

# Extrinsic and Intrinsic Factors Regulating Juvenile Refractive Development and Eye Growth

Kai Yip Choi<sup>1</sup> and Henry Ho-lung Chan<sup>1-3</sup>

<sup>1</sup>The Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Kowloon, Hong Kong

<sup>2</sup>Centre for Eye and Vision Research (CEVR), 17W Hong Kong Science Park, Hong Kong

<sup>3</sup>Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Hong Kong

Correspondence: Henry H.-I. Chan, School of Optometry, The Hong Kong Polytechnic University, 11 Yuk Choi Road, Hung Hom, Kowloon, Hong Kong; [henryhl.chan@polyu.edu.hk](mailto:henryhl.chan@polyu.edu.hk)

**Received:** July 21, 2021

**Accepted:** October 30, 2021

**Published:** November 19, 2021

Citation: Choi KY, Chan HHL. Extrinsic and intrinsic factors regulating juvenile refractive development and eye growth. *Invest Ophthalmol Vis Sci.* 2021;62(14):21. <https://doi.org/10.1167/iovs.62.14.21>

**PURPOSE.** Peripheral refraction and accommodation are intrinsic factors that were once hypothesized to trigger myopia but are now controversial. Previously, home nearwork environment (i.e., extrinsic factor) was reported to be associated with myopia progression. In this study, we aimed to evaluate the potential interaction between extrinsic and intrinsic factors with juvenile refractive development.

**METHODS.** Nearwork environmental parameters were measured for 50 children (aged  $9.3 \pm 1.2$  years), including net amount and dispersion of defocus. Refraction was measured at near distances and in central field ( $\pm 30^\circ$  horizontal) at 3m. The relative peripheral refraction (RPRE) was obtained and presented in a vectoral approach. The linear regression coefficient was extracted ( $m_{Acc}$ ) from the accommodative stimulus-response curve. RPRE was quadratically regressed against field eccentricity, and the first coefficients ( $a_M$ ,  $a_{J0}$ ,  $a_{P90}$ , and  $a_{P180}$ ) were extracted. Relationships between RPRE, baseline accommodation, and 1-year myopia progression ( $\Delta M$ ), controlled for the nearwork environment, were evaluated.

**RESULTS.** Coefficients of RPRE were independent of  $\Delta M$ . However, additional nearwork environmental parameters significantly improved the variance in  $\Delta M$  explained by  $a_M$  and  $a_{P180}$  ( $P < 0.03$ ). The relationship between intrinsic factor and  $\Delta M$  was stronger when the extrinsic risk was low ( $P \leq 0.01$ ), whereas the relationship was abolished when extrinsic risk was high. For  $m_{Acc}$ , it also significantly improved the variance in  $\Delta M$  explained by nearwork environmental parameters.

**CONCLUSIONS.** The interaction between extrinsic (environment) and intrinsic (RPRE and accommodation) factors is speculated to contribute to juvenile myopia progression. Our findings may also explain the inconsistencies of such intrinsic factors in the literature.

**Keywords:** myopia, environment, nearwork, accommodation, peripheral refraction

Myopia (nearsightedness) affects billions of people worldwide, but especially in developed countries.<sup>1</sup> Its development is largely attributed to an excessive axial elongation of the eyeball,<sup>2</sup> and the subsequent thinning of the posterior ocular structure is associated with various ocular diseases, including glaucoma, rhegmatogenous retinal detachment, and myopic macular degeneration,<sup>3,4</sup> which can lead to irreversible vision loss. Once thought to be an inherited and ethnicity-prone condition, myopia is now suggested to be more associated with visual experience, especially in early life.<sup>5,6</sup>

The effect of peripheral refraction on myopia progression has received considerable attention over the past few decades. Peripheral hyperopia and myopia were associated with on-axis myopia and hyperopia along the horizontal meridian, respectively.<sup>7-9</sup> Animal experiments also showed that axial eye growth can be regulated by not only by the central retina but also the peripheral retina,<sup>10-12</sup> in which peripheral hyperopic and myopic defocus cause on-axis myopic and hyperopic shifts, respectively. However, epidemiology studies have shown that the presence of base-

line peripheral hyperopia was not able to predict subsequent myopia progression in children.<sup>13,14</sup> To date, the effect of peripheral refraction on myopia development is under debate.<sup>15,16</sup>

Childhood myopia is strongly associated with environmental factors,<sup>17</sup> in which the living environment plays a crucial role.<sup>18-22</sup> Previously, this group revealed a relationship between home size and refractive error<sup>21</sup> and speculated that within a constricted living space, children would be exposed to more peripheral hyperopic defocus, which may accelerate myopia progression. Such a scene defocus profile (i.e., spatial dioptric content) varies greatly according to the viewing distance, especially between an outdoor scene and an indoor scene.<sup>23,24</sup> In a recent home visit study, using a depth sensing camera, the visual scene of the nearwork environment was quantified, and it was determined that a more dispersed and a more hyperopic paracentral defocus profile at a child's reading desk was associated with faster myopia progression.<sup>22</sup>

Another controversy in eye growth modulation has been proximal accommodation in children. Lag of accommoda-



tion was found to be greater in myopic children, who tend to focus behind the near fixation object, creating hyperopic defocus.<sup>25</sup> However, the magnitude of accommodative lag did not precede myopia progression.<sup>26</sup> In the external environment, not only does defocus profile vary with viewing distance, as mentioned previously, but various viewing distances also exert different accommodative stimuli. The accuracy of the proximal accommodative response would alter the perceived defocus stimuli by the eye, in which lag of accommodation would lead to a hyperopic shift in defocus profile and vice versa.

Dioptric stimuli of the visual scene over the central and paracentral retina may explain the inconsistent findings of peripheral refraction and accommodation on myopia progression in previous studies. In theory, all three aspects (i.e., the dioptric distances of objects in the external visual scene, the accommodative response, and the peripheral refractive error) interact to affect the retinal image clarity and possibly act as a cue for modulating emmetropization. The current study aimed to preliminarily evaluate the effect of peripheral refraction, as well as accommodation, on myopia progression and axial elongation in children while controlling for the factors in the defocus profile in a home nearwork environment. The results may provide insights into myopia control regimens in terms of manipulating the peripheral refractive error and the home environment setup for children.

