Season of Birth, Natural Light, and Myopia

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Purpose: To investigate the possible roles of season of birth and perinatal duration of daylight hours (photoperiod) in the development of myopia.

Design: Retrospective, population-based, epidemiological study.

Participants: A total of 276 911 adolescents (157 663 male, 119 248 female) 16 to 22 years old. All were Israeli-born conscripts to the Israeli Defense Forces who were examined during the 5-year period 2000 through 2004.

Methods: Noncycloplegic refraction was determined by autorefractometer and validated by qualified optometrists. Myopia, defined on the basis of right eye spherical equivalence, was classified as mild (−0.75 to −2.99 diopters [D]), moderate (−3.0 to −5.99 D), or severe (−6.0 D or worse). The photoperiod was recorded from astronomical tables and classified into 4 categories. Using multivariate logistic regression models, we calculated odds ratios (ORs) for several risk factors of myopia including season of birth.

Main Outcome Measure: The OR for photoperiod categories as risk factors for myopia.

Results: Overall prevalences of mild, moderate, and severe myopia were 18.8%, 8.7%, and 2.4%, respectively. There were seasonal variations in moderate and severe myopia according to birth month, with prevalence highest for June/July births and lowest for December/January. On multivariate logistic regression, the ORs of photoperiod categories for moderate and severe myopia were highly significant and demonstrated a dose–response pattern. Odds ratios for severe myopia were highest for the shortest versus the longest photoperiods (1.24; 95% confidence interval, 1.15–1.33; $P<0.001$). Mild myopia was not associated with season of birth or perinatal light exposure. Other risk factors were gender (1.14 for female), education level (1.32 for age above 12), and father's origin (1.31 for Eastern vs. Israeli origin).

Conclusion: Myopia in this population is associated with birth during summer months. The exact associating mechanism is not known but might be related to exposure to natural light during the early perinatal period. *Ophthalmology 2007;xx:xxx © 2007 by the American Academy of Ophthalmology.*

The prevalence of myopia is increasing worldwide,[1,2] but its pathogenesis is still unclear. Genetic factors are probably the most important[3–5]; other environmental risk factors include near work, education, and intelligence.[5–7] Disruption of diurnal lighting rhythms disturbs emmetropization processes in chicks.[8–10] However, continuous light exposure does not induce refractive error in rhesus monkeys, despite some reported patterns of abnormal emmetropization.[11] A study by Quinn et al[12] of an association between night lighting and myopia in children sparked a continuing discussion over the effect of the light/dark cycle on the development of myopia in humans. Some studies in humans[13–15] have failed to show an association between myopia and light, whereas in other studies such an association was shown to exist.[16–20] Vannas et al,[17] for example, reported a trend towards higher prevalence of myopia among people living above the Arctic Circle, suggesting the possible participation of natural light in the pathogenesis of myopia. It is possible that the effect of light on the emmetropization process is small or masked by other factors; therefore, to verify its effect a large number of cases are needed. Nevertheless, when such an effect is detected, the finding is always that more light is associated with more myopia. Such findings might suggest that the amount of light exposure generates a biological signal that can influence the emmetropization process.

The purpose of this study was to evaluate the effect of season of birth and perinatal photoperiod on the prevalence of myopia.

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Materials and Methods

Subjects

Military service in Israel is compulsory except for specific minority populations. All candidates undergo an evaluation process that includes a test of best-corrected visual acuity (BCVA). Candidates for inclusion in our study comprised all Israeli-born male and female subjects between 16 and 22 years old who were examined in the years 2000 through 2004. All were drawn from the database of the Israel Defense Forces induction center, without any details of personal identity. The inclusion of only Israeli-born candidates (about 75% of all candidates) ensured that all participants had been exposed to the same perinatal seasonal variation. The number of years of education was reported by each candidate on a standardized form and was grouped into 3 categories. Origin was defined, according to the father's country of birth, as Israeli, Western (countries of Europe, the Americas, or Oceania), or Eastern (Asian or African countries).

