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Letter to the editor **Open Access**

Low color temperature artificial lighting can slow myopia development: Long-term study using juvenile monkeys

The incidence of myopia has increased rapidly in recent decades, suggesting that environmental factors, such as light, may be an important cause. Correlated color temperature (CCT) is a commonly used index to quantify the spectral composition of light. Here, we used 32 juvenile monkeys (16 females and 16 males) and selected four kinds of light with typical but different CCTs to study the relationship between CCT and ocular axial elongation. After 365 days of observation, ocular axial elongation under low-CCT light was smaller than that under high-CCT light and this effect was robust and stable over the entire observation period. As excessive axial elongation is the main cause of juvenile myopia, these results provide a new approach for the prevention of juvenile myopia.

The incidence rate of myopia has increased rapidly in recent decades, suggesting that environmental factors, such as light, may be an important cause (Morgan et al., 2012). With the evolvement of light-emitting diode (LED) technology, the spectral composition of artificial lighting has changed significantly, with an increase in short wavelength (e.g., blue) and decrease in long wavelength (e.g., red) components (Behar-Cohen et al., 2011). Studies have also shown that different light spectra, e.g., violet (Jiang et al., 2021a; Mori et al., 2021) and red light (Hung et al., 2018; Jiang et al., 2021b; Smith et al., 2015) can affect myopia development in humans and animals. Given the importance of the light spectrum to the occurrence and development of myopia, the compositional transformation of artificial light spectra in recent years may be related to the increase in myopia incidence.

CCT, which characterizes the proportions of different wavelength components in light, is commonly used to quantify the spectral composition of a light source. High CCT usually indicates richness in short wavelength components, while low CCT indicates dominance of long wavelength components. Regarding effects on humans, most studies have explored the impact of CCT on visual comfort, cognition, and fatigue under different artificial lighting conditions (Davis & Ginthner, 1990; Keis et al., 2014; Knez, 2001; Lan et al., 2021; Lin et al., 2019; Lucas et al., 2014; Zhu et al., 2019), with the relationship between CCT and myopia development yet to be clarified. Furthermore, no direct study on the relationship between daily lighting CCT and myopia development has been reported in animals.

Due to their close evolutionary proximity, rhesus monkeys share a similar visual system as humans, with highly similar structures and functional organization. As such, we selected 32 (16 males and 16 females) juvenile rhesus macaques (age: 2.3±0.08 years) as study subjects to increase the possibility of valid extrapolation of the experimental results to humans. Before the start of the experiment, all candidate monkeys underwent an ophthalmic examination and ocular baseline data collection, including ocular axial length, keratometry radius, anterior chamber depth, and refractive status. Monkeys with cataracts or other ophthalmic diseases were excluded from the subject pool.

We selected three kinds of LED lamps with typical CCTs

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and one traditional incandescent lamp (IL, 2700 K) as experimental light sources (Figure 1A, B). The same CCT can originate from different spectra. Thus, to ensure comparability among different CCT lighting conditions, we selected a commercial LED light with a typical spectrum (Figure 1A, LED 4 000 K) and generated two other LED lights with different CCTs by varying the ratio of their long and short wavelengths (Figure 1A, LED 3 000 K and LED 5 000 K).

Using the above four lights, we quantitatively studied the relationship between light CCT and ocular axial elongation, which is an important and reliable index for myopia development (Rucker, 2019). All four lamps were panel lights of the same size, mounted on the ceiling, and hung about ~ 1 m above the top of each single monkey cage (please see Supplementary Materials for details). The intensities of each CCT light condition were 3.42±0.07 W/m^2 (IL 2700 K), 1.49±0.03 W/m^2 (LED 3000 K), 1.48±0.02 W/m^2 (LED 4000 K), and 1.50±0.02 W/m^2 (LED 5000 K).

The 32 monkeys were divided into four groups (each CCT lighting condition) of eight according to their axial lengths, so that mean axial lengths were comparable among groups (Supplementary Table S1, $F_{3,\ 60}$=0.001, P=1.00, please see Supplementary Materials for details). At the start of the experiment, the four groups were randomly assigned to four experimental rooms with pre-installed experimental lights. Each experimental room housed eight single cages arranged in two columns along each side of the room. All animals were transferred into the single cages (0.8 m×0.8 m×0.8 m) in the experimental rooms on the same day. During the experiment, illumination at the center of each cage was maintained at ~500 lx by careful measurement and adjustment at regular intervals (28–32 days). The daily light cycle was 12 h light/ 12 h dark, with lights on from 0700 h to 1900 h. The monkeys were only exposed to artificial light (IL and LED) after transfer to the indoor cages. All animals had free access to food and water and were inspected daily by experienced veterinarians.

