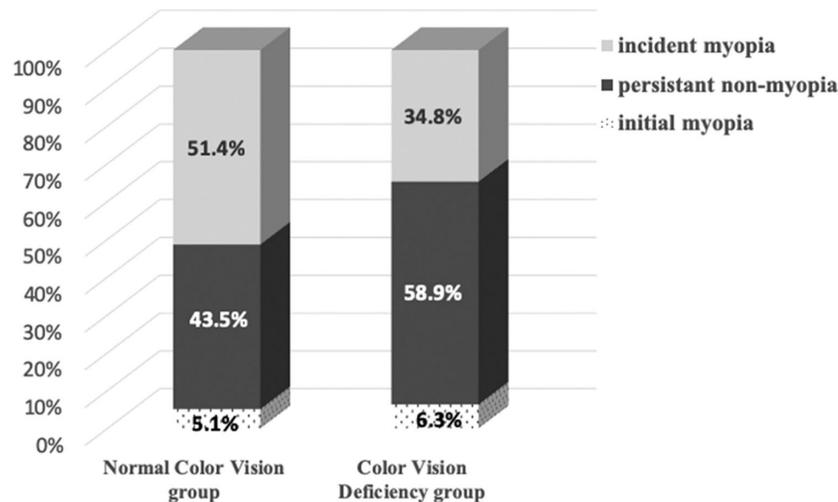
\* Indicates statistical significance between the normal color vision group and the color vision deficiency group ( $P < 0.05$ ).

[2.8%] and 2 girls [0.16%]). Of the 48 children with CVD, 44 had deutan defects, and four had protan defects. [Table 1](#) summarizes the baseline characteristics of the children. The baseline SER was  $0.98 \pm 0.95$  D, and the baseline axial length was  $22.71 \pm 0.75$  mm. Myopia was present in 6.3% and 6.6% of the CVD and CN subjects, respectively.

After five years, the cumulative incidence of myopia was 56.1% for all children. [Table 2](#) summarizes the percentages of students with incident myopia, the mean SER, and the mean axial length at the last follow-up visit in the CN and CVD groups. As shown in [Figure 1](#), the five-year cumulative incidence of myopia was 35.4% in the CVD group (17 of 48 participants [95% confidence interval [CI], 21.9% to 49.0%])

and 55.4% in the CN group (1107 of 2000 participants [95% CI, 52.6% to 57.2%]) ( $P = 0.003$ ). [Table 2](#) also indicates that at the last visit, the mean SERs of both protan and deutan groups were significantly less myopic than that of the CN group ( $P < 0.001$  for both groups).

[Table 3](#) presents results for boys only. At baseline, there were no significant differences between the two groups in SER, the prevalence of myopia, the number of myopic parents, time outdoors, or near work. However, boys in the CVD group had shorter axial lengths (by 0.30 mm,  $P = 0.005$ ) than boys in the CN group. After five years of follow-up, the boys in the CVD group had significantly less myopic progression (by 0.55 D,  $P = 0.012$ ), less axial elongation



**FIGURE 1.** The cumulative myopia incidence in the normal color vision group and color vision deficiency group at the 5-year follow-up period. Initial myopia was defined as the proportion of subjects who were myopic at baseline, persistent nonmyopia was defined as the proportion of subjects who were not myopic at both baseline and the follow-up period, and incident myopia was defined as the proportion of subjects who were not myopic at baseline and developed myopia during the follow-up period.

**TABLE 3.** Summary of Ocular and Behavioral Profiles of Boys in CN and CVD Groups and Statistical Comparisons of the Same

Variable	Normal Color Vision	Color Vision Deficiency	P Value
Baseline			
SER (D)	0.91 ± 0.99	1.19 ± 1.06	0.051
Axial length (mm)	22.96 ± 0.70	22.66 ± 0.72	0.005*
Myopia, n (%)	112 (7.1%)	2 (4.4%)	0.47
Parental myopia, n (%)			
None	928 (63.7%)	27 (58.7%)	
One	419 (28.7%)	14 (30.4%)	
Both	111 (7.6%)	5 (10.9%)	
Time outdoors (h/d)	1.02 ± 0.62	1.04 ± 0.70	0.54
Time on near work (h/d)	1.76 ± 0.74	1.79 ± 0.63	0.57
5-year follow-up			
Myopia progression (D)	-2.13 ± 1.54	-1.58 ± 1.12	0.012*
Axial elongation (mm)	1.44 ± 0.65	1.13 ± 0.57	0.003*
Incident myopia, n (%)	512 (51.4%)	16 (34.8%)	0.028*

\* Indicates statistical significance between the normal color vision group and the color vision deficiency group ( $P < 0.05$ ).