## METHOD

### Participants

Fifty Hong Kong children ( $9.3 \pm 1.2$  years of age) with normal ocular and general health were recruited at the university optometry clinic, without any restriction in refractive error. All participants had corrected visual acuity of equal to or better than logMAR 0.00 and received full-spectacle prescription after the baseline examination. Participants who had received myopia control intervention, including atropine, multifocal contact lens, orthokeratology, and progressive addition/bifocal/defocus incorporated multiple-segment lens, and those with strabismus were excluded. All clinical procedures followed the tenets of the Declaration of Helsinki. Informed consent and written assent were obtained from the parents and the children, respectively.

### Home Scene Measurement

Home environment parameters were measured in a baseline home visit as described elsewhere.<sup>22</sup> In brief, the scene at the children's reading desk from the children's position of view was captured by the Kinect (Microsoft, Redmond, WA, USA), which consists of an infrared emitter and a sensor to measure the depth map across a  $70^\circ \times 60^\circ$  field of view.<sup>27,28</sup> The depth map was then converted into a scene dioptric defocus profile with respect to the child's working distance to the primary visual target (i.e., objects closer than the visual target create hyperopic scene defocus, while objects farther away than the visual target create myopic scene defocus). The dioptric volume (DV, the total amount of net scene defocus) and standard deviation of the defocus ( $SD_D$ , the dispersion of the scene defocus values) over the central  $\pm 30^\circ$  circular field of view were calculated. Figure 1 summarizes the process of scene defocus profile acquisition.

## Eye Examination

Eye examination was conducted at the Optometry Research Clinic of The Hong Kong Polytechnic University. Cycloplegic central and peripheral refractions were measured at a  $10^\circ$  interval up to  $30^\circ$  along the horizontal visual field on each side (i.e., seven points in total) and was measured five times<sup>29</sup> by NVision K5001 (Shin-Nippon, Osaka, Japan), which enabled peripheral refraction measurements at a far viewing distance with good repeatability and reproducibility.<sup>30–32</sup> 30 minutes after instillation of two drops of 1% cyclopentolate with a 5-minute separation. The fixation targets were placed 3 m away from the participant, who rotated his or her eyes to fixate at the peripheral targets while keeping the head straight ahead.<sup>33</sup> Refraction results were converted into vector form using the following formulas<sup>34</sup>:

$$M = S + \frac{C}{2}$$

$$J_0 = -\frac{C}{2} \cos 2\alpha$$

$$P(90) = M - J_0$$

$$P(180) = M + J_0$$

Relative peripheral refraction (RPRE) at each peripheral position was obtained by subtracting the central values from the peripheral values. RPRE along the horizontal visual field was fitted with a quadratic equation,  $RPRE = a(\text{Eccentricity} - b)^2 + c$ , to obtain the second-order coefficients ( $a_M$ ,  $a_{J_0}$ ,  $a_{P(90)}$ , and  $a_{P(180)}$ ).<sup>7</sup> Positive and negative  $a_M$  represented relative hyperopic and myopic shift, respectively, to the periphery, while  $a_{J_0}$  decreased with the steepening rate of the peripheral astigmatism profile.<sup>7</sup> Magnitude of  $a_{P(90)}$  and  $a_{P(180)}$  represented the blurriness of radial and tangential orientation of the image on the peripheral visual field, respectively.  $J_{45}$  was not analyzed as the magnitude was much smaller than other peripheral refraction vectors.

Accommodative responses were measured by NVision K5001 with habitual correction before the cycloplegia at near distances, including 20, 25, 33, 40, and 50 cm, which exerted from 2 to 5 diopters (D) of accommodative stimuli by 0.40 logMAR paragraphs. Spectacle correction was allowed because the accommodative responses were measured, as were the children accommodating in a nearwork environment with habitual spectacles. A linear accommodative stimulus–response relationship was assumed<sup>25</sup>: Response =  $m_{Acc} \cdot \text{Stimulus} + c'$ , in which  $c' = 0$  (i.e., the equation passes through the origin, implying zero accommodative response at an infinite distance), and the stimulus/response slope was extracted ( $m_{Acc}$ ). The flatter the slope, the more lag of accommodation the children would experience. Axial length was the secondary outcome and was measured five times with a signal-to-noise ratio  $>2.0$  by IOL Master (Carl Zeiss Meditec AG, Jena, Germany), which is efficient in measurement with good repeatability.<sup>35</sup> Refraction and axial length were measured at baseline and 1 year later to obtain myopia progression ( $\Delta M$ ) and axial elongation ( $\Delta AL$ ). Only results from the right eye were analyzed.