Refraction

The visual examination is described in detail elsewhere.[1] In short, BCVA was determined in each candidate by a qualified optometrist using a standard Snellen chart. Those who were able to read all the letters in the 6/6 line with not more than one mistake were assumed to have no refractive error. When using optical correction, subjects who could read at least all but one of the letters on the 6/6 line were assumed to be properly refracted. All other candidates underwent subjective noncycloplegic refraction. The visual assessment was carried out only once. Only those candidates in whom both eyes had undergone complete examination were included in the study (comprising about 96% of conscripts examined). For each subject, we calculated the spherical equivalent of the right eye only. Myopia was classified into 3 categories: mild (between −0.75 and −2.99 diopters [D]), moderate (between −3.0 and −5.99 D), and severe (−6.0 D or worse).

The visual examination is one of the compulsory requirements during the recruiting process, and therefore, informed consent was not needed. The data were analyzed anonymously from the computerized database, and the subjects' privacy was protected according to the guidelines published in the Helsinki Declaration.

Photoperiod Categories

Daylight times were recorded from astronomical tables (Wise Observatory Astronomical Calendar, Tel-Aviv University, http://wise-obs.tau.ac.il). For each day of the year, we averaged the photoperiod of the following 30 days. These averages were further grouped into 4 categories (90–91 days each) with photoperiods of 10.1–10.8 hours, 10.81–12.2 hours, 12.21–13.57 hours, and 13.58–14.23 hours (means: 10.3 hours, 11.5 hours, 12.9 hours, and 14 hours) for categories 1 to 4, respectively. The specific photoperiod category for each month of the year is recorded in Figure 1.

Statistics

Univariate analysis was used to determine possible risk factors for myopia. In addition, multivariate logistic regression models were used to adjust for possible confounding factors. We compared the prevalence of the 3 categories of myopia (mild, moderate, severe) in relation to the 4 photoperiod categories while adjusting for gender, origin, and education. When analyzing the odds ratio (OR) for one category, other degrees of myopia were considered as missing values. The ORs and 95% confidence intervals (CIs) from the logistic regression models were used to assess the strength of association of risk factors with myopia. A value of $P<0.05$ was considered statistically significant. Data were analyzed using SPSS (version 12, SPSS Inc., Chicago, IL).

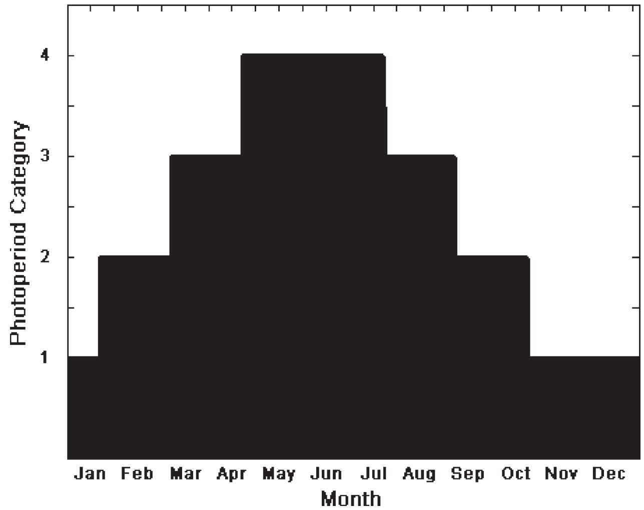

Figure 1. Photoperiod categories according to month of birth.

Results

Included in the study were 276 911 adolescents (157 663 male [56.9%], 119 248 female [43.1%]) between 16 and 22 years old. Mean age, education, origin (father's country of birth), and photoperiod categories for subjects' birth dates are recorded in Table 1. The overall prevalence of myopia was 29.9%, and specific prevalences of mild, moderate, and severe myopia were 18.8%, 8.7%, and 2.4%, respectively. Table 2 records the prevalence of the various degrees of myopia in relation to photoperiod category, gender, origin, and level of education.

Univariate analysis revealed that long photoperiod, female gender, non-Israeli origin, and higher education level were all related to higher prevalence of myopia (data not shown). Multivariate logistic regression analysis disclosed that all of these risk factors were significantly and independently associated with myopia prevalence (Table 3). Education level, gender, and country of origin are well-known risk factors for myopia and are not discussed here.

Figure 2 shows the prevalence of moderate and severe myopia according to month of birth. Variations in moderate and severe myopia according to birth month can be seen, with peak prevalences during June/July (9.2% and 2.6%, respectively) and the nadir during December/January (8.4% and 2.0%, respectively). The monthly averaged photoperiod in Israel is included in the figure, and its length appears to be closely related to myopia prevalence. Similar seasonal variations of mild myopia were minor and are not shown.