**TABLE 4.** Mean Myopia Progression and Axial Elongation at the Follow-up Time Points in the Normal Color Vision and Color Vision Deficiency Groups (Mean, 95% CI)

Follow-Up, Year	1	2	3	4	5
SER (D)					
Normal color vision	-0.32 (-0.38~-0.26)	-0.80 (-0.86~-0.74)*	-1.38 (-1.44~-1.32)*,†	-1.88 (-1.95~-1.82)*,†,‡	-2.41 (-2.48~-2.34)*,†,‡,§
Color vision deficiency	-0.24 (-0.70~0.06)	-0.45 (-0.98~-0.22)	-0.91 (-1.39~-0.63)*	-1.23 (-1.71~-0.95)*,†	-1.63 (-2.19~-1.43)*,†,‡
Protan	-0.34	-0.44	-0.69	-1.00	-1.44
Deutan	-0.21	-0.45	-0.94	-1.25	-1.65
P value	1.00	0.30	0.06	0.005	0.002
Axial length (mm)					
Normal color vision	0.42 (0.34~0.50)	0.60 (0.53~0.68)*	0.90 (0.81~0.99)*,†	1.19 (1.11~1.27)*,†,‡	1.51 (1.41~1.60)*,†,‡,§
Color vision deficiency	0.25 (0.23~0.74)	0.47 (0.01~0.96)	0.72 (0.24~1.21)	0.93 (0.44~1.41)	1.21 (0.73~1.70)
Protan	0.24	0.44	0.65	0.91	1.22
Deutan	0.23	0.47	0.73	0.93	1.15
P value	0.51	0.61	0.48	0.29	0.24

\* Indicates statistical significance compared with year 1 ( $P < 0.05$ ).

† Indicates statistical significance compared with year 2 ( $P < 0.05$ ).

‡ Indicates statistical significance compared with year 3 ( $P < 0.05$ ).

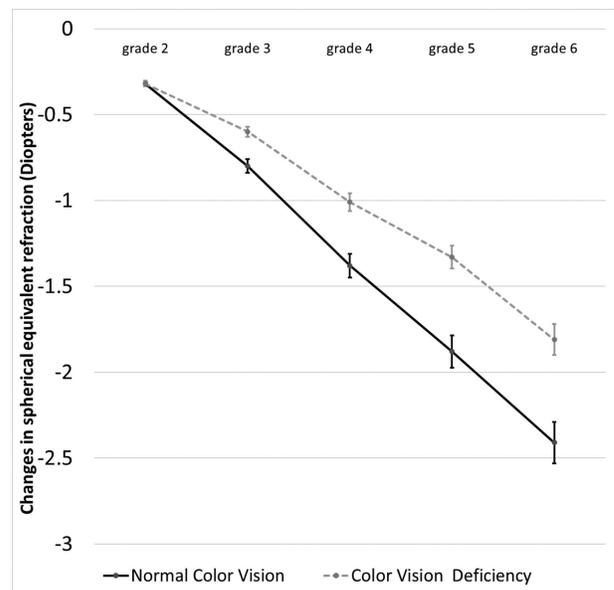
§ Indicates statistical significance compared with year 4 ( $P < 0.05$ ).

|| Indicates statistical significance between the normal color vision group and the color vision deficiency group ( $P < 0.05$ ).