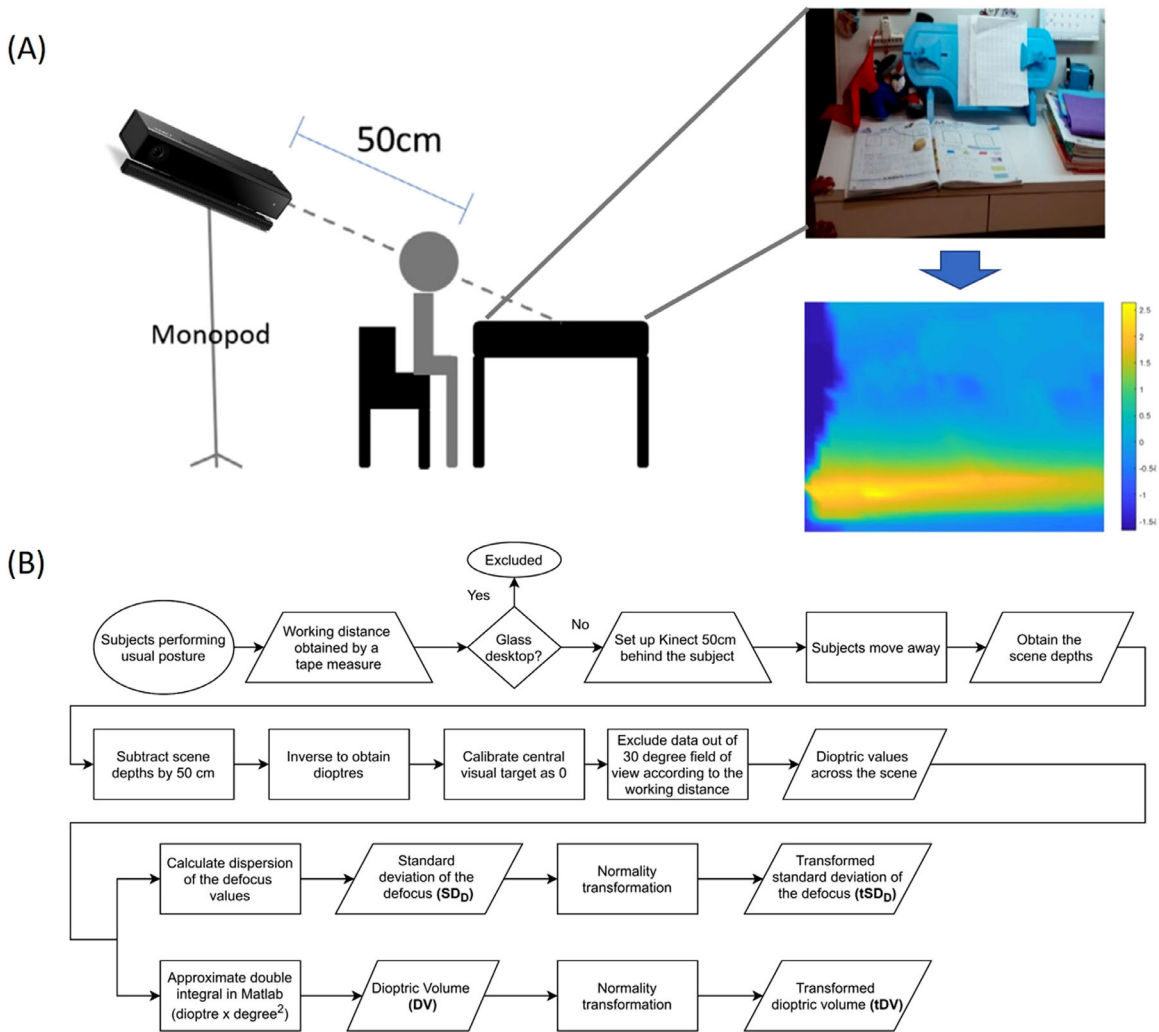


FIGURE 1. Home environment for nearwork.<sup>22</sup> (A) Measurement setup. (B) Measurement flow chart. Modified images from part A reprinted from Choi KY, Mok AY-T, Do C-W, Lee PH, Chan HH-L. The diversified defocus profile of the near-work environment and myopia development. *Ophthalmic Physiol Opt.* 2020;40(4):463–471. Available under a CC BY license.

**Data Analysis**

Hierarchical multiple linear regressions were performed to assess the association between RPRE/accommodation and  $\Delta M/\Delta AL$ . The change in  $R^2$  value from the null model was used to represent the proportion of variance in  $\Delta M$  and  $\Delta AL$  explained by additional independent variables: RPRE, baseline refraction, and home scene parameters. The regressions were performed after normality transformation<sup>36</sup> on the home scene parameters to satisfy the parametric assumptions. To investigate the interaction between peripheral refraction and home scene parameter in our sample, the participants were median-split by the  $SD_D$ . The relationship between RPRE and  $\Delta M$  was evaluated by correlation analyses. In a previous study,<sup>22</sup> a significant association was reported between home scene parameters ( $DV/SD_D$ ) and change in refractive error ( $\Delta M$ ). Hierarchical regression was then applied to investigate whether controlling for the accommodation ( $m_{Acc}$ ) would significantly improve such relationship. Hochberg’s adjustment was applied when

appropriate,<sup>37</sup> and the base significance level was set as  $P \leq 0.05$ .

**RESULTS**

**Basic Refractive Outcomes**

The baseline and change in refraction over 1 year (mean  $\pm$  SD [range]) were  $-1.51 \pm 2.02$  ( $-6.25$  to  $+1.38$ ) D and  $-0.56 \pm 0.45$  ( $-1.95$  to  $+0.57$ ) D, respectively. Corresponding results for axial length were  $24.02 \pm 1.01$  (22.35 to 26.11) mm and  $0.33 \pm 0.16$  (0.05 to 0.77) mm, and baseline cylindrical error was  $0.77 \pm 0.61$  (0.00 to 2.50) D. The number of participants stratified by types of refractive error and their change in refractive error, as well as RPRE and accommodation, are listed in Table 1. Baseline RPRE against field eccentricity is shown in Figure 2. The correlation between baseline M and  $\Delta M$  was not significant (Pearson’s  $r = 0.21$ ,  $P = 0.14$ ), nor was that between baseline AL and  $\Delta AL$  (Pearson’s  $r = 0.07$ ,  $P = 0.65$ ). Twenty percent of the participants

TABLE 1. Myopia Progression, RPRE, and Lag of Accommodation Stratified by Baseline Refractive Error (Mean  $\pm$  SD)

Characteristic	N (Corrected Before Baseline)	$\Delta M$	$\Delta AL$	$a_M (\times 10^{-3})$	$a_{J0} (\times 10^{-3})$	$a_{P90} (\times 10^{-3})$	$a_{P180} (\times 10^{-3})$	$m_{Acc}$	DV (D <sup>0.05</sup> )	SD <sub>D</sub> (D)
Hyperope (M > +0.50 D)	8 (1)	-0.34 $\pm$ 0.16	0.21 $\pm$ 0.12	0.66 $\pm$ 1.01	-1.00 $\pm$ 0.57	1.65 $\pm$ 1.09	-0.36 $\pm$ 1.23	0.88 $\pm$ 0.10	1.61 $\pm$ 1.56	0.46 $\pm$ 0.29
Emmetrope (0.50 $\geq$ M > -0.50 D)	10 (4)	-0.53 $\pm$ 0.38	0.33 $\pm$ 0.14	0.20 $\pm$ 1.17	-0.93 $\pm$ 1.12	1.10 $\pm$ 0.66	-0.70 $\pm$ 2.20	0.90 $\pm$ 0.06	3.39 $\pm$ 2.78	0.88 $\pm$ 0.65
Myope (M $\leq$ -0.50 D)	32 (28)	-0.63 $\pm$ 0.50	0.36 $\pm$ 0.16	1.78 $\pm$ 1.21	-0.85 $\pm$ 0.74	2.63 $\pm$ 0.94	0.91 $\pm$ 1.77	0.84 $\pm$ 0.09	1.94 $\pm$ 2.37	0.56 $\pm$ 0.46
ANOVA <i>P</i> value		0.25	0.06	0.001	0.88	<0.001	0.03	0.11	0.19	0.13
Non-astigmatism (Cyl < 1.00 D)	38 (22)	-0.54 $\pm$ 0.50	0.33 $\pm$ 0.17	1.11 $\pm$ 1.36	-0.93 $\pm$ 0.83	2.03 $\pm$ 1.09	0.17 $\pm$ 1.97	0.87 $\pm$ 0.09	2.32 $\pm$ 2.51	0.65 $\pm$ 0.56
Astigmatism (Cyl $\geq$ 1.00 D)	12 (11)	-0.63 $\pm$ 0.22	0.33 $\pm$ 0.11	1.84 $\pm$ 1.13	-0.76 $\pm$ 0.67	2.58 $\pm$ 1.09	1.08 $\pm$ 1.54	0.82 $\pm$ 0.07	1.73 $\pm$ 1.99	0.46 $\pm$ 0.13
<i>t</i> -test <i>P</i> value		0.54	0.97	0.10	0.51	0.14	0.15	0.07	0.46	0.06