We did not intervene with visual development in the monkeys but allowed it to develop naturally under artificial lighting to mimic the developmental process of the ocular axis in children under indoor activity conditions.

Measurements of ocular axial length, corneal curvature radius, anterior chamber depth, and spherical equivalent (SE) refractive errors were performed on the monkeys before the experiment and then regularly after the experiment started. Ocular measurements were carried out following standard protocols used in previous studies (Ivers et al., 2011; Qiao-Grider et al., 2007). All data were collected between 1200 h and 1630 h on the testing day. For details on data collection, please see Supplementary Materials.

Upon completion of ocular measurements, data from both eyes of each monkey were pooled after statistical analyses showed no significant differences between them. The change trends in ocular parameters over the experimental period were analyzed and compared using a generalized linear mixed model (GLMM) followed by Bonferroni correction for *post hoc* tests, as commonly used in the field (Lee et al., 2020; Lin & Tsai, 2016). At the end of the experiment, the last set of ocular data were analyzed by repeated measures one-way analysis of variance (ANOVA) followed by the LSD *post hoc* test, with data from both eyes controlled for within subject effects (Armstrong, 2013). All statistical analyses were performed using SPSS Statistics v27.0 (IBM Corp., USA).

After data analysis, significant differences in the increasing trend of ocular axial length were observed among the three LED groups (Figure 1C). Based on GLMM, CCT had a significant effect on ocular axial growth over the lighting period ($F_{2,\ 374}$=24.48, P<0.001). Paired comparative analysis of the GLMM further demonstrated that the ocular axial growth rate under low-CCT light (3 000 K) was smaller than that under higher CCT light (P<0.001 for 4 000 K; P<0.001 for 5 000 K). In addition, there was no significant difference in ocular axial growth rate between the two higher CCT groups (P=0.907). We also analyzed the last set of data collected to determine the differences in ocular axial growth among the three different CCT LED groups. Results demonstrated that LED lights with different CCTs had different effects on ocular axial growth in the juvenile monkeys (repeated measures ANOVA: $F_{2,\ 19}$=8.857, P=0.0104, Figure 1D). The increase in ocular axial length under artificial light with low CCT (3 000 K) (0.32±0.10 mm, mean±standard deviation (*SD*)) was significantly smaller than that under higher CCT (0.49±0.12 mm under 4 000 K, P=0.004; 0.46±0.09 mm under 5 000 K, P=0.017, *post-hoc* test, LSD). Thus, lights with higher CCT induced greater elongation (~0.15 mm) during the one-year experiment. There was no significant difference between the two higher CCT groups (Figure 1D).

We also compared the axial growth rates in different time periods of the experiment. From days 1 to 63, the axial length elongation rates were 0.058±0.037 mm/month for the LED 3 000 K group, 0.108±0.046 mm/month for the LED 4 000 K group, and 0.114±0.061 mm/month for the LED 5 000 K group. Thus, axial length elongation in the LED 3 000 K group was 53.7% and 50.9% that of the LED 4000 K and LED 5 000 K groups, respectively. From days 64–365, the axial length elongation rates were 0.019±0.011 mm/month for the LED 3 000 K group, 0.026±0.007 mm/month for the LED 4 000 K group, and 0.022±0.007 mm/month for the LED 5 000 K group. Thus, axial length elongation in the LED 3 000 K group was 73.1% and 86.4% that of the LED 4 000 K and LED 5 000 K groups, respectively. These results indicated that the inhibitory effects of low CCT light were stronger during the earlier stage of the experiment.

Collectively, compared with high-CCT lighting, low-CCT lighting slowed ocular axial growth in juvenile monkeys, and this effect was robust and stable over the entire observation period.

As LEDs have a different spectrum from that of traditional lights, we wanted to know whether the above findings were specific to LEDs. Therefore, we investigated the effects of a traditional IL with a similar CCT (2 700 K) but different spectrum as the 3 000 K LED on ocular axial development in juvenile monkeys (IL 2 700 K group). Results showed no significant differences in the increasing trend of ocular axial length between the two conditions (GLMM: $F_{1,246}$=1.709, P=0.192; Figure 1E). After one year of IL exposure, the ocular axial length increased by 0.40±0.08 mm, very close to that under 3 000 K LED exposure (repeated measures ANOVA: $F_{1,\ 12}$=2.951, P=0.112; Figure 1F). These results clearly show

