

Contribution of Ambient Light Intensity vs Spectral Contents of Short Wavelength on Refractive Development in Young Rabbits

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Research Article

Keywords: emmetropization, myopia, hyperopia, refractive error, illuminance, blue light

Posted Date: March 16th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1423252/v1>

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Abstract

Background: The aim of this study was to compare the effects of manipulating lighting levels versus manipulating the short wavelength contents of ambient lighting on refractive development in young rabbits.

Methods: A total of 32 healthy 3-week-old rabbits were randomly assigned to one of four groups with 8 in each group. Normal blue at normal illuminance (control, NC) group and normal blue at high illuminance lighting (HI) group were exposed to light emitted by ordinary LED lamps with low content in the short wavelength range. High-blue at high illuminance (Simulating natural light, S-NL) group and high-blue at normal illuminance (High-blue, HB) group were exposed to the light with high content in the short wavelength range provided by ordinary LED and blue LED lamps. The approximate mean illuminance (in human lux) on the cage floor was (NC:341lux, HI:5057lux, HB:342lux, S-NL: 5051lux). Refractive error, axial dimensions and corneal curvature radius were assessed by retinoscopy, ultrasonography and keratometry, respectively. Average data of both eyes for each animal were compared across groups.

Results: During the intervention, all animals had an emmetropization period. The refractive development of HI group was similar to S-NL group, both significantly slower than that of HB and NC group ($p < 0.001$). While the decrease of group refraction in HB paralleled to the control group ($p = 0.381$). At the 12th week, the group refraction of S-NL ($3.000 \pm 0.267D$) was similar to HI ($3.250 \pm 0.267D$), more hyperopic than HB ($2.219 \pm 0.281D$) and NC ($1.938 \pm 0.291D$). The vitreous chamber depth of S-NL ($7.421 \pm 0.168mm$) was shorter than HB ($7.785 \pm 0.230mm$) and NC ($7.825 \pm 0.313mm$), similar to that of HI group ($7.264 \pm 0.256mm$). The other components were less effected by light conditions ($p > 0.05$).

Conclusions: Extrapolated from rabbits, these findings suggest that high illuminances per se but not the rich in short wavelengths determine the inhibitory effect of ambient lighting on myopia after increasing time outdoors.

Background

Myopia, also known as nearsightedness, is a common eye condition with an increasing prevalence in recent years.^[1]

In 2020, Wang et al.^[2] reported that the prevalence of myopia in primary school students in China had reached 63.1% and increased with grade in a non-linear manner to 90% by grade 10 or above. Furthermore, it is estimated that the global prevalence of myopia will account for 52% by 2050.^[3] Previous studies believed that only high myopia will add to the burden of sight-threatening ocular complications such as cataract, retinal detachment, macular degeneration and glaucoma, but a current systematic analysis showed that even moderate or low myopia also has considerable risks.^[4] Because of the higher incidence and serious complications, myopia has been recognized as an important public health concern.^[5, 6]

It is well established that time spent indoors increases the risk of myopia onset in children, whereas time spent outdoors reduces the risk of myopia. Results from a variety of laboratory animals, like chickens,^[7, 8] guinea pig,^[9] primates,^[10] and tree shrews^[11] supported the idea that the significantly higher illuminance encountered outdoors reduces the risk for myopia. Furthermore, the differences in the spectral composition of lighting between typical indoor and outdoor environments is still responsible. Typical outdoor sunlight contains a preponderance of blue light,^[12] while tungsten, fluorescent lights and light emitting diode (LED) lamps were weaker in short wavelengths. Numbers of experiments confirmed that animals kept in blue light, such as fish,^[13] chicks,^[14] and guinea pigs^[15] had a lower refraction change or remained more hyperopic compared to those kept in red light. It has also been proposed that in order to maximize luminance contrast, the eye would become relatively myopic in typical indoor scenes that are dominated by relatively long-wavelength lighting.^[16]

However, the difference between light intensity and short wavelengths on refractive development has not been reported. A study performed by Smith, et al.^[17] also assumed that increasing light intensity did not alter the final amount of myopia change in monkeys wearing monocular - 3.0D lenses. Furthermore, in recent years, studies also indicated that long wavelength light (red light) can effectively alter the process of emmetropization^[18-22] and blue light promoted the development of refraction error,^[18] which strongly impact the view that high content of blue light were beneficial to reduce the myopia change. These contradictory findings of the effect of light on refractive development, uncertain risk factors outdoors and potentially detrimental effects caused by long-term exposure to short wavelengths, such as sunburn, macular degeneration and increased risk of skin cancers,^[23] all urge us to further explore the effects of lighting levels and the content of short wavelengths on refractive development and axial growth and guide us to optimize potential treatment strategies for myopia.

As a kind of mammal, young rabbits have been used in ophthalmic research for a long time.^[24, 25] The transmittance of electromagnetic radiation through the ocular media of the rabbit eyes^[26] was similar to the transmittance spectra of the human crystalline lens.^[27] The evidence that rabbits use visual cues to emmetropize also have been provided.^[28] Therefore, in this study, we analyzed and clarified the changes of refractive development and axial components in young, pigmented rabbits after rearing them in different ambient lighting conditions to provide reference for clarifying the main factor that affect the refractive development by light.

Methods

Animals

This study was approved and supervised by the Experimental Animal Ethics Committee of North Sichuan Medical College (NSMC Appl. No. 2021 [24]). In this study, 32 healthy pigmented young male/female rabbits, aged 3-week with weight of 250–450 g provided by the Experimental Animal Centre of North Sichuan Medical College were used. Animals with refractive medium opacity or fundus abnormalities

were excluded. The animals were then raised in rabbit cages, which was surrounded by black shading cloth to simulate an independent rearing space, in the North Sichuan Medical College Experimental Animal Centre for 12 weeks. Food was regularly supplied in the morning, at noon and in the evening every day with unrestricted access to water. The room temperature was kept at 24 ± 2 C with air circulation. All these conditions remained unchanged during treatment.

Grouping and Lighting

All rabbits were randomly divided into 4 groups (randomly designated by non-breeders), 8 for each group, namely normal blue at normal illuminance (control, NC) group, normal blue at high illuminance lighting (HI) group, high-blue at high illuminance (Simulating natural light, S-NL) group and high-blue at normal illuminance (High-blue, HB) group. At the top of each rearing space, lighting equipment was installed on the simulated ceiling with a 12-hour light/12-hour dark cycle (light from 07:00 to 19:00). Control group was fed in space with normal room light, which was composed by 3 ordinary LED lamps (OPPLE12-LE-47026, 5W, Luminous color: warm) to simulate the lighting with normal short wavelengths at normal illuminance (300-350lux). The high illuminance group (HI) was put into space with 20 ordinary LED lamps to simulate the lighting with normal short wavelengths at high illuminance (5000-5100lux). The high-blue at normal illuminance group was reared in space with 2 ordinary LED lamps and 1 blue LED lamp to simulate the lighting with higher short wavelengths at normal illuminance (300-350lux), and the high-blue at high illuminance group was raised in space with 17 ordinary LED lamps and 9 blue LED lamps to simulate the lighting with high short wavelengths at high illuminance (5000-5100lux). Before the start of the experiment, the lighting parameters and the relative spectral distribution of each group were measured at the horizontal position of the eyes of rabbits in the feeding cage with the spectral illuminance analyzer (OHSP-350, HOPOOCOLOR). The lighting parameters and relative spectral distribution were shown in Table 1 and Fig. 1.

Table 1
Lighting parameters of light conditions.