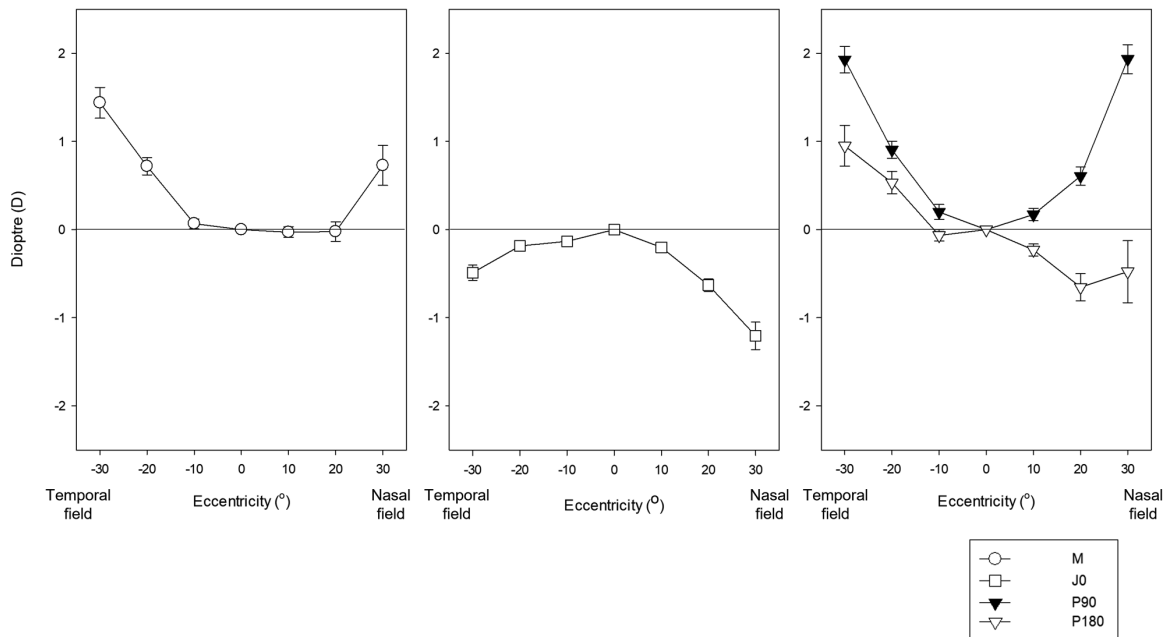


FIGURE 2. Baseline RPREs in terms of M, J0, P(90), and P(180) across eccentricity from temporal 30° to nasal 30° visual field.

had peripheral myopia (i.e.,  $a_M < 0$ ). While 24% of the participants had a lead of accommodation ( $m_{Acc} > 1$ ), the remainder had a lag of accommodation.

### Relative Peripheral Refractive Error ( $a_M/a_{J0}/a_{P90}/a_{P180}$ )

The myopia progression was negatively associated with RPRE, that is, the more hyperopic the  $a_M$  and  $a_{P180}$ , and the flatter the  $a_{J0}$ , the faster the myopia progression (Fig. 3), respectively, but only  $a_{J0}$  was associated with axial elongation (Fig. 4). Table 2 shows the changes in coefficients of determination, and the detailed statistical results for the hierarchical regressions are listed in Supplementary Tables S1 and S2. After controlling for the baseline refraction (model 2), the RPRE was independent of  $\Delta M$  and  $\Delta AL$ . Home scene parameters were then added as a covariate in the regression models. The introduction of the normality-transformed dioptric volume variable explained an additional 9% ( $P = 0.03$ ) and 8% ( $P = 0.03$ ) of variation in  $\Delta M$  for the  $a_M$  and  $a_{P180}$  models, respectively. The corresponding results for  $\Delta AL$  were 11% ( $P = 0.02$ ) for both the  $a_M$  and  $a_{P180}$  models. Furthermore, the introduction of the normality-transformed standard deviation of scene defocus variable explained an additional 10% ( $P = 0.02$ ) of the variation in  $\Delta M$  for both the  $a_M$  and  $a_{P180}$  models. The corresponding results for  $\Delta AL$  were 21% ( $P = 0.001$ ), 18% ( $P = 0.001$ ), 19% ( $P < 0.01$ ), and 20% ( $P < 0.001$ ) for  $a_M$ ,  $a_{J0}$ ,  $a_{P90}$ , and  $a_{P180}$  models, respectively.

The myopia progression in children was different in high versus low scene defocus dispersion (i.e.,  $SD_D$ ) and steep versus flat peripheral refraction ( $a_M$ ,  $a_{J0}$ , and  $a_{P180}$ ), by median split (Fig. 5). When the participants were equally divided into two groups according to their  $SD_D$ , the RPRE of participants with low  $SD_D$  was significantly associated with  $\Delta M$  with improved correlation coefficients (low  $SD_D$ :  $a_M$  vs.  $\Delta M$ :  $r = -0.58$ ,  $P < 0.01$ ;  $a_{J0}$  vs.  $\Delta M$ :  $r = -0.50$ ,  $P = 0.01$ ;