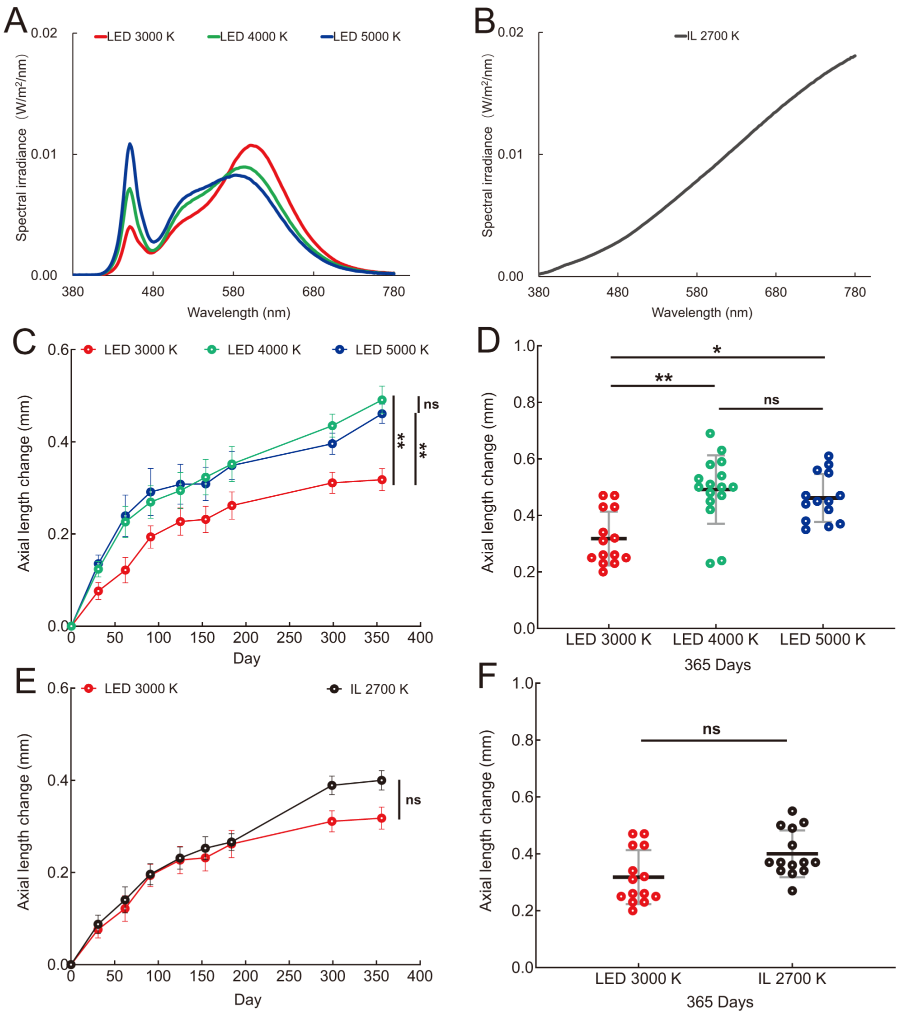

Figure 1 1Spectral power distributions of four lights and increased ocular axial length in juvenile monkeys under different CCT LED lighting during one-year experiment

A: Spectral power distributions of three LEDs with similar spectral profiles. Due to differences in ratio of blue and yellow green light bands in each light, CCT increased with increasing blue light band ratio. CCTs of three groups were 2 883±30 K, 3 803±14 K, and 4 740±13 K, respectively (measured by spectral flicking irradiance meter SFIM-400, Everfine Corporation, Hangzhou, China). B: Spectral power distributions of incandescent lamps (CCT: 2 709±74 K). C: Increased ocular axial length over time under three different LED lighting conditions. Ocular axial growth rate under artificial light with lower CCT (3 000 K; red circles) was significantly smaller than that under light with higher CCT (4 000 K, green circles; 5 000 K, blue circles). Differences in growth rates between two higher CCT conditions were not significant (ns). D: LED 3 000 K group (red circles) showed lowest increase in ocular axial length after one year compared with LED 4 000 K (green circles) and LED 5 000 K groups (blue circles). There was no significant difference in axial length between LED 4 000 K and LED 5 000 K groups. E, F: Effects of conventional incandescent lamp (2 700 K; black circles) and LED with comparable CCT (3 000 K; red circles) on development of ocular axial length in juvenile rhesus macaques. Statistical analysis showed no significant differences in axial growth trends throughout experiment (E) or in ocular axial growth between two groups at end of experiment (F). *: $P<0.05$; ** $P<0.01$. Data are presented as mean±*SEM*.

that artificial illumination with low-CCT light, whether traditional IL (2 700 K) or modern LED (3 000 K), can slow axial growth, largely independent of the light source.