Group	Illuminance (lux)	Irradiance (mW/cm ²)	Output Ratio(%)		
			Red light	Green light	Blue light
NC	341	118.09	22.2	76	1.8
HB	342	179.48	13.7	81.1	5.2
HI	5057	1553.94	22.4	76	1.6
S-NL	5052	1705.49	16.1	79	4.9

Illuminance, Irradiance, Output Ratio(%) all measured by spectral illuminance analyzer (OHSP-350, HOPOOCOLOR). Red light: the light with wavelength between 700-780nm. Green light: the light with wavelength between 500-700nm; Blue light: the light with wavelength between 380-500nm; NC: normal

blue at normal illuminance lighting (normal room light); HB: high-blue at normal illuminance lighting; HI: normal blue at high illuminance lighting; S-NL: high-blue at high illuminance lighting.

Ocular Biometry

All measures were taken while the animals were awake. Refractive state was measured in darkness every two weeks at the same time of day (around 10:00 am) during the intervention by retinoscopy and the data were recorded as the mean of three measurements. No cycloplegic agent was used during all the examinations because the data tested before found no difference between using cycloplegic agents and not using cycloplegic agents and that McBrien et al.^[29] reported cycloplegic agents may interfere with refractive development. The anterior radius of curvature of the cornea was measured at the beginning (3-week-old) and end of intervention at the same time of day (around 15:00 pm) by keratometry (OM-4; Topcon Co., Japanese) and the data also calculated from the average of three readings. Axial dimensions were measured in all animals at the beginning (3-week-old) and end of intervention at the same time of day (around 19:00 pm) with A-scan ultrasonography (11 MHz, Cinescan A/B, Quantel Co., France) after topical anesthesia with one drop of 0.4% oxybuprocaine hydrochloride (Santen Co., Osaka, Japan) and the data were recorded as the mean of ten measurements. The velocities of sound were assumed as :1532 m/s in the aqueous and vitreous humours and 1641 m/s in the lens. The A-mode ultrasound provides and stores waveforms with peaks that correspond to the front and back of the cornea, front and back of the lens and the internal limiting membrane of the retina. Off-line, the analysis cursors were moved to each pair of peaks to provide measures of anterior chamber depth, lens thickness and vitreous chamber depth.

Statistical Analysis

The Statistical Package for the Social Sciences V.22 (SPSS 22.0) was used to describe statistics and analysis data. Data were expressed as mean \pm standard deviation ($\bar{x} \pm s$). Normal distributions and equal variances were determined for each test. Intergroup differences of refraction recorded from NC, HB, HI and S-NL groups were analyzed by two-way repeated measures analysis of variance (ANOVA) after Bonferroni corrections. One-way analysis of variance (ANOVA) was used to analysis the differences in refraction and ocular biometric parameters of each group at the end of intervention. Differences were defined as being significant at values of p less than 0.05.

Results

Among all the animals participating in the experiment, the refractive state and other ocular component dimensions were not different in both eyes. Therefore, we present the average data of the right and left eyes for each animal as statistics.^[30] At the beginning of intervention, there was no significant difference in refraction and other ocular components among the four groups ($p > 0.05$) (Table 2).

Table 2
Refraction and ocular parameters during the intervention.

	NC	HB	HI	S-NL	$F_{31,3}$	P
<i>Refraction(D)</i>						
Begin	4.688 ± 0.417	4.750 ± 0.423	4.688 ± 0.417	4.656 ± 0.421	0.070	0.975
2w	4.094 ± 0.442	4.468 ± 0.432	4.656 ± 0.421	4.594 ± 0.441		
4w	3.250 ± 0.443	3.687 ± 0.417	4.251 ± 0.422	4.156 ± 0.421		
6w	2.875 ± 0.422	3.156 ± 0.441	3.968 ± 0.410	3.843 ± 0.421		
8w	2.468 ± 0.431	2.812 ± 0.417	3.781 ± 0.410	3.625 ± 0.422		
10w	1.968 ± 0.311	2.343 ± 0.325	3.312 ± 0.320	3.156 ± 0.325		
12w	1.937 ± 0.291	2.218 ± 0.281	3.150 ± 0.267*#	3.000 ± 0.267*#	40.549	0.001
Two-way ANOVA(P)		0.380	0.001	0.001		
<i>R(mm)</i>						
Begin	5.476 ± 0.234	5.500 ± 0.179	5.405 ± 0.207	5.450 ± 0.232	0.298	0.827
12w	6.730 ± 0.158	6.721 ± 0.178	6.745 ± 0.151	6.728 ± 0.192	0.027	0.994
<i>ACD(mm)</i>						
Begin	2.120 ± 0.060	2.144 ± 0.043	2.160 ± 0.048	2.090 ± 0.050	2.875	0.054
12w	2.346 ± 0.029	2.296 ± 0.059	2.270 ± 0.058	2.300 ± 0.069	2.547	0.076
<i>LT(mm)</i>						
Begin	5.011 ± 0.078	4.996 ± 0.079	5.005 ± 0.082	5.021 ± 0.072	0.147	0.931

D, Diopter; R, Radius of curvature of the cornea; ACD, Anterior chamber depth; LT, Lens thickness; VCD, Vitreous chamber depth; Values given as the mean ± SD. * indicated values with significantly difference compered with NC; # indicated values with significantly difference compered with HB.

	NC	HB	HI	S-NL	$F_{31,3}$	P
12w	6.041 ± 0.078	5.994 ± 0.094	6.040 ± 0.104	5.970 ± 0.041	1.417	0.259
<i>VCD(mm)</i>						
Begin	6.109 ± 0.283	6.195 ± 0.252	6.017 ± 0.305	6.278 ± 0.265	1.305	0.292
12w	7.825 ± 0.313	7.785 ± 0.229	7.263 ± 0.255*#	7.421 ± 0.168*#	9.901	0.001
D, Diopter; R, Radius of curvature of the cornea; ACD, Anterior chamber depth; LT, Lens thickness; VCD, Vitreous chamber depth; Values given as the mean ± SD. * indicated values with significantly difference compered with NC; # indicated values with significantly difference compered with HB.						

Before the start of intervention, all young rabbits were hyperopic. During all the different light exposure regimens, all animals emmetropized towards less hyperopic refractions (Fig. 2). All individuals in groups indicated the consistency of this process.

Figure 2A showed the refractive development of young rabbits in response to normal room light (control group), the eyes (principally the vitreous chamber) grew rapidly so that at the end of intervention they were less than two diopters hyperopic ($1.938 \pm 0.291D$) (Table 2, Fig. 3A). As shown in Table 2 and Fig. 3B, the depth of their vitreous chamber was the largest of the four groups at the end of intervention ($7.825 \pm 0.313mm$).

Figure 2B compared the longitudinal changes in refraction of animals exposed to normal blue at high illuminance light with the animals exposed to normal room light. All rabbits exposed to normal blue at high illuminance light had significantly higher hyperopia refraction than that of animals in control group over time ($p < 0.001$). At the end of intervention, the group refraction ($3.250 \pm 0.267D$) was significantly higher than that of the control group at the same age ($p = 0.001$) (Table 2, Fig. 3A). The depth of their vitreous chamber was short. It was significantly shorter than vitreous chamber depth in control group ($p < 0.001$) (Table 2, Fig. 3B). The result indicated that exposure to normal blue at high illuminance light can significantly reduced the development of myopia in young rabbits by delaying the growth rate of the vitreous chamber depth.