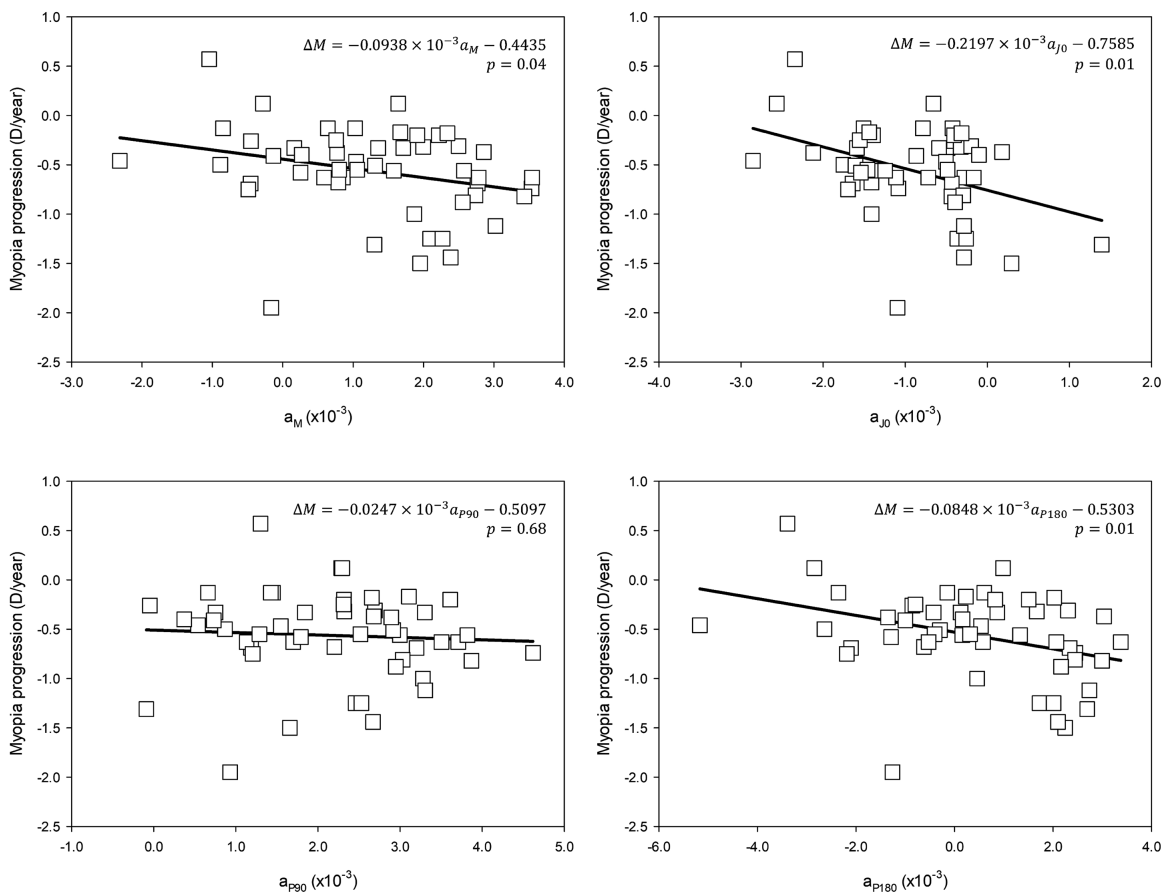
$a_{P180}$  vs.  $\Delta M$ :  $r = -0.62$ ,  $P = 0.001$ ), while those with high  $SD_D$  were independent of  $\Delta M$  (high  $SD_D$ :  $a_M$  vs.  $\Delta M$ :  $r = -0.14$ ,  $P = 0.49$ ;  $a_{J0}$  vs.  $\Delta M$ :  $r = -0.27$ ,  $P = 0.20$ ;  $a_{P180}$  vs.  $\Delta M$ :  $r = -0.21$ ,  $P = 0.32$ ).

### Lag of Accommodation ( $m_{Acc}$ )

The partial correlation between  $\Delta M$  and DV, controlled for the baseline M, was insignificant (Spearman's  $\rho = -0.25$ ,  $P = 0.08$ ) while that of  $SD_D$  was significant (Spearman's  $\rho = -0.42$ ,  $P < 0.01$ ).<sup>22</sup> After adding  $m_{Acc}$  as a covariate, both DV (Spearman's  $\rho = -0.32$ ,  $P = 0.03$ ) and  $SD_D$  (Spearman's  $\rho = -0.47$ ,  $P < 0.001$ ) were significantly correlated with  $\Delta M$ . The hierarchical regression showed a significant improvement in  $R^2$  after the addition of the lag of accommodation (Table 3) over home scene parameters and baseline refraction.

## DISCUSSION

In the current study, the home nearwork environment was demonstrated to be a contributing factor to juvenile myopia development, as in our previous study.<sup>22</sup> Although neither peripheral refraction nor accommodation could predict subsequent myopia progression or axial elongation in children after controlling for the baseline refraction and axial length, as in the epidemiology studies, peripheral refraction, in terms of  $a_M$ ,  $a_{J0}$ , and  $a_{P180}$ , and accommodation, in terms of  $m_{Acc}$ , were significantly associated with subsequent myopia progression and axial elongation after the addition of home scene parameters as covariates. Hierarchical multiple regression analysis further demonstrated an increase in coefficients of determination after addition of home scene parameters in the models, indicating the significance of the home nearwork environment on account of the variances of myopia progression and axial elongation, as well as the interactive effect between extrinsic factors (i.e., visual stimuli



**FIGURE 3.** Relationship between the fitted first coefficients of RPRES and myopia progression ( $\Delta M$ ). *Top left:*  $a_M$ . *Top right:*  $a_{J0}$ . *Bottom left:*  $a_{P90}$ . *Bottom right:*  $a_{P180}$ .

from the environment) and intrinsic factors (i.e., peripheral refraction and accommodation) on myopia.

The findings in the current study are consistent with the literature in that myopes had a higher lag of accommodation than emmetropes and hyperopes (baseline  $M$  vs.  $m_{Acc}$ :  $r = 0.27$ ,  $P = 0.05$ ),<sup>25</sup> but lag of accommodation alone could not predict subsequent myopia progression ( $P = 0.12$ ).<sup>26</sup> However, it is speculated to be a bridge between the extrinsic and intrinsic factors—the dioptric distances in the external visual scene were refracted by the accommodative and peripheral optics, reaching the resultant internal defocus. Table 3 shows the relationship between nearwork scene parameters and myopia progression, in which part of the results were reported in our previous study.<sup>22</sup> Furthermore, the coefficients of determination can be improved by controlling the lag of accommodation, which appeared to affect the defocus profile to which the eye is exposed. With the peripheral refractive error being relatively stable throughout accommodation to a near-working distance,<sup>38,39</sup> the defocus profile is expected to have a hyperopic shift regardless of the eccentricity, by which myopes would be exposed to a greater hyperopic shift than hyperopes and emmetropes and hence the DV. However, the lag of accommodation is speculated not to affect the  $SD_D$ , maintaining the scene defocus dispersion.