Figure 3 records cumulative prevalences of moderate and severe myopia in relation to photoperiod categories. Both moderate and severe myopia were significantly more prevalent in subjects born in months with longer photoperiods than in those born during shorter photoperiods (χ^2 for trend, 41.98; $P<0.001$).

The ORs for photoperiod categories for subjects with mild myopia were low and of borderline significance only when the longest photoperiod category was compared to the shortest (OR, 1.03; 95% CI, 1.00–1.06). The ORs for moderate and severe myopia were all highly significant (except for the difference between categories 1 and 2 in moderate myopia). The ORs for severe

Table 1. Age, Origin, Education Level, and Photoperiod Category of Participants

	Male (n = 157 663)	Female (n = 119 248)	Total (n = 276 911)
Mean age (SD)	17.3 (0.5)	17.1 (0.3)	17.2 (0.4)
Origin (father's country of birth)			
Israel (%)	17 843 (11.34)	9918 (8.34)	27 761 (10.05)
West (%)	55 745 (35.44)	44 644 (37.53)	100 389 (36.34)
East (%)	83 706 (53.22)	64 389 (54.13)	148 095 (53.61)
Missing (%)	369 (0.2)	297 (0.2)	666 (0.2)
Education level (yrs)			
<12 (%)	13 296 (8.4)	4153 (3.5)	17 449 (6.3)
12 (%)	141 272 (89.6)	114 708 (96.2)	255 980 (92.4)
>12 (%)	3095 (2.0)	387 (0.3)	3482 (1.3)
Photoperiod category (hrs)			
1 (10.1–10.8)	40 287 (25.55)	30 071 (25.22)	70 358 (25.41)
2 (10.8–12.2)	39 535 (25.08)	29 510 (24.75)	69 045 (24.93)
3 (12.2–13.57)	39 440 (25.02)	30 119 (25.26)	69 559 (25.12)
4 (13.58–14.23)	38 401 (24.36)	29 548 (24.78)	67 949 (24.54)

SD = standard deviation.

myopia were highest for the comparison of photoperiod categories 1 and 4 (OR, 1.24; 95% CI, 1.15–1.33; $P<0.001$). Furthermore, for both moderate and severe myopia the ORs demonstrated a dose–response pattern within photoperiod categories: the longer the photoperiod, the more prevalent the myopia (Table 3). None of the interactions between identified risk factors for myopia was found to be statistically significant.

The presence of family-related cases (siblings and cousins) might constitute a bias in a statistical analysis, in which case independence is assumed. To address this possible problem, we carried out an additional analysis after identifying and excluding 47 422 sibling pairs. The results were similar to those of the analysis in which all cases had been included (e.g., the OR for photoperiod category 4 vs. photoperiod category 1 was 1.225 [95% CI, 1.135–1.323; $P<0.001$]).

Discussion

The overall costs of correcting myopia in the United States in 1990 were estimated at about $4.6 billion.[21] Moreover, the rising prevalence of myopia and, especially, severe myopia presents an increasing economic burden as a result of ocular complications such as retinal detachment and choroidal neovascularization. Myopia can therefore be viewed as a major public health problem, thus necessitating preventive measures.

Our analysis in this study revealed a correlation between season of birth and the prevalence of moderate or severe myopia. Season of birth, however, is a nonspecific factor whose effect can apparently be mediated and confounded by various other factors, including the perinatal photoperiod, seasonal variations in pregnancy, birth complications, weather, infectious agents, and family characteristics such as socioeconomic status and education. Moreover, it is possible that our findings can be explained, at least in part, by an association between parental education, parental refractive state, and the subject's season of birth. Thus, for example, better educated (and myopic) parents might prefer to have their babies born in the summer, with consequently