Then, Fig. 2C showed that high-blue at normal illuminance light had little effect on refractive development. The refractive response was similar to that with control group ($p = 0.380$). The refractive state at the end of intervention was not significantly different from the refraction in control group. Vitreous chamber depth of this group was significantly longer than vitreous chamber depth of animals exposed to normal blue at high illuminance light or high-blue at high illuminance light ($p < 0.001$, $p < 0.001$), but was not significantly longer than that of control group ($p = 0.311$) (Table 2, Fig. 3).

Figure 2D compared the effects of high-blue at high illuminance light on refractive development: the time-course of the group average refraction were similar to that of the animals reared in normal blue at high illuminance light during the intervention period, significantly higher than that of the animals reared in normal room light ($p = 0.001$) and high-blue at normal illuminance light ($p = 0.019$). At the end of intervention, the refractive state and vitreous chamber depth were all similar to that of the high illuminance group, significantly different from that of the control group and high-blue at normal illuminance group (Table 2, Fig. 3).

Then **the** anterior chamber depth, lens thickness and anterior radius of curvature of the cornea were less affected by illuminance and special composition. At the end of intervention, there was no significant difference between the four groups ($p > 0.05$)(Table 2).

The association between the change in refraction and other components also showed that the correlation between amount of change in vitreous chamber depth and the change in refraction was highly significant ($p = 0.002$, $R^2 = 0.271$), values of the anterior chamber depth, lens thickness and corneal radius to refraction were small (Fig. 4).

Given the difference of light conditions and eye parameters, we analyzed the effect on the changes in refraction and axial components according to the proportion of short wavelengths without considering the light intensity. The effects of light illuminance on refraction and axial components were also analyzed according to illuminance without considering the proportion of short wavelengths. Figure 5A and Fig. 5B showed that the changes of refraction, vitreous chamber depth, anterior chamber depth and lens thickness in the group of higher proportion of short wavelengths(S-NL + HB) were relatively smaller than lower proportion of short wavelengths group (NC + HI), but the difference was not significant. However, the changes in refraction and vitreous chamber depth in higher illuminance group (HI + S-NL) were all smaller than that in lower illuminance group (NC + HB), and the difference were statistically significant, as showed in Fig. 5C and Fig. 5D. The results further confirmed that illuminance is the main factor to affect the refractive development by retarding the growth rate of vitreous chamber length.

Discussion

The main finding of this study was that high illuminance rather than relatively high short wavelengths is the main factor for the difference of myopia risk between indoor and outdoor environments. Specifically, regardless of whether the content of short wavelengths was increased or not, high illuminance light can significantly retard the progress of myopia compared with normal illuminance light. Under the condition of high illuminance, the effect of light with increased short wavelengths or with normal short wavelengths on refractive state and ocular components were the same. Further grouping analysis also showed the same result. There was no significant difference in refractive state and axial parameters between these two groups which was divided by the content of short wavelengths; At the same time, the result showed that high illuminance (no matter the content of short wavelengths) can significantly retard the progress of myopia and delay the increasing of vitreous chamber compared to the low illuminance group.

Previous studies have shown that individuals who spend more time outdoors have more hyperopic refractive errors and a lower prevalence of juvenile-onset myopia.^[31-34] The protective effect of time outdoors is not associated with sporting activities, nor the time spent in near work. Instead, it is the total amount of time outdoors that appears to be important.^[34, 35] Although the mechanisms underlying this protective effect are not well understood, a review conducted by Lingham, et al.^[36] reported that bright light and spectral composition were relatively significant among all the evidence listed.

In this study, even if the blue LED lamps were added to increase the content of short wavelengths, the difference in refractive development and ocular components between animals raised in lower proportion of short wavelengths lighting and higher proportion of short wavelength lighting were not significant when the illuminance were the same. On the contrary, the decreasing of hyperopia and the increasing of vitreous chamber of animals reared in high illuminance light were obviously smaller than that of the low illuminance group, no matter the spectral composition. Research in chickens has provided that high lighting levels, either from sunlight or intense laboratory lights, all reduces the degree of axial myopia produced by form deprivation by 65% over a 4-day treatment period.^[37] In chicks reared with normal visual development, emmetropization is also slowed by high light levels, leading to more hyperopic refractive errors.^[38] Though it is not reasonable to extrapolate the results from chickens to humans, because of the differences in species and eye size. Smith et al.^[10] found that absolute light levels can have a significant impact on vision-dependent ocular growth in primates (rhesus monkeys). Hua et al.^[39] also found that increasing the light levels in classrooms can reduce the incidence of myopia in children and have a protective effect on myopia. Recently, Lanca et al.^[40] reported that even if certain protective measures were taken, the illuminance of outdoor light was significantly higher than that of indoor light, which played a protective role on the progress of myopia. Although there will be some differences between the spectral composition after protection with indoor light, it also means that light intensity plays a majority role in reducing the risk for myopia after increasing time outdoors, and the role of spectral composition is relatively limited.

However, not all studies support the protective effect of intense indoor lights on myopia. Smith, et al.^[17] assumed that increasing light intensity did not alter the final amount of myopia change in monkeys wearing monocular - 3.0D lenses. But exposure to sunlight for 3 hours a day significantly reduced the progress of refractive myopia in normal eyes and negative lens-induced eyes of young monkeys.^[41] Similar findings were also confirmed in the research conducted by Yang et al.^[42] Considering the significant difference in light levels and spectral composition between indoor and outdoors, and the theory that relative myopic defocus over a large portion of the retina have been shown to produce clinically meaningful reductions in myopia progression.^[43-45] In their opinion, the protective effect of increasing outdoor time on myopia is also related to spectral components and the mechanisms might be both complex and phase-dependent. Because the differences in the spectral composition of ambient lighting could interfere with the eye's ability to recognize the sign of optical defocus.^[46]

In this study, high-blue at normal illuminance lighting had little effect on refractive development compared with normal room light, the refractive response was similar to that seen with control group (Fig. 2D, $p = 0.381$). At the end of intervention, the refraction and ocular components were all similar to that of control group ($p > 0.05$). In the past, a study performed by Rohrer et al.^[47] found that refractive development in chickens was not different from controls in white light for either red or near-ultraviolet light. Similarly, animals exposed to ultraviolet light or white light also have no significant difference in compensation for myopia induced by negative lenses.^[48] Recently, results from Liu et al.^[49] still conformed that no significant difference in mean refraction was observed between the rhesus monkeys raised in blue light and white light. The results of this study were basically consistent with the research above. But study performed by Foulds et al.^[14] assumed that chicks developed hyperopia when reared in light consisting mainly of shorter wavelengths, and a large number of studies confirmed that short wavelength light can protect against myopia progression in different species in recent 10 years.^[15, 50-52] In their opinion, tipping the balance towards activation of S-cones by enhancing the contrast of short wavelengths could be protective against myopia for enhanced S-syndrome may be more hyperopic.^[16] In addition, short wavelengths can focus in front than long wavelengths after passing through the refractive system of the eye to form myopic defocus, which can inhibit the growth rate of eye length. Unfortunately, such protective effects have not been found in this work, though the blue cones are distributed in rabbit retina.^[53] Furthermore, Long et al.^[54] and Tori et al.^[55, 56] found that even in an environment exceeding species' spectral sensitivity, the animals also experienced different refractive compensation compared with normal room lighting, and this phenomenon can not be explained by vision defocus or the activation of S-cones. Besides, combined with the refractive development of the eye, almost all vertebrates (including humans) show hyperopia in their refractive state in infancy.^[57] Even if the content of short wavelengths in illumination is increased, the focus plane is still behind the retina, which cannot form the so-called "myopic defocus effect". Therefore, the reason for spectral differences which affect the emmetropization process need to be explained by other characteristics of light.