Eye growth, and hence refractive development, was once suggested to be a homeostasis of the organ itself (i.e., the eye was adapting to the visual task after a long period

of nearwork).<sup>40</sup> In such an environment, the scene defocus profile was generated by the external stimuli, in which objects closer than the fixation point create hyperopic scene defocus, while those farther away create myopic scene defocus. In our recent study, a more dispersed and hyperopic nearwork scene defocus profile was revealed to be associated with faster myopia progression.<sup>22</sup> Furthermore, in the current study, the peripheral refraction was also found to be a significant factor in refractive development in children if nearwork scene defocus profile was taken into account. It is speculated that the extrinsic factor (i.e., the defocus profile of the nearwork environment) would interact with the intrinsic factor (i.e., the peripheral refraction of the children) during myopia development. Thus, from Figure 5, greater  $a_M$ ,  $a_{J0}$ , and  $a_{P180}$  appeared to accelerate myopia progression, when the external scene defocus profile was more uniform. In contrast, if the defocus profile was more dispersed, the effect of RPRES on myopia progression was diminished. This interaction may address the importance of the visual scene in the external environment on account of the inconsistencies of peripheral refraction in predicting myopia progression in children.

There are several limitations restricting a comprehensive interpretation in the current study. A relatively small sample size was adopted in this preliminary evaluation, which had led to insufficient statistical power in some analyses (Tables 2 and 3). Accommodation was measured with habitual optical corrections, if any, assuming the participants would wear

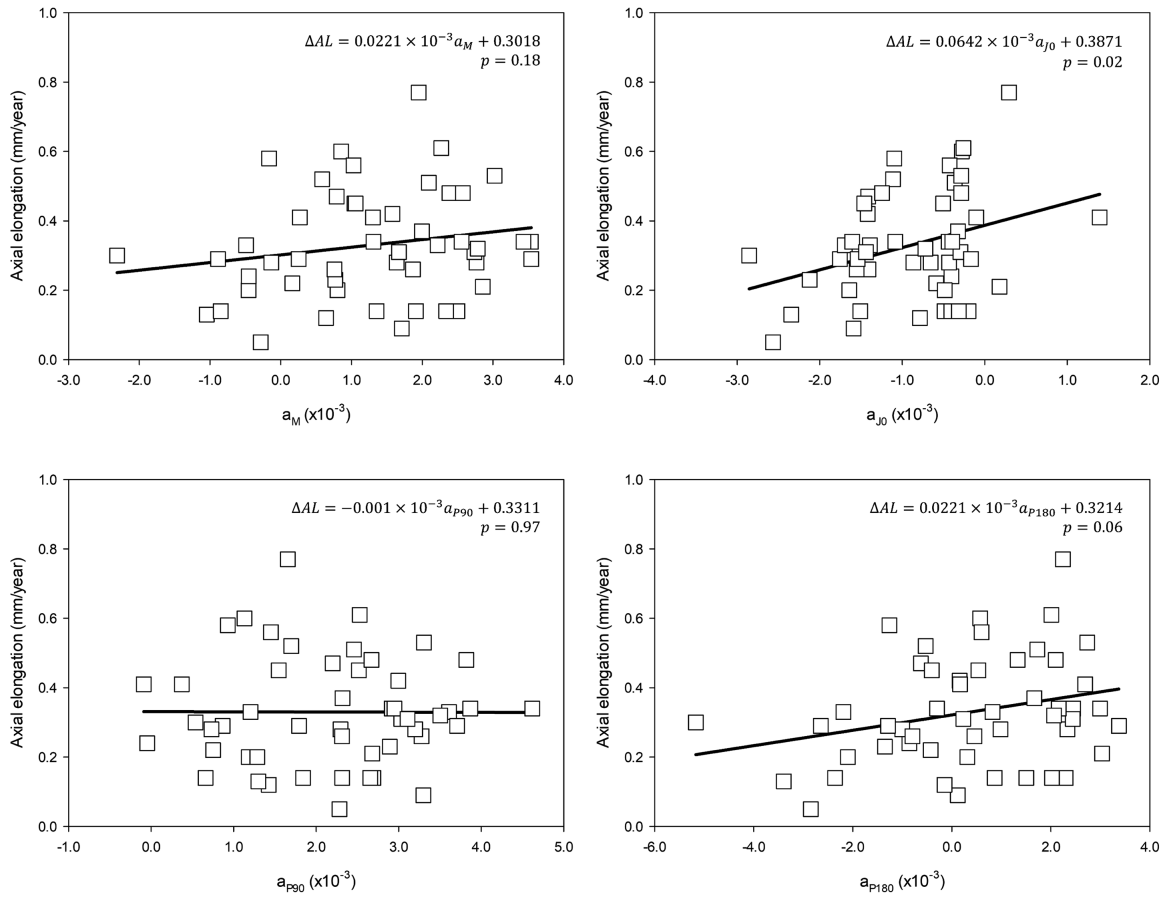


FIGURE 4. Relationship between the fitted first coefficients of RPRES and ΔAL. Top left:  $a_M$ . Top right:  $a_{J0}$ . Bottom left:  $a_{P90}$ . Bottom right:  $a_{P(180)}$ .

TABLE 2. Changes in Coefficients of Determination in Hierarchical Multiple Regressions ( $\Delta R^2$  [P]) for RPRES

Characteristic	Model 1	Model 2	Model 3a	Achieved Power, %	Model 3b	Achieved Power, %
$\Delta M$						
M	0.08 (0.05)	0.01 (0.48)	<b>0.09 (0.03)</b>	74	<b>0.10 (0.02)</b>	80
J0	<b>0.15 (&lt;0.01)</b>	0.05 (0.10)	0.06 (0.07)	92	0.07 (0.04)	95
P(90)	0.00 (0.68)	0.05 (0.13)	0.05 (0.10)	42	0.08 (0.05)	50
P(180)	<b>0.13 (0.01)</b>	0.01 (0.41)	<b>0.08 (0.03)</b>	81	<b>0.10 (0.02)</b>	86
$\Delta \Delta L$						
M	0.04 (0.18)	0.00 (0.97)	<b>0.11 (0.02)</b>	67	<b>0.21 (0.001)</b>	88
J0	<b>0.11 (0.02)</b>	0.01 (0.43)	0.09 (0.03)	91	<b>0.18 (0.001)</b>	98
P(90)	0.00 (0.97)	0.01 (0.60)	0.09 (0.04)	54	<b>0.19 (&lt;0.01)</b>	80
P(180)	0.07 (0.06)	0.00 (0.92)	<b>0.11 (0.02)</b>	71	<b>0.20 (&lt;0.001)</b>	90

Bolding indicates statistical significance after Hochberg's adjustment.

Model 1:  $\Delta M/\Delta \Delta L$  versus the coefficient ( $a_M/a_{J0}/a_{P90}/a_{P180}$ ) over null model.

Model 2:  $\Delta M/\Delta \Delta L$  versus the coefficient + baseline M over model 1.