In summary, compared with high-CCT light (4 000 and 5 000 K), low-CCT lights (2 700 and 3 000 K) slowed ocular axial growth in juvenile monkeys. This effect was robust and stable over the entire observation period and was largely independent of the light source. This study presents a new approach for the prevention and treatment of juvenile myopia due to excessive ocular axial elongation. This interdisciplinary study bridges an important gap in the research of lighting and ocular development and is of great importance for understanding the effect of CCT on the development of myopia. Creating a low-CCT lighting environment in places of study, such as classrooms, could be a useful method for protecting children’s eyesight. At the same time, exposure to high-CCT light may help maintain heightened mood and alertness. As beneficial effects are also related to illumination levels (Davis & Ginthner, 1990; Kruithof, 1941; Wang et al., 2017), illumination should be appropriately increased when using low-CCT lamps to maintain a high level of alertness and good emotional state (Davis & Ginthner, 1990).

Although the precise mechanism is currently unclear, recent studies have indicated that long wavelength red light can inhibit ocular axial development in rhesus monkeys and tree shrews (closest relatives of primates) (Gawne et al., 2017; Hung et al., 2018; Smith et al., 2015). In addition, exposure to low-level red light (650 nm) twice a day (3 min each time) can effectively inhibit the development of myopia in children (Jiang et al., 2021b). Low-CCT light contains a large red-light component, which may explain why it can slow axial growth.

In addition, spending more than 3 h outdoors every day can significantly reduce the incidence rate of myopia in school children (French et al., 2013; Rose et al., 2008), with sunlight likely playing a very important role. Short wavelength blue light (Rucker et al., 2015, 2018) and violet light (Jiang et al., 2021a; Mori et al., 2021; Torii et al., 2017) are also implicated in the inhibition of myopia. The relationship between these different research results and our findings is still unclear and needs to be further studied.

As our study was limited to macaques, corresponding human verification studies are required. Further research using microarray analysis of genome-wide expression patterns and single-cell sequencing is also needed to explore the underlying mechanisms. The effect of light intensity and CCT interactions on myopia is another important research direction.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

Y.Z.H., H.Y., H.L., L.B.L., J.W., Z.Z., and Y.H.Z. performed the experiments. Y.Z.H., F.F.Y., and S.H.F. analyzed the data. X.T.H, H.Y., Q.Q., C.B.H., J.P.Z., and S.X.W. designed the project. Y.Z.H, X.T.H., and H.Y. wrote the manuscript. C.B.H., S.X.W., J.P.Z., H.L., and X.T.H. revised the manuscript. All authors read and approved the final version of the manuscript.

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Ying-Zhou Hu[1,#], Hua Yang[7,8,9,#], Hao Li[1,#], Long-Bao Lv[2], Jing Wu[1], Zhu Zhu[1], Yu-Hua Zhang[1], Fang-Fang Yan[3,4], Shu-Han Fan[3,4], Shu-Xiao Wang[5,*], Jian-Ping Zhao[5,*], Qiang Qi[1,*], Chang-Bing Huang[3,4,*], Xin-Tian Hu[1,2,6,*]

[1] *Key Laboratory of Animal Models and Human Disease Mechanisms of the Chinese Academy of Sciences and Yunnan Province*, *Kunming Institute of Zoology*, *Chinese Academy of Sciences*, *Kunming*, *Yunnan* 650223, *China*

[2] *National Resource Center for Non-human Primates*, *Kunming Primate Research Center*, *and National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility)*, *Kunming Institute of Zoology*, *Chinese Academy of Sciences*, *Kunming*, *Yunnan* 650107, *China*

[3] *Key Laboratory of Behavioral Science*, *Institute of Psychology*, *Chinese Academy of Sciences*, *Beijing* 100101, *China*

[4] *Department of Psychology*, *University of Chinese Academy of Sciences*, *Beijing* 100049, *China*

[5] *China Academy of Building Research*, *Beijing* 100013, *China*

[6] *Center for Excellence in Brain Science and Intelligence Technology*, *Chinese Academy of Sciences*, *Shanghai* 200031, *China*

[7] *Institute of Semiconductors*, *Chinese Academy of Sciences*, *Beijing* 100083, *China*

[8] *Center of Materials Science and Optoelectronics Engineering*, *University of Chinese Academy of Sciences*, *Beijing* 100049, *China*

[9] *Center for the 3rd Generation Semiconductor Materials and Application*, *Beijing* 100083, *China*

[#]Authors contributed equally to this work

*Corresponding authors, E-mail: wangshuxiao417@163.com; zhaojianping@cabr.com.cn; qqi@cashq.ac.cn; huangcb@psych.ac.cn; xthu@mail.kiz.ac.cn

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