As a kind of electromagnetic wave, the propagation of light is also a kind of energy transmission. Combined with the photon energy of different wavelengths and the application of photo biotherapy in recent years,^[58] we speculate that the influence of light on refractive development may also be related to the irradiance of light and the energy conversion of different wavelengths received by retina. As shown in Table 1, high illuminance always means high irradiance; under the same illuminance, more short wavelengths is related to more irradiance. The retina of animals exposed to high illuminance or high short wavelengths lighting receives greater energy than ordinary indoor lighting after light passes through the refractive system of the eye. Experiment conducted by Torii et al.^[55] confirmed the inhibitory effect of ultraviolet on myopia progress in chickens. Even if the focal plane was behind the retina due to negative lens induction, the myopia changes of chickens raised in lighting with ultraviolet was significantly lower than that of the animals raised in lighting without ultraviolet. Moreover, when the irradiance is the same, no matter the white lighting with ultraviolet or only monochromatic blue light, the inhibition effects on lens-induced myopia of chickens were almost the same. However, in this study, the output of short

wavelengths we controlled in high-blue groups were more suitable for the outdoor lighting in real life, significantly lower than other experimental studies. Therefore, even if the content of short wavelengths was increased, the difference of overall irradiance is still low. Which may be one of the reasons for a lack of statistical difference of refractive development between normal blue groups and high-blue groups.

Conclusions

In summary, we present evidence indicating that high illuminance not the high content of short wavelengths is the main factor to affect the development of refraction and the growth rate of vitreous chamber depth. However, there are limitations in our study (e.g., lacks the data of the peak of the rabbit blue cone and the data of pupil size during the intervention period), and there is still much to be learned about the mechanism(s) by which high illuminance light prevents the development of myopia. Therefore, further studies are needed to confirm it.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

All authors participated in the design, interpretation of the studies and analysis of the data and review of the manuscript; ZYC, XPT and ZJT designed the experiment, analyzed the data, wrote and modified the manuscript. XPT, and HBF conducted the experiments and participated in ocular biometry. AH modified the manuscript.

Funding

This study was supported by Scientific Research Project of Affiliated Hospital of North Sichuan Medical College (No 2018ZX002), Sichuan Medical Research Project (No: S18034) and Science and Technology Project City-School Science and Technology Strategic Cooperation Project of Nanchong (No.18SHZ0386).

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request. Or all relevant datasets related to the study can be found in the specified (database. <https://figshare.com/s/2e9f6420ce220c84a2d4>).

Ethics approval and informed consent

The study that has been performed according to the ARRIVE guidelines was approved by the Medical Ethics Committee of North Sichuan Medical College and supervised throughout the process (NSMC Appl. No. 2021 [24]) and this study adhered to the ethical guidelines published by International Council for Laboratory Animal Science (ICLAS).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Dolgin E. *The myopia boom*. *Nature* 2015; *519*(7543): 276–278
2. Wang J, Ying GS, Fu X, Zhang R, Meng J, Gu F, Li J. *Prevalence of myopia and vision impairment in school students in Eastern China*. *Bmc Ophthalmol* 2020; *20*(1): 2
3. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. *Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050*. *Ophthalmology* 2016; *123*(5): 1036–1042
4. Haarman A, Enthoven CA, Tideman J, Tedja MS, Verhoeven V, Klaver C. *The complications of myopia: A review and Meta-Analysis*. *Invest Ophthalmol Vis Sci* 2020; *61*(4): 49
5. Chen M, Wu A, Zhang L, Wang W, Chen X, Yu X, Wang K. *The increasing prevalence of myopia and high myopia among high school students in Fenghua city, eastern China: A 15-year population-based survey*. *Bmc Ophthalmol* 2018; *18*(1): 159
6. Wong TY, Ferreira A, Hughes R, Carter G, Mitchell P. *Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: An evidence-based systematic review*. *Am J Ophthalmol* 2014; *157*(1): 9–25
7. RS A, F S. *The effect of bright light on lens compensation in chicks*. *Invest Ophth Vis Sci* 2010; *51*(10): 5247–5253
8. Backhouse S, Collins AV, Phillips JR. *Influence of periodic vs continuous daily bright light exposure on development of experimental myopia in the chick*. *Ophthalmic & physiological optics: the journal of the British College of Ophthalmic Opticians (Optometrists)* 2013; *33*(5): 563–572

9. Zhang L, Qu X. *The effects of high lighting on the development of Form-Deprivation myopia in guinea pigs*. Invest Ophth Vis Sci 2019; 60(13): 4319–4327
10. EL S, LF H, J H. *Protective effects of high ambient lighting on the development of form-deprivation myopia in rhesus monkeys*. Invest Ophth Vis Sci 2012; 53(1): 421–428
11. Siegwart JT WANT. *Moderately elevated fluorescent light levels slow form deprivation and minus lens-induced myopia development in tree shrews*. Invest Ophthalmol Vis Sci 2012; 53 ARVO E-abstract 3457
12. Ngo C, Saw SM, Dharani R, Flitcroft I. *Does sunlight (bright lights) explain the protective effects of outdoor activity against myopia?* Ophthalmic Physiol Opt 2013; 33(3): 368–372
13. Kroger RH, Wagner HJ. *The eye of the blue acara (Aequidens pulcher, Cichlidae) grows to compensate for defocus due to chromatic aberration*. J Comp Physiol a 1996; 179(6): 837–842
14. Foulds WS, Barathi VA, Luu CD. *Progressive myopia or hyperopia can be induced in chicks and reversed by manipulation of the chromaticity of ambient light*. Invest Ophth Vis Sci 2013; 54(13): 8004–8012
15. Jiang L, Zhang S, Schaeffel F, Xiong S, Zheng Y, Zhou X, Lu F, Qu J. *Interactions of chromatic and lens-induced defocus during visual control of eye growth in guinea pigs (Cavia porcellus)*. Vision Res 2014; 94: 24–32
16. Yoon HH, Taylor CP, Rucker FJ. *Indoor illuminants, S-Cone stimulation, and eye growth in chicks*. Invest Ophth Vis Sci 2018; 59(9)
17. EL S, LF H, B A, J H. *Negative lens-induced myopia in infant monkeys: Effects of high ambient lighting*. Invest Ophth Vis Sci 2013; 54(4): 2959–2969
18. Gawne TJ, Siegwart JJ, Ward AH, Norton TT. *The wavelength composition and temporal modulation of ambient lighting strongly affect refractive development in young tree shrews*. Exp Eye Res 2017; 155: 75–84
19. Yang J, Yang L, Chen R, Zhu Y, Wang S, Hou X, Wei B, Wang Q, Liu Y, Qu J, Zhou X. *A role of color vision in emmetropization in C57BL/6J mice*. Sci Rep 2020; 10(1): 14895
20. LF H, B A, Z S, L O, EL S. *Narrow-band, long-wavelength lighting promotes hyperopia and retards vision-induced myopia in infant rhesus monkeys*. Exp Eye Res 2018; 176: 147–160
21. TJ G, AH W, TT N. *Long-wavelength (red) light produces hyperopia in juvenile and adolescent tree shrews*. Vision Res 2017; 140: 55–65
22. EL S, LF H, B A, BA H, M N, J N. *Effects of Long-Wavelength lighting on refractive development in infant rhesus monkeys*. Invest Ophth Vis Sci 2015; 56(11): 6490–6500
23. Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P, Melchi CF. *Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure*. European journal of cancer (Oxford, England: 1990) 2005; 41(1): 45–60
24. Lin Z, Chen X, Ge J, Cui D, Wu J, Tang F, Tan J, Zhong X, Gao Q. *Effects of direct intravitreal dopamine injection on sclera and retina in Form-Deprived myopic rabbits*. J Ocul Pharmacol Th 2008;