Table 2. Prevalence of Myopia in Relation to Various Possible Risk Factors

Risk Factors	Mild Myopia		Moderate Myopia		Severe Myopia	
	Prevalence	*95% CI*	*Prevalence*	*95% CI*	*Prevalence*	*95% CI*
Photoperiod category (hrs)						
1 (10.1–10.8)	18.6%	(18.35–18.92)	8.5%	(8.25–8.66)	2.2%	(2.08–2.3)
2 (10.8–12.2)	18.6%	(18.33–18.91)	8.6%	(8.4–8.81)	2.4%	(2.27–2.49)
3 (12.2–13.57)	18.9%	(18.62–19.21)	8.9%	(8.67–9.09)	2.4%	(2.29–2.51)
4 (13.58–14.23)	18.9%	(18.64–19.23)	9.0%	(8.81–9.24)	2.7%	(2.55–2.79)
Gender						
Male	17.3%	(17.13–17.51)	8.2%	(8.08–8.35)	2.3%	(2.24–2.39)
Female	20.7%	(20.47–20.93)	9.4%	(9.26–9.59)	2.5%	(2.45–2.62)
Origin (father's country of birth)						
Israel	15.7%	(15.28–16.14)	6.8%	(6.51–7.1)	1.9%	(1.77–2.1)
West	19.4%	(19.16–19.65)	9.1%	(8.94–9.3)	2.6%	(2.48–2.67)
East	18.9%	(18.72–19.12)	8.8%	(8.7–8.99)	2.4%	(2.31–2.47)
Education (yrs)						
<12	12.7%	(12.25–13.24)	5.7%	(5.39–6.08)	2.0%	(1.75–2.17)
12	19.2%	(19.01–19.31)	8.9%	(8.83–9.06)	2.4%	(2.38–2.5)
>12	20.6%	(19.28–21.96)	8.6%	(7.68–9.55)	2.3%	(1.8–2.8)

CI = confidence interval.

Table 3. Multivariate Logistic Regression for Assessment of Myopia Risk Factors

Risk Factors	Mild Myopia		Moderate Myopia		Severe Myopia	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Photoperiod category (hrs)						
1 (10.1–10.8)	Ref.	0.086*	Ref.	0.001*	Ref.	<0.001*
2 (10.8–12.2)	1.00 (0.98–1.03)	0.757	1.03 (0.99–1.06)	0.207	1.09 (1.02–1.17)	0.014
3 (12.2–13.57)	1.03 (1.00–1.05)	0.079	1.06 (1.02–1.10)	0.002	1.11 (1.03–1.19)	0.004
4 (13.58–14.23)	1.03 (1.00–1.06)	0.033	1.08 (1.04–1.13)	<0.001	1.24 (1.16–1.33)	<0.001
Gender						
Male	Ref.	<0.001*	Ref.	<0.001*	Ref.	<0.001*
Female	1.25 (1.22–1.27)	<0.001	1.18 (1.15–1.21)	<0.001	1.14 (1.08–1.19)	<0.001
Origin (father's country of birth)						
Israel	Ref.	<0.001*	Ref.	<0.001*	Ref.	<0.001*
West	1.30 (1.25–1.35)	<0.001	1.40 (1.33–1.48)	<0.001	1.41 (1.28–1.55)	<0.001
East	1.27 (1.23–1.32)	<0.001	1.37 (1.30–1.44)	<0.001	1.31 (1.19–1.44)	<0.001
Education (yrs)						
<12	Ref.	<0.001*	Ref.	<0.001*	Ref.	<0.001*
12	1.63 (1.55–1.71)	<0.001	1.68 (1.57–1.80)	<0.001	1.34 (1.20–1.50)	<0.001
>12	1.91 (1.73–2.10)	<0.001	1.72 (1.50–1.97)	<0.001	1.32 (1.03–1.70)	0.026

CI = confidence interval; OR = odds ratio; ref. = reference for OR calculation.
Myopia is significantly associated with birth during months with longer photoperiods after adjustment for gender, origin, and education.
*For the overall difference.

a higher prevalence of myopia in subjects born during the summer period. Partial adjustment for this possible confounding factor was achieved here by defining education level as one of the risk factors in the regression model. A more satisfactory way to address these concerns would be to adjust also for the refractive state of the parents, but unfortunately, this information was not available to us. As a reasonable substitute, we conducted an analysis of sibling data (unpublished). Data on siblings' refractive states were available for 47 422 sibling pairs. When adjusting for sibling refractive state in addition to the other 4 risk factors defined in this study, the logistic regression model disclosed that the photoperiod effect remained almost exactly as reported (OR, 1.18 [95% CI, 0.98–1.42]; OR, 1.26 [95% CI, 1.05–1.51]; and OR, 1.30 [95% CI, 1.09–1.56], for photoperiod categories 2, 3, and 4, respectively). These results suggest that there is statistical independence between the effect of light on myopia and the sibling refractive state.