Model 3a:  $\Delta M/\Delta \Delta L$  versus the coefficient + baseline M + normality-transformed dioptric volume over model 2.

Model 3b:  $\Delta M/\Delta \Delta L$  versus the coefficient + baseline M + normality-transformed standard deviation of scene defocus over model 2.

glasses during nearwork. The common optometric practice was to encourage full-time wear of spectacles or least during nearwork, but the  $m_{Acc}$  may have been totally different if the participants had been unaided. The home environment was measured at baseline only, instead of longitudinally monitoring the scene defocus. The measurement could be further enhanced with the incorporation of more advanced depth sensors and mobile eye trackers in future studies.

The current study focused only on the nearwork environment at home, where children in Hong Kong spend hours tackling their homework. On the other hand, other environments, particularly the school environment, could also contribute to myopia progression. While a previous study reported the effect of time spent on nearwork and outdoors in these participants and their joint effect with nearwork environment on myopia progression,<sup>22</sup> future research

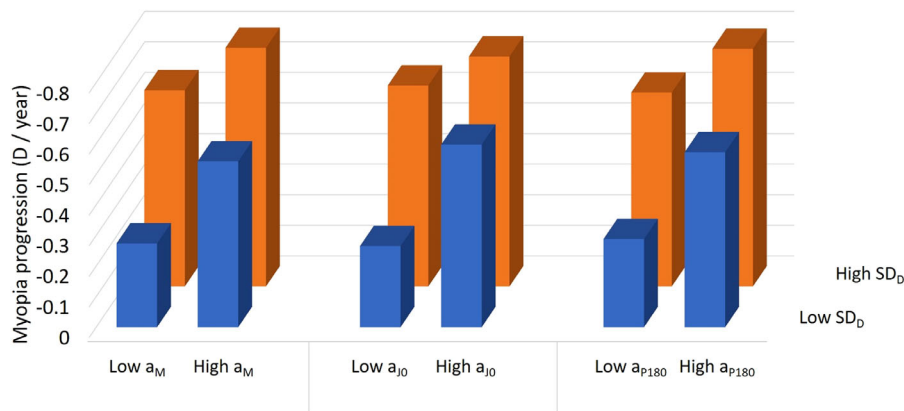


FIGURE 5. Myopia progression versus scene defocus profile and peripheral refraction. High SD<sub>D</sub>: more dispersed defocus profile; low SD<sub>D</sub>: more uniform defocus profile; low a<sub>M</sub>: more peripheral myopia; high a<sub>M</sub>: more peripheral hyperopia; low a<sub>J0</sub>: steeper peripheral astigmatism profile; high a<sub>J0</sub>: flatter peripheral astigmatism profile; low a<sub>P180</sub>: more myopic peripheral vertical component; high a<sub>P180</sub>: more hyperopic peripheral vertical component.

TABLE 3. Hierarchical Regression for the Lag of Accommodation

Characteristic	Raw B	95% CI	Standardized B	P Value	VIF
Model 1a					
tDV	-0.10	-0.22 to 0.02	-0.25	0.09	1.03
BL M	0.06	-0.01 to 0.12	0.25	0.08	1.03
Model 2a: Change in R <sup>2</sup> = 0.08, P = 0.04, achieved power = 55%					
tDV	-0.13	-0.24 to -0.01	-0.30	0.04	1.06
BL M	0.05	-0.01 to 0.11	0.21	0.13	1.05
m <sub>Acc</sub>	1.56	0.11 to 3.01	0.30	0.04	1.06
Model 1b					
tSD <sub>D</sub>	-0.12	-0.24 to -0.00	-0.29	0.04	1.02
BL M	0.06	-0.01 to 0.12	0.26	0.07	1.02
Model 2b: Change in R <sup>2</sup> = 0.09, P = 0.03, achieved power = 59%					
tSD <sub>D</sub>	-0.14	-0.26 to -0.03	-0.33	0.02	1.05
BL M	0.05	-0.01 to 0.11	0.21	0.12	1.04
m <sub>Acc</sub>	1.58	0.16 to 3.01	0.30	0.03	1.06

BL M, baseline spherical equivalent refraction; CI, confidence interval; m<sub>Acc</sub>, slope of accommodation stimulus-response curve; tDV, normality-transformed dioptric volume; tSD<sub>D</sub>, normality-transformed standard deviation of scene defocus; VIF, Variance Inflation Factor.

should put effort in optimizing both home and school environment (e.g., in terms of defocus profile and spatial frequency) for better childhood and adolescent ocular development.<sup>41,42</sup>

CONCLUSION

To our knowledge, the current study is the first to preliminarily incorporate the intrinsic and extrinsic factors, which were the peripheral refraction and home nearwork scene defocus profile, respectively, to relate with refractive development in children. The results agreed that only peripheral refraction or accommodation alone was not predictable of myopia progression. However, with the additional consideration of the nearwork scene profile, which the children were exposed to over a long period of time, peripheral refraction became a significant factor in predicting refractive error development. Our findings further suggest that the peripheral refractive error may be a conjugate of the exter-

nal environmental stimulus, which in turn modulates myopia progression. We speculate that in addition to myopia control interventions by optical means, modification of the nearwork environment could be another strategy aiding in retardation of myopia progression, which can be put on trials.

Acknowledgments

The authors thank Maureen Boost for proofreading the manuscript.

Supported by the General Research Fund from the Research Grants Council of the Hong Kong Special Administrative Region, China (PolyU 151001/17M) and Collaborative Research (Industrial) Fund from SEED Co. Ltd. (ZG7B).

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Disclosure: K.Y. Choi, None; H.H.-L. Chan, None

References

- Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123:1036–1042.
- Grosvenor T, Scott R. Role of the axial length/corneal radius ratio in determining the refractive state of the eye. *Optom Vis Sci*. 1994;71:573–579.
- Verkharla PK, Ohno-Matsui K, Saw SM. Current and predicted demographics of high myopia and an update of its associated pathological changes. *Ophthalmic Physiol Opt*. 2015;35:465–475.
- Tideman JW, Snabel MCC, Tedja MS, et al. Association of axial length with risk of uncorrectable visual impairment for Europeans with myopia. *JAMA Ophthalmol*. 2016;134:1355–1363.
- Wallman J, Turkel J, Trachtman J. Extreme myopia produced by modest change in early visual experience. *Science*. 1978;201:1249–1251.
- Morgan IG, Ohno-Matsui K, Myopia Saw SM. *Lancet*. 2012;379:1739–1748.
- Atchison DA, Pritchard N, Schmid KL. Peripheral refraction along the horizontal and vertical visual fields in myopia. *Vision Res*. 2006;46:1450–1458.