24(6): 543–550

25. Nie HH, Huo LJ, Yang X, Gao ZY, Zeng JW, Trier K, Cui DM. *Effects of 7-methylxanthine on form-deprivation myopia in pigmented rabbits*. Int J Ophthalmol 2012; 5(2): 133–137
26. Algvere PV, Torstensson PA, Tengroth BM. *Light transmittance of ocular media in living rabbit eyes*. Invest Ophthalmol Vis Sci 1993; 34(2): 349–354
27. Eto T, Teikari P, Najjar RP, Nishimura Y, Motomura Y, Kuze M, Higuchi S. *A Purkinje image-based system for an assessment of the density and transmittance spectra of the human crystalline lens in vivo*. Sci Rep 2020; 10(1): 16445
28. Tong L, Cui D, Zeng J. *Topical bendazol inhibits experimental myopia progression and decreases the ocular accumulation of HIF-1 α protein in young rabbits*. Ophthalmic Physiol Opt 2020; 40(5): 567–576
29. McBrien NA, Stell WK, Carr B. *How does atropine exert its anti-myopia effects?* Ophthalmic & physiological optics: the journal of the British College of Ophthalmic Opticians (Optometrists) 2013; 33(3): 373–378
30. Ederer F. *Shall we count numbers of eyes or numbers of subjects?* Arch Ophthalmol 1973; 89(1): 1–2
31. Jones-Jordan LA, Sinnott LT, Cotter SA, Kleinstein RN, Manny RE, Mutti DO, Twelker JD, Zadnik K. *Time outdoors, visual activity, and myopia progression in juvenile-onset myopes*. Invest Ophthalmol Vis Sci 2012; 53(11): 7169–7175
32. Jones LA, Sinnott LT, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K. *Parental history of myopia, sports and outdoor activities, and future myopia*. Invest Ophthalmol Vis Sci 2007; 48(8): 3524–3532
33. Rose KA, Morgan IG, Smith W, Burlutsky G, Mitchell P, Saw SM. *Myopia, lifestyle, and schooling in students of Chinese ethnicity in Singapore and Sydney*. Archives of ophthalmology (Chicago, Ill.: 1960) 2008; 126(4): 527–530
34. Rose KA, Morgan IG, Ip J, Kifley A, Huynh S, Smith W, Mitchell P. *Outdoor activity reduces the prevalence of myopia in children*. Ophthalmology 2008; 115(8): 1279–1285
35. Dirani M, Tong L, Gazzard G, Zhang X, Chia A, Young TL, Rose KA, Mitchell P, Saw SM. *Outdoor activity and myopia in Singapore teenage children*. The British journal of ophthalmology 2009; 93(8): 997–1000
36. Lingham G, Mackey DA, Lucas R, Yazar S. *How does spending time outdoors protect against myopia? A review*. Brit J Ophthalmol 2020; 104(5): 593–599
37. R A, A O, F S. *The effect of ambient illuminance on the development of deprivation myopia in chicks*. Invest Ophthalmol Vis Sci 2009; 50(11): 5348–5354
38. Y C, M B, O Y, AS S, U P. *Dependency between light intensity and refractive development under light-dark cycles*. Exp Eye Res 2011; 92(1): 40–46
39. Hua WJ, Jin JX, Wu XY, Yang JW, Jiang X, Gao GP, Tao FB. *Elevated light levels in schools have a protective effect on myopia*. Ophthalmic Physiol Opt 2015; 35(3): 252–262

40. Lanca C, Teo A, Vivagandan A, Htoon HM, Najjar RP, Spiegel DP, Pu SH, Saw SM. *The effects of different outdoor environments, sunglasses and hats on light levels: Implications for myopia prevention*. *Transl Vis Sci Technol* 2019; *8*(4): 7
41. Y W, H D, WK S, L L, S L, H L, X Z. *Exposure to sunlight reduces the risk of myopia in rhesus monkeys*. *Plos One* 2015; *10*(6): e127863
42. Yang X, Yang Y, Wang Y, Wei Q, Ding H, Zhong X. *Protective effects of sunlight exposure against PRK-induced myopia in infant rhesus monkeys*. *Ophthalmic & physiological optics: the journal of the British College of Ophthalmic Opticians (Optometrists)* 2021; *41*(4): 911–921
43. Sankaridurg P, Holden B, Smith E, Naduvilath T, Chen X, de la Jara PL, Martinez A, Kwan J, Ho A, Frick K, Ge J. *Decrease in rate of myopia progression with a contact lens designed to reduce relative peripheral hyperopia: One-year results*. *Invest Ophth Vis Sci* 2011; *52*(13): 9362–9367
44. Anstice NS, Phillips JR. *Effect of dual-focus soft contact lens wear on axial myopia progression in children*. *Ophthalmology* 2011; *118*(6): 1152–1161
45. Kakita T, Hiraoka T, Oshika T. *Influence of overnight orthokeratology on axial elongation in childhood myopia*. *Invest Ophth Vis Sci* 2011; *52*(5): 2170–2174
46. Kim EC, Morgan IG, Kakizaki H, Kang S, Jee D. *Prevalence and risk factors for refractive errors: Korean National Health and Nutrition Examination Survey 2008–2011*. *Plos One* 2013; *8*(11): e80361
47. B R, F S, E Z. *Longitudinal chromatic aberration and emmetropization: Results from the chicken eye*. *The Journal of physiology* 1992; *449*: 363–376
48. Hammond DS, Wildsoet CF. *Compensation to positive as well as negative lenses can occur in chicks reared in bright UV lighting*. *Vision Res* 2012; *67*: 44–50
49. R L, M H, JC H, XT Z, JH D, XM Q, H L, RY C. *The effects of monochromatic illumination on early eye development in rhesus monkeys*. *Invest Ophth Vis Sci* 2014; *55*(3): 1901–1909
50. F R, S B, C T. *Color and temporal frequency sensitive eye growth in chick*. *Invest Ophth Vis Sci* 2018; *59*(15): 6003–6013
51. Rucker F, Britton S, Spatcher M, Hanowsky S. *Blue light protects against temporal frequency sensitive refractive changes*. *Invest Ophthalmol Vis Sci* 2015; *56*(10): 6121–6131
52. Timucin OB, Arabaci M, Cuce F, Karatas B, Onalan S, Yasar M, Yildirim S, Karadag MF. *The effects of light sources with different spectral structures on ocular axial length in rainbow trout (*Oncorhynchus mykiss*)*. *Exp Eye Res* 2016; *151*: 212–221
53. Famiglietti EV. *Wide-field cone bipolar cells and the blue-ON pathway to color-coded ganglion cells in rabbit retina*. *Vis Neurosci* 2008; *25*(1): 53–66
54. Q L, D C, R C. *Illumination with monochromatic long-wavelength light promotes myopic shift and ocular elongation in newborn pigmented guinea pigs*. *Cutan Ocul Toxicol* 2009; *28*(4): 176–180
55. H T, T K, Y S, K N, K O, T I, M K, X J, S K, M M, Y M, Y K, K M, K K, K T, H G, M O, M H, K T. *Violet light exposure can be a preventive strategy against myopia progression*. *Ebiomedicine* 2017; *15*: 210–219