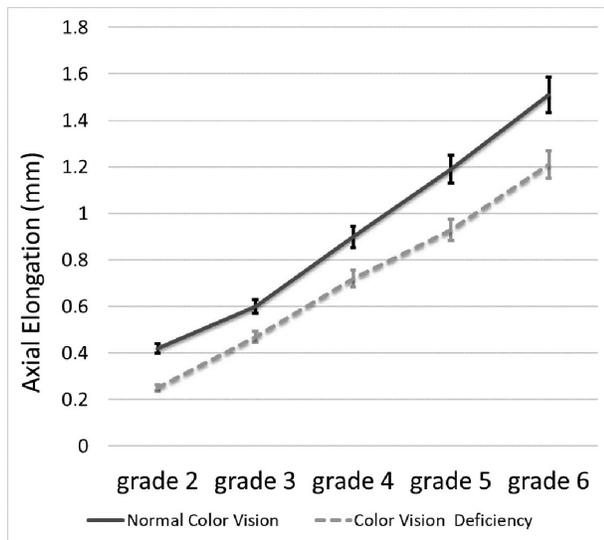
(by 0.31 mm,  $P = 0.003$ ), and lower cumulative incidence of myopia (16.6%,  $P = 0.028$ ) than boys in the CN group.

Table 4 presents the myopic progression by color vision group. As shown in Figure 2, the difference between the CVD and CN groups in mean change in SER increased with the follow-up period, with a significantly smaller myopic shift in the CVD group than in the CN group at the fourth and fifth follow-up visits (e.g., -1.81 D vs. -2.41 D at the fifth visit [ $P = 0.002$ ]). Linear mixed effects models (Supplementary Table S2) show that myopic progression was significantly affected by the type of color vision ( $P < 0.001$ ), follow-up period ( $P < 0.001$ ), gender ( $P < 0.001$ ), time spent on near work ( $P = 0.006$ ), and the number of myopic parents ( $P < 0.001$ ). However, no interaction was found for myopic progression with type of color vision × follow-up period ( $F_{7,42} = 1.61, P = 0.17$ ).

As shown in Figure 3, the mean axial elongations of the CN and CVD groups over five years were 1.51 mm and 1.21 mm, respectively ( $P = 0.24$ ). The axial elongation at each visit relative to baseline was greater in the CN group than in the CVD group (Table 4), although there was no significant difference at any visit between the two groups. Linear mixed effects models (Supplementary Table S2) summarises the significant effects on axial elongation during the follow-up period and the number of myopic parents (both  $P < 0.001$ ).



**FIGURE 2.** Mean myopia progression in the normal color vision and color vision deficiency groups. Myopia progression was calculated as the change in the cycloplegic SE between the measurements acquired at baseline and at a follow-up point. Error bars: 95% CI of means.



**FIGURE 3.** Mean axial elongation (95% CI) in the color normal and color vision deficiency groups. Axial elongation was calculated as the change in axial length between the measurements acquired at baseline and at a follow-up point. Error bars: 95% CI.

## DISCUSSION

To the best of our knowledge, this is the first longitudinal study reporting the relationship between CVD and myopic progression in children. Over five years, children in the CVD group had a lower incidence of myopia (35.4% [95% CI, 21.9% to 49.0%]) than children in the CN group (55.4% [95% CI, 52.6% to 57.2%]). The CVD group also had less myopic refractive errors ( $\sim 0.87$  D), and shorter axial lengths ( $\sim 0.36$  mm) than the CN group at the five-year visit. Myopia progression was also smaller in the CVD group than in the CN group over the five-year follow-up period. Previously Qian et al.<sup>22</sup> and Ostadimoghaddam et al.<sup>23</sup> also found lower myopic prevalence in CVD than in CN children, while Rajavi et al. reported no difference.<sup>24</sup>

Because most of the CVD group were boys, we compared the characteristics of boys in the two groups and found that boys in the CVD group had shorter axial lengths at baseline and a lower incidence of myopia after five years (34.8% [95% CI, 20.3% to 48.40%]) than boys in the CN group (51.4% [95% CI, 50.3% to 56.2%]) (Table 3).

As shown in Figures 2 and 3, there was a mismatch in the patterns of change in refractive errors and axial lengths over the five-year monitoring period. At the first visit, the axial length changes showed a greater, but not significant, difference ( $\sim 0.2$  mm) between the two groups than those of the following visits, whereas the refraction changes between the two groups increased gradually and became significantly different at the last two visits. The discrepancy may result from the reason that changes in refraction are determined by axial length, as well as corneal curvature and lens power.<sup>33,34</sup> Although axial length may be the predominant determinant of myopia, the smaller, but significant, myopic shifts in the CVD group relative to the CN group at the last two visits may be due to contributions from corneal curvature and lens power changes.