8. Sng CCA, Lin XY, Gazzard G, et al. Change in peripheral refraction over time in Singapore Chinese children. *Invest Ophthalmol Vis Sci.* 2011;52:7880–7887.
9. Li S-M, Li S-Y, Liu L-R, et al. Peripheral refraction in 7- and 14-year-old children in central China: the Anyang Childhood Eye Study. *Br J Ophthalmol.* 2015;99:674–679.
10. Miles FA, Wallman J. Local ocular compensation for imposed local refractive error. *Vision Res.* 1990;30:339–349.
11. Smith EL, Hung LF, Huang J. Relative peripheral hyperopic defocus alters central refractive development in infant monkeys. *Vision Res.* 2009;49:2386–2392.
12. Zeng G, Bowrey HE, Fang J, Qi Y, McFadden SA. The development of eye shape and the origin of lower field myopia in the guinea pig eye. *Vision Res.* 2013;76:77–88.
13. Mutti DO, Sinnott LT, Mitchell GL, et al. Relative peripheral refractive error and the risk of onset and progression of myopia in children. *Invest Ophthalmol Vis Sci.* 2011;52:199–205.
14. Atchison DA, Li SM, Li H, et al. Relative peripheral hyperopia does not predict development and progression of myopia in children. *Invest Ophthalmol Vis Sci.* 2015;56:6162–6170.
15. Smith EL, Campbell MCW, Irving E. Does peripheral retinal input explain the promising myopia control effects of corneal reshaping therapy (CRT or ortho-K) & multifocal soft contact lenses? *Ophthalmic Physiol Opt.* 2013;33:379–384.
16. Rosén R, Lundström L, Unsbo P, Atchison DA. Have we misinterpreted the study of Hoogerheide et al.(1971)? *Optom Vis Sci.* 2012;89:1235–1237.
17. Morgan IG, Rose KA. How genetic is school myopia? *Prog Retin Eye Res.* 2005;24:1–38.
18. Ip JM, Rose KA, Morgan IG, Burlutsky G, Mitchell P. Myopia and the urban environment: findings in a sample of 12-year-old Australian school children. *Invest Ophthalmol Vis Sci.* 2008;49:3858–3863.
19. He M, Zheng Y, Xiang F. Prevalence of myopia in urban and rural children in mainland China. *Optom Vis Sci.* 2009;86:40–44.
20. Wu X, Gao G, Jin J, et al. Housing type and myopia: the mediating role of parental myopia. *BMC Ophthalmol.* 2016;16:151.
21. Choi KY, Yu WY, Lam CHI, et al. Childhood exposure to constricted living space: a possible environmental threat for myopia development. *Ophthalmic Physiol Opt.* 2017;37:568–575.
22. Choi KY, AYt Mok, Cw Do, Lee PH, HHL Chan. The diversified defocus profile of the near-work environment and myopia development. *Ophthalmic Physiol Opt.* 2020;40(4):463–471.
23. Flitcroft DI. The complex interactions of retinal, optical and environmental factors in myopia aetiology. *Prog Retin Eye Res.* 2012;31:622–660.
24. Tse DY, Lam CSY, Guggenheim JA, et al. Simultaneous defocus integration during refractive development. *Invest Ophthalmol Vis Sci.* 2007;48:5352–5359.
25. Gwiazda J, Thorn F, Bauer J, Held R. Myopic children show insufficient accommodative response to blur. *Invest Ophthalmol Vis Sci.* 1993;34:690–694.
26. Mutti DO, Mitchell GL, Hayes JR, et al. Accommodative lag before and after the onset of myopia. *Invest Ophthalmol Vis Sci.* 2006;47:837–846.
27. Khoshelham K, Elberink SO. Accuracy and resolution of Kinect depth data for indoor mapping applications. *Sensors.* 2012;12:1437–1454.
28. Zhang Z. Microsoft Kinect sensor and its effect. *IEEE Multi-media.* 2012;19:4–10.
29. Tang WC, Tang YY, Lam CSY. How representative is the 'representative value' of refraction provided by the Shin-Nippon NVision-K5001 autorefractor? *Ophthalmic Physiol Opt.* 2014;34:89–93.
30. Chat SWS, Edwards MH. Clinical evaluation of the Shin-Nippon SRW-5000 autorefractor in children. *Ophthalmic Physiol Opt.* 2001;21:87–100.
31. Davies LN, Mallen EAH, Wolffsohn JS, Gilmartin B. Clinical evaluation of the Shin-Nippon NVision-K 5001/Grand Seiko WR-5100K autorefractor. *Optom Vis Sci.* 2003;80:320–324.
32. Sheppard AL, Davies LN. Clinical evaluation of the Grand Seiko auto ref/keratometer WAM-5500. *Ophthalmic Physiol Opt.* 2010;30:143–151.
33. Radhakrishnan H, Charman WN. Peripheral refraction measurement: does it matter if one turns the eye or the head? *Ophthalmic Physiol Opt.* 2008;28:73–82.
34. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci.* 1997;74:367–375.
35. Chan B, Cho P, Cheung SW. Repeatability and agreement of two A-scan ultrasonic biometers and IOLMaster in non-orthokeratology subjects and post-orthokeratology children. *Clin Exp Optom.* 2006;89:160–168.
36. Templeton GF. A two-step approach for transforming continuous variables to normal: implications and recommendations for IS research. *Commun Assoc Inf Syst.* 2011;28.
37. Hochberg Y. A sharper Bonferroni procedure for multiple tests of significance. *Biometrika.* 1988;75:800–802.
38. Calver R, Radhakrishnan H, Osuobeni E, O'Leary D. Peripheral refraction for distance and near vision in emmetropes and myopes. *Ophthalmic Physiol Opt.* 2007;27:584–593.
39. Davies LN, Mallen EAH. Influence of accommodation and refractive status on the peripheral refractive profile. *Br J Ophthalmol.* 2009;93:1186–1190.
40. Wallman J, Winawer J. Homeostasis of eye growth and the question of myopia. *Neuron.* 2004;43:447–468.
41. Zhou Z, Chen T, Wang M, et al. Pilot study of a novel classroom designed to prevent myopia by increasing children's exposure to outdoor light. *PLoS One.* 2017;12:e0181772.
42. Choi KY, Chan SS-H, Chan HH-L. The effect of spatially-related environmental risk factors in visual scenes on myopia [published online October 6, 2021]. *Clin Exp Optom.*