56. Torii H, Ohnuma K, Kurihara T, Tsubota K, Negishi K. *Violet light transmission is related to myopia progression in adult high myopia*. *Sci Rep-Uk* 2017; 7(1): 14523
57. DO M, LT S, G LM, LA J, NE F, SL F, WK L. *Ocular Component Development during Infancy and Early Childhood*. *Optometry and vision science: official publication of the American Academy of Optometry* 2018; 95(11): 976–985
58. Kaynezhad P, Tachtsidis I, Jeffery G. *Optical monitoring of retinal respiration in real time: 670 nm light increases the redox state of mitochondria*. *Exp Eye Res* 2016; 152: 88–93

Figures

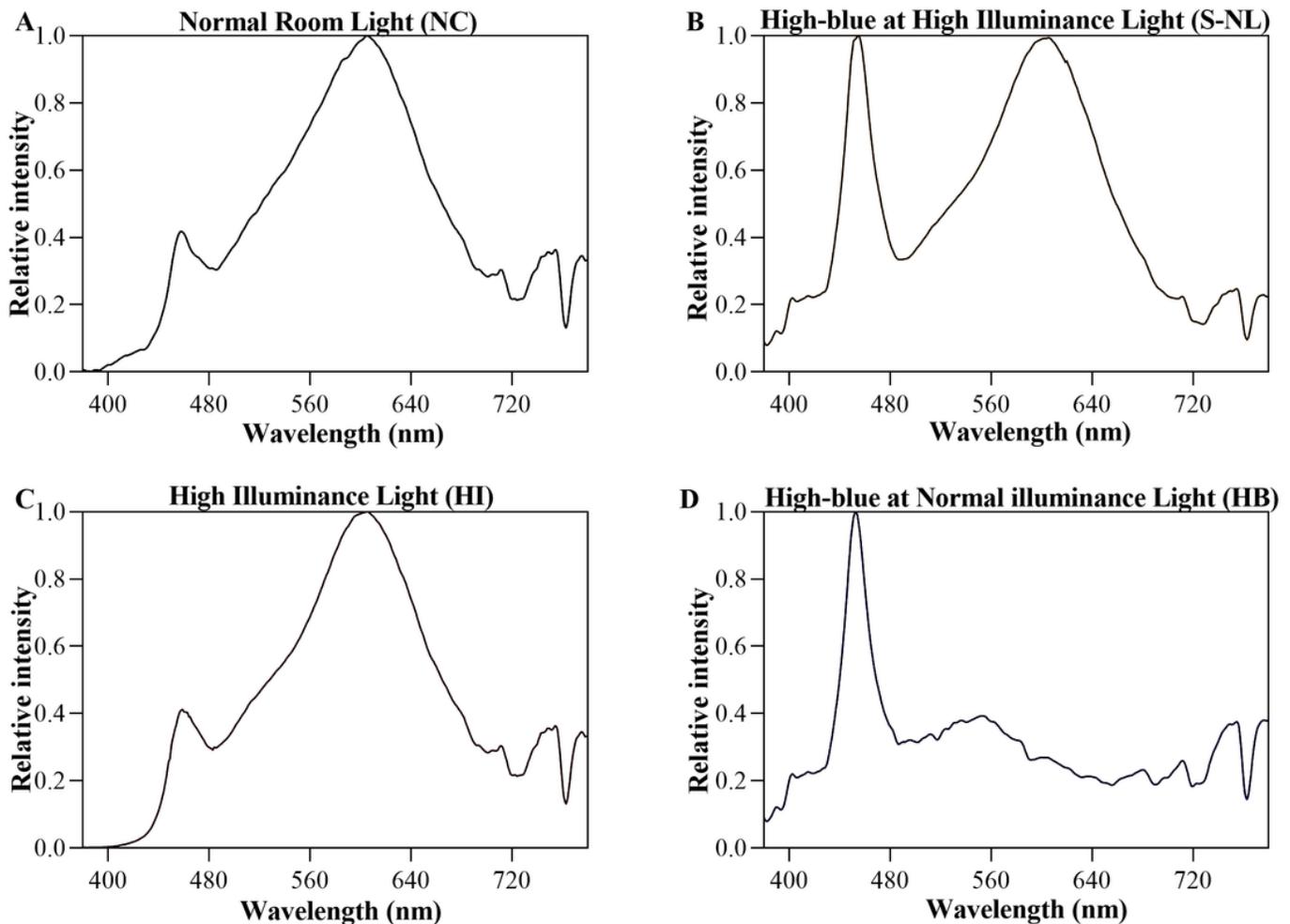


Figure 1

Relative spectral distribution of light conditions. y-axis indicate the relative intensity. x-axis indicate the wavelength. A and C shows the spectral distribution of normal room light and normal blue at high illuminance light were the same. The proportion of short-wavelength light with wavelength below 500nm was small. B: The spectral distribution of high-blue at high illuminance light. The relative power ratio of short wavelengths with wavelength less than 500nm were higher than that of the control group. D: The

spectral distribution of high-blue content light. The relative power ratio of short wavelengths with wavelength less than 500nm were similar to high-blue at high illuminance light, significantly higher than normal room light and normal blue at high illuminance light.