A summary of studies of CVD prevalence in children is presented as Supplementary Table S1 in the Supplementary Material. In our study, the prevalence of CVD was

1.7% (2.8% and 0.2% in boys and girls, respectively). Qian et al.<sup>22</sup> reported a CVD prevalence of 2.2% in Chinese high school students in Shanghai and Xinjiang Province, among whom 1.9% were confirmed to have red-green CVD; this result was similar to our results. Compared with most other countries, the prevalence of CVD in Chinese children is low. Race-related variations in CVD prevalence has been reported, with figures of 6% in European white males, 4% or less in African males, and 2.6% in Hispanic males, respectively.<sup>19,35</sup> It should be noted that the prevalence of CVD in our study was lower than in two previous studies of Chinese adults, which found a prevalence of 4% to 6.5% in adult males and 0.7% to 1.7% in adult females.<sup>19,36</sup> However, data analyzed in these studies were collected before 1960 when travel was difficult over long distance and most marriages would have been with near neighbors. Different color vision testing methods used and sampling biases may have contributed also to differences.

Observations from Scandinavian countries provide an interesting parallel with the findings in the current study, in that they show a low prevalence of myopia but a relatively high prevalence of color vision deficiencies.<sup>37</sup> Recent studies have shown that the prevalence of myopia is 10% in Sweden,<sup>38</sup> 13% in Norway,<sup>39</sup> and 18% in Denmark.<sup>40</sup> A recent review found no evidence of an increase in myopia prevalence in Denmark over a 140-year period, which runs counter to the increasing prevalence in Asian countries.<sup>41</sup>

Some mechanisms have been postulated to explain the association between myopia and color vision. One is that the L- and M-cone ratio is associated with myopia susceptibility. Evidence from full-field ERGs found that females with normal color vision and a high L/M cone ratio tend to have lower degrees of myopia.<sup>20</sup> In addition, the mean L/M cone ratio in East Asians has been reported to be lower than that in Caucasians, with higher myopia prevalence in the former.<sup>42,43</sup> In contrast, McClements et al.<sup>17</sup> found a low ratio associated with myopia. Further investigation into the relationship between L/M cone ratios and myopia susceptibility is warranted.

Another focus of myopia research relates to the role of longitudinal chromatic aberration in emmetropization.<sup>44</sup> Evidence indicates that the emmetropization process uses wavelength-dependent defocus and chromatic signals from longitudinal chromatic aberration.<sup>10,11,45</sup> Given that protan eyes have low sensitivity to long wavelengths, an image position is favored that is in front of that favored for CN eyes.<sup>46</sup> This could lead to shorter axial lengths and lower degrees of myopia for the protan eyes. On the other hand, the finding that deutan subjects have shorter axial length and lower myopia cannot be explained by the same wavelength-dependent defocus mechanism. Qian et al.<sup>22</sup> suggested that the [L+M]/S chromatic mechanisms might be involved in myopia development,<sup>45,47-53</sup> so CVD subjects who have absent or altered L or M cones would exhibit highly altered cone contrast (the difference between responses from the S cone and the summed responses from the L- and M-cones) compared with CN subjects and therefore slow eye growth via [L+M]/S chromatic mechanisms. Further research is needed to investigate how cone contrast or [L+M]/S chromatic mechanisms affect myopia development.

There are some limitations of the present study. One was that the numbers of participants in the CN and CVD groups were highly imbalanced and that there were fewer than expected protan defects, which makes separately analyzing deutan and protan defects not very meaningful. Further

work is required to assess whether these findings can be replicated in a larger CVD group. Another limitation was that the children were from a single geographical region with a reasonably homogeneous ethnic background. Thus caution should be exercised when extrapolating these results to other ethnic groups. In addition, the diagnosis of CVD was based on results from a pseudoisochromatic plate test and the City University test; we did not use an anomaloscope, which would have provided a more definitive diagnosis. Thus some mild anomalous color vision defects may have been misdiagnosed as normal using this approach.

In summary, this prospective cohort study found that children with color vision deficiencies had a lower incidence of myopia, slower myopic progression, and less axial elongation than children with normal color vision. These findings suggest that individuals with CVD are less susceptible to myopia onset and progression, and this may be related to altered cone ratios or cone contrast. More studies should be conducted to further investigate the relationship of color vision status with myopia progression and axial elongation in different racial populations.

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