Another statistical finding of this study further strengthens the argument against family planning as a confounding factor for the association between myopia and perinatal photoperiod. When the subjects' photoperiods were replaced by the photoperiods of their respective siblings, application of the same regression model yielded no statistical correlation between siblings' photoperiod and subjects' myopia (ORs were 1.02 [95% CI, 0.86–1.21; $P = 0.82$], 1.1 [95% CI, 0.93–1.3; $P = 0.27$], and 1.07 [95% CI, 0.90–1.28; $P = 0.46$], for sibling photoperiod categories 2, 3, and

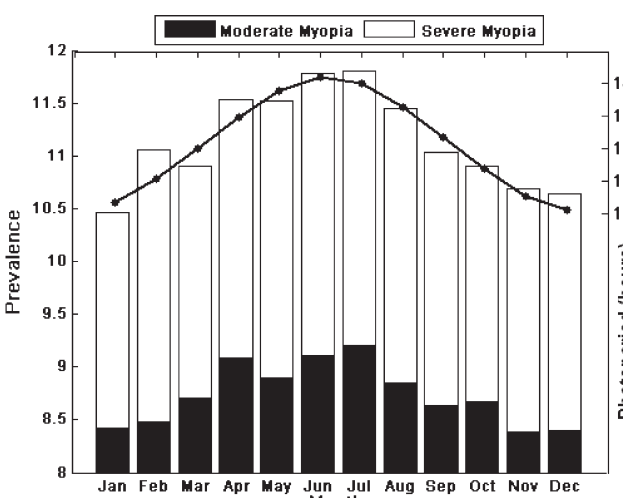

Figure 2. Season of birth and prevalence of myopia. Prevalence (%) of moderate and severe myopia plotted against month of birth. Myopia prevalence shares the same seasonal variation as the photoperiod. The y-axis begins at 8% for better graphic demonstration of the seasonal effects. Moderate and severe myopia are more prevalent during summer months than in the winter. Line, monthly averaged daily photoperiod.

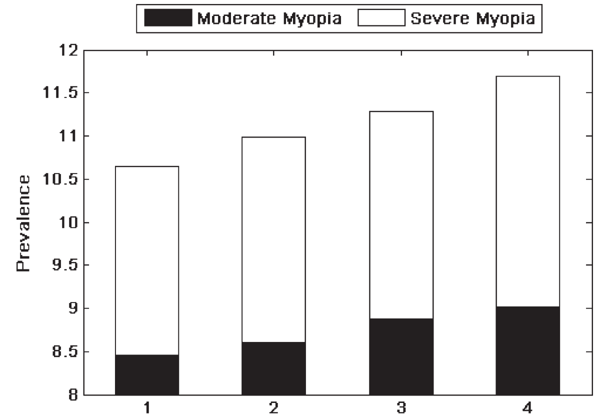

Figure 3. Myopia and perinatal photoperiod. Prevalence (%) of moderate and severe myopia plotted against photoperiod categories. The prevalence of myopia increases with lengthening of the perinatal photoperiod.

4, respectively). If family planning was a confounding factor for the association between myopia and photoperiod, not only the subjects' but also the siblings' photoperiod should have been identifiable as a risk factor. The absence of a statistical association between sibling date of birth and subject myopia weakens any claim that family planning affects the correlation observed here between myopia and season of birth.

The observed correlation between myopia and season of birth might be explained by differences in the light exposure of babies born in different seasons. Animal studies have demonstrated that the light/dark cycle plays a role in the emmetropization process.[8–10] Li et al showed that at least 4 hours of darkness are needed for normal emmetropization in chicks.[22] Diurnal growth rhythm in ocular elongation was demonstrated in chicks,[23,24] with maximal elongation occurring during the day and growth rate slowing during the night. Diurnal variations reportedly occur in human eye axial length[25] as well as in anterior chamber depth (ACD),[26] with maximum length measured at midday. Whereas Hoffmann and Schaeffel[27] concluded that "melatonin is not involved in the retinal signaling pathway translating visual experience to deprivation myopia," Rada and Wiechmann[28] recently detected the melatonin receptors Mel(1a), Mel(1b), and Mel(1c) in the cornea, choroid, sclera, and retina of chicks, leading these authors to suggest that observed fluctuations in ACD are attributable to a mechanism mediated by melatonin. In that study, systemic administration of melatonin resulted in significant changes in the morphology and growth of the anterior chamber, vitreous chamber, choroid, and retina, and some of these melatonin effects were blocked by a melatonin-receptor antagonist. Li and Howland[29] also suggested that circulating melatonin is responsible for growth of the anterior segment of the chick eye. Consistent with this suggestion is the finding of Lauber et al,[30] who reported an association between daily patterns of corneal mitotic activity and plasma melatonin levels. Taken together, these findings support the notion that the normal melatonin–dopamine balance plays a role in emmetropization and that disruption of this balance can result in a refractive error.[31]