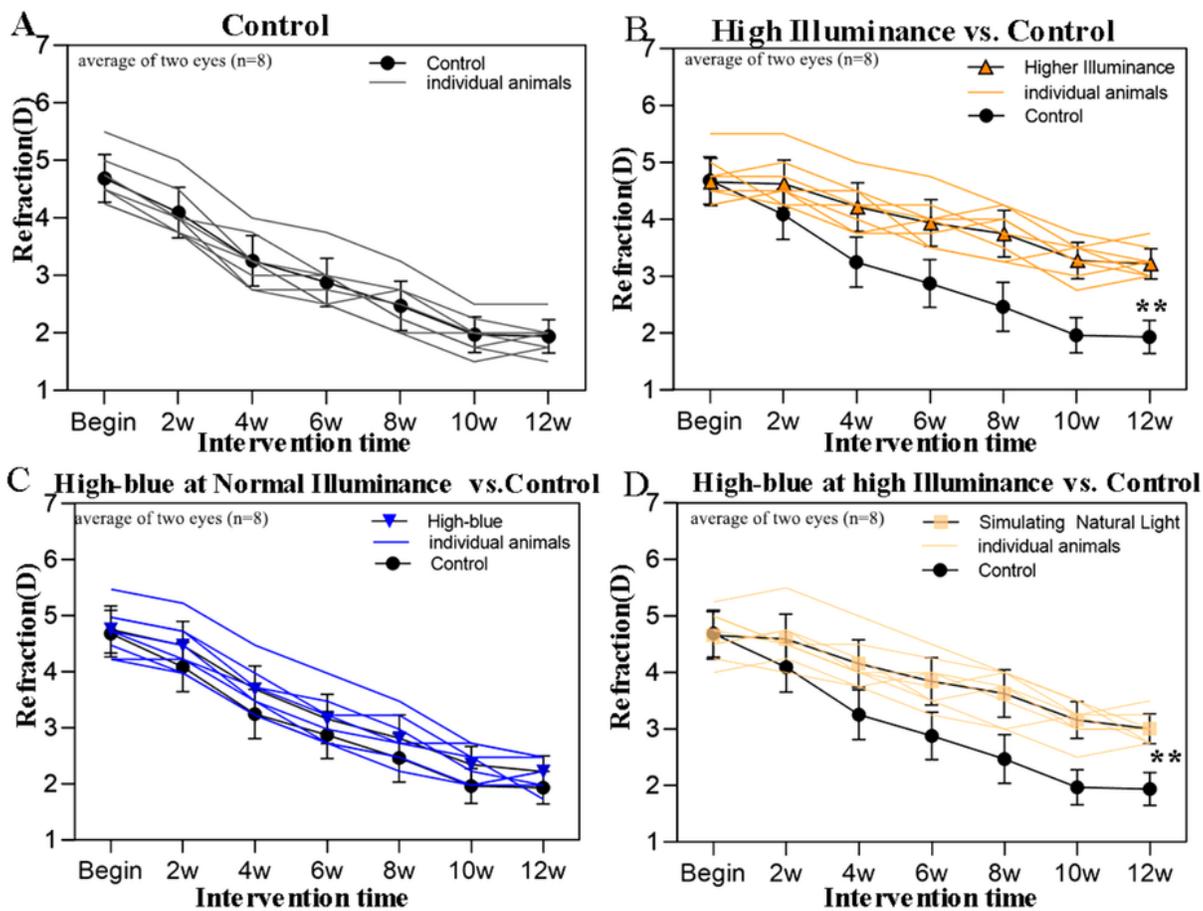


Figure 2

The effect on refractive development in young rabbit of different light conditions. y-axis indicate refractive error, x-axis indicate the intervention time. Thin lines show individual animals (mean of the two eyes). Error bars denote SD. During the intervention, all had an emmetropization period with the decreasing of hyperopia. A: Refractive response of animals exposure to normal room light (black, circle symbols). B: Refraction of 8 young rabbits raised in normal blue at high illuminance light (orange red, regular triangle symbols) was significantly higher hyperopia than that of animals raised in normal room light. C: Exposure to high-blue at normal illuminance light. Refractive rate (blue, inverted triangle symbols) was closer to control group. D: Refraction (yellow, square symbols) of animals exposure to high-blue at high illuminance light (stimulating natural light) was closer to high illuminance light group, significantly higher than control group. The asterisk indicates the statistical value compared with the control group. ** means $p < 0.01$

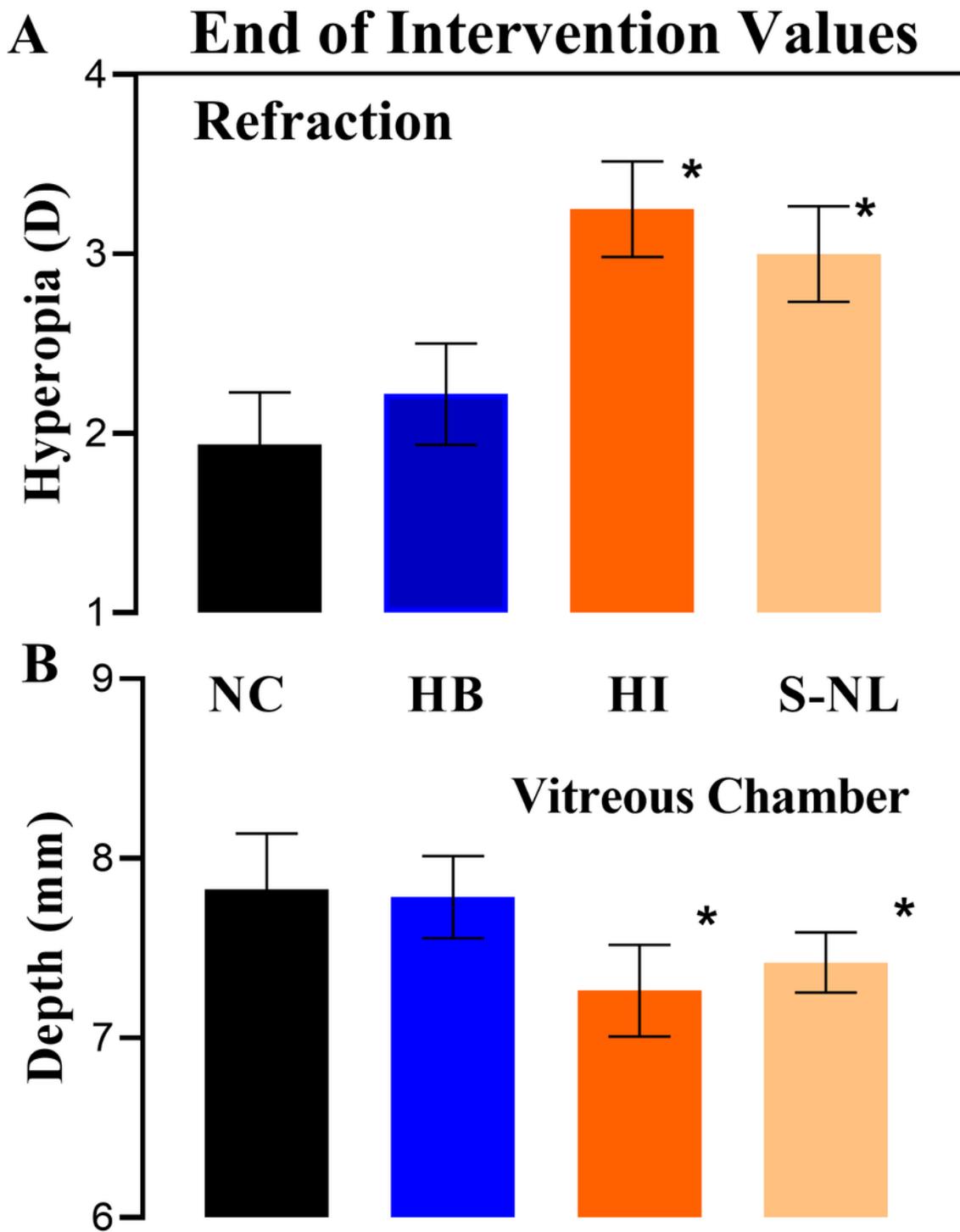


Figure 3

Refractive state and Vitreous chamber depths of the four groups at the end of the intervention. Values are the average of the right and left eyes. A: Refractive state of four groups. After 12 weeks, rabbits reared in high-blue at high illuminance light had $3.000 \pm 0.267D$ hyperopia and rabbits reared in normal blue at high illuminance light had $3.250 \pm 0.267D$ hyperopia, both significantly more hyperopia than animals raised in normal room light ($1.938 \pm 0.291D$) and high-blue at normal illuminance light ($2.219 \pm 0.281D$). B: Vitreous

chamber depths. The more hyperopic group had the shorter vitreous chambers depth. Vitreous chamber depth of animals raised in normal room light and high-blue at normal illuminance light was greater than that of animals raised in both high illuminance groups.. Asterisks indicated values with significantly difference (One-way analysis of variance).

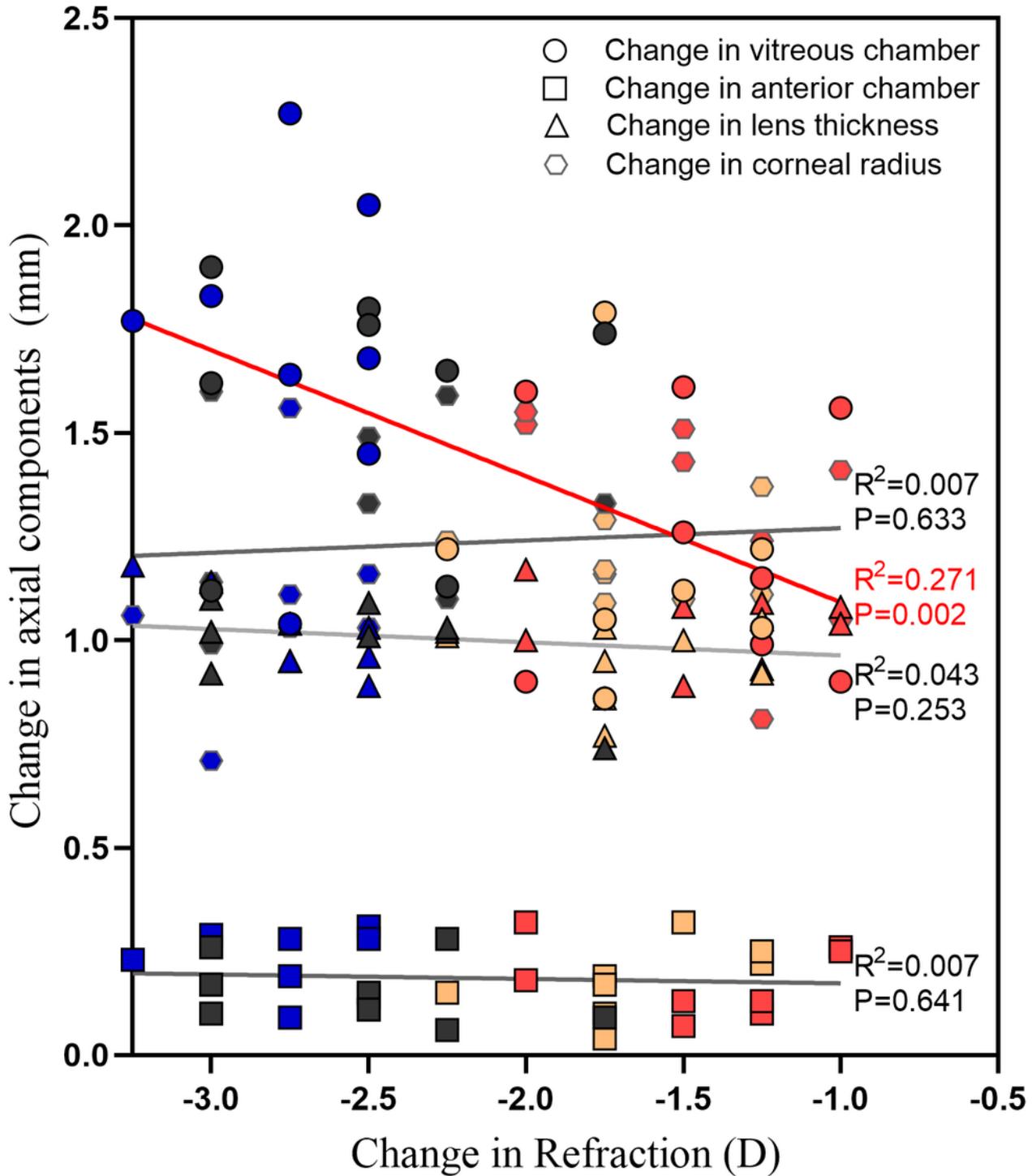


Figure 4

Association between the change in refractive state and ocular components. Values are the average of the right and left eyes. Different groups are represented by different colors. The correlation between amount of change in vitreous chamber depth and refraction was highly significant. While values of the anterior chamber depth, lens thickness and corneal radius to refraction were small.

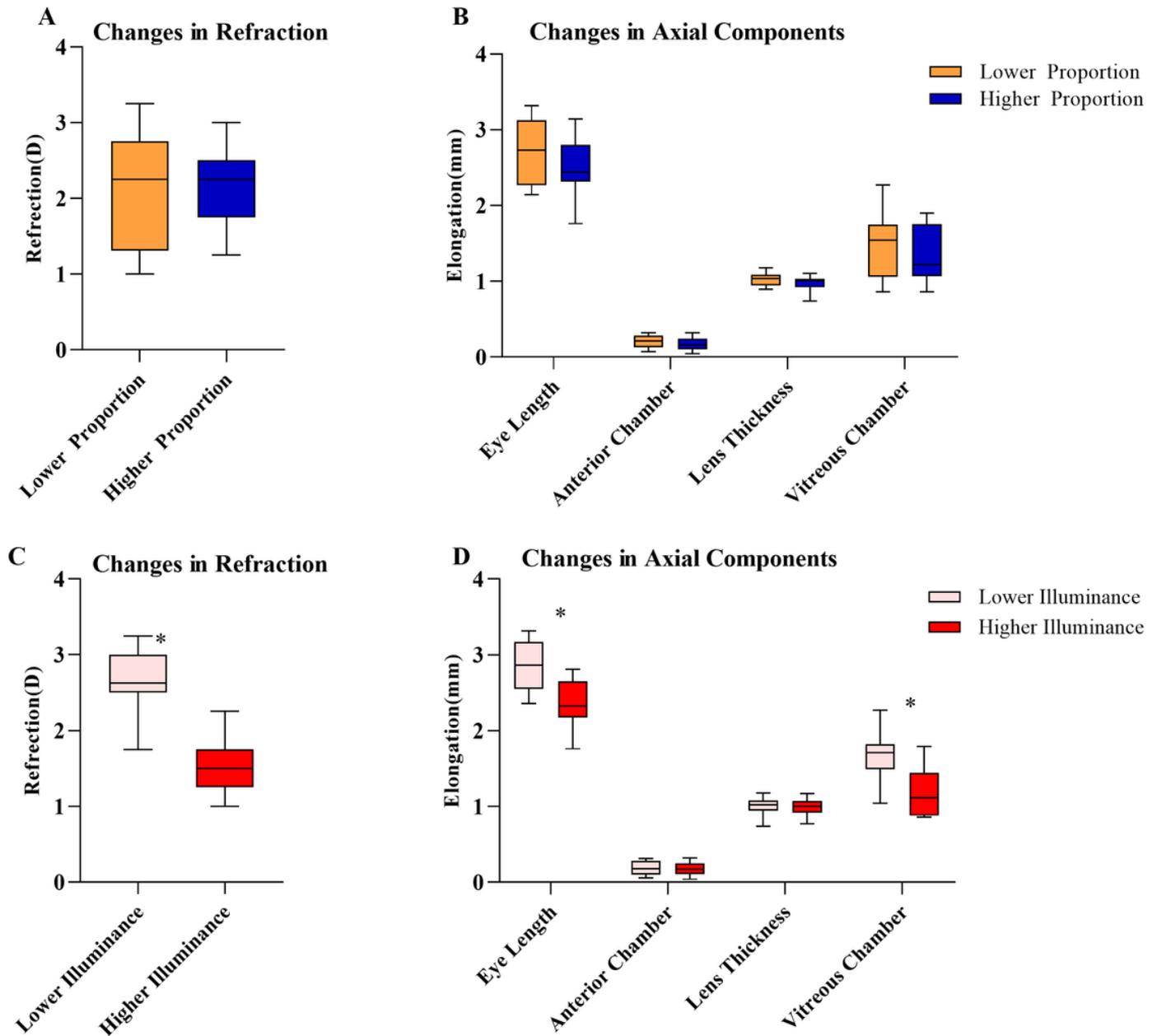


Figure 5

Changes of eye parameters grouped by short wavelengths proportion and illuminance. A and B showed there were no significant difference between the changes in refraction and axial components in low or high proportion of short wavelengths. C and D showed that high illuminance light significantly inhibited

the changes in refraction and vitreous chamber depth, and the changes were significantly lower than those in low illuminance group. * means $p < 0.05$.