The correlation observed in this study between perinatal photoperiod and the prevalence of myopia might be explained in terms of the melatonin–dopamine balance. Studies in humans showed that turnover of the neurotransmitter dopamine in adults born in Sweden is related to their season of birth, with a peak around the birth months of November/December and a nadir for birth during May/June, suggesting a long-term effect of the photoperiod during the perinatal period on dopamine turnover in adulthood.[32] Furthermore, a study conducted in Israel demonstrated a significant effect of the birth month on production of melatonin (6-sulfatoxymelatonin) at the age of 8 weeks, with peak levels observed in infants born in June and a nadir in those born in December. This seasonal variation was no longer detectable when the infants were 16 weeks old.[33] Season of birth is reportedly also related to certain personality traits, suicidal behavior, degree of morningness or eveningness of subjects, and other psychosocial functions in adults,[34–36] as well as the age of menopause.[37] Thus, although season of birth is a one-time early life exposure, it might have a prolonged and even lifetime effect on the reproductive system and some neurobehavioral properties, as well as on certain CNS neurotransmitters, including dopamine and melatonin.

The effect of the photoperiod on babies born in Israel is expected to be small because the greatest difference in photoperiod between the summer and winter in Israel is only 4.2 hours. However, the effect could be significantly magnified because of the natural tendency to spend more time outdoors during summer. A study by Sivan et al[33] showed that even the small difference in seasonal photoperiod in Israel is sufficient to affect the neonate's melatonin system. It is not clear whether the photoperiod effect is exerted on the newborn directly or, as suggested by Natale et al,[38] through the maternal melatonin system.

We calculated the population-attributable risks for subjects born in photoperiods 2, 3, and 4. These were 2.2%, 2.7%, and 5.6%, respectively, meaning that 2.2% to 5.6% of severe myopia in the population is attributable to factors associated with season of birth or perinatal light.

Some authors suggest that severe myopia is more likely to be an inherited characteristic and that, in less severe cases, the etiology is multifactorial, with environmental factors playing a more prominent role.[3,39,40] Other authors maintain, however, that the genetics of different degrees of myopia are similar.[41,42] Interestingly, the photoperiod effect was found in our study to increase the risk of severe myopia more than that of moderate or mild myopia. This might be explained in terms of genetic/environmental interaction. Qualitative evidence for such interaction in ocular refraction was obtained in a population study of twins.[5] Evidence for genetic/environmental interaction was also reported by Saw et al,[43,44] who found an increased effect of near-work activity on myopia in subjects in whom both parents were myopic. Different results, however, were reported by Mutti et al,[45] who found no evidence of genetic predisposition to different sensitivities to near work in children with myopic parents. It should be pointed out that in those studies the authors analyzed all levels of myopia and not only severe myopia, and their conclusions therefore cannot be simply projected to the genetics of severe myopia. Nevertheless, it seems reasonable to assume that only a fraction of the population might be genetically prone to develop myopia if exposed to environmental risk factors such as a long perinatal photoperiod. This might explain our present finding of a differential response of the more severe type of myopia to season of birth or light.

It should be noted, however, that none of the interactions between the 4 risk factors of myopia (gender, father's country of origin, education, photoperiod category) was found to be statistically significant in our regression model, indicating that the effect of light on myopia development is not modified by any of the risk factors tested here.

In conclusion, our results demonstrate a correlation between season of birth and prevalence of myopia. Although the mechanism that relates season of birth and myopia might be difficult to identify, it is possible that the emmetropization process in humans exhibits the same sensitivity to the dark/light cycle as that demonstrated in animal studies. Further exploration of the mechanisms underlying the effects of light on the development and progression of myopia in humans will be needed to devise effective preventive measures.

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