Concerning Manuscript “Bright Light Suppresses Form-Deprivation Myopia Development With Activation of Dopamine D1 Receptor Signaling in the ON Pathway in Retina”

A longitudinal randomized clinical trial has reported that increasing time of outdoor activities could reduce the incidence of myopia in school-aged children. However, the potential neurobiological signal mechanism of its protective effect remains unclear, and this has attracted researcher interest recently. We read with great interest the article by Chen et al. regarding bright light suppressing form deprivation myopia (FDM). We appreciate the rigorous methods and massive statistical analysis in their research. However, we have some concerns about the authors’ work.

First, the researchers randomly divided 262 C57BL/6 mice for exposure to normal light (NL) or bright light (BL). Then, mice in each group were assigned to differently treated subgroups (normal vision or FDM; SCH39166 or vehicle) for 4 weeks. They used another 20 C57BL/6 mice for immunostaining to probe phosphorylated tyrosine hydroxylase (p-TH) and 8 Drd1a-ttdTomato mice to double label with c-fos and neuron type-specific markers. However, these mice were only raised for 2 days. Thus, it seems like the myopia modeling and biological experiments were separated. Different durations of light exposure may result in different refractive development. Furthermore, the authors only showed us the refraction and ocular biometric outcomes of animals after 4 weeks of treatment. Related data about the animals exposed to light for 2 days were not available. Thus, it is unclear whether this short period of light exposure could make any significant difference between groups (NL versus BL). Why didn’t the researchers just obtain the retina tissues from the 4-week treatment group for analysis like other studies have? Additionally, immunofluorescence results suggest the retinal dopamine (DA) synthesis and D1R expressions of 2-day tissues may be different from that of 4-week tissue. Results from the 2-day tissues might not properly reveal the real situation of the 4-week tissues. This is because it is possible that the DA production, release, and metabolism during the experimental period of 4 weeks experienced a dynamic change with fluctuation.

Second, these authors chose 100 to 200 and 1500 to 3300 lux for NL and BL luminance, respectively. The former’s intensity was similar to other studies, but the latter was lower than commonly used. Other researchers usually set approximately 50, 500, and 10,000 to 20,000 lux for the low, standard, and high light conditions, respectively. Outdoor light intensity on a sunny day exceeds 100,000 lux, and even on a cloudy day, it would reach a typical level of 10,000 to 20,000 lux. Therefore, the BL luminance used in this study may be insufficient to mimic “high,” “elevated,” or “bright” situations. The authors clarified in the Discussion that the light intensity in this study was lower than in other studies. So why didn’t the researchers choose more bright light in the study design? As mentioned before, the short 2-day lighting condition with 1500 to 3300 lux may not be sufficient to elaborate the relative bright light effects on myopia development.

Third, the effects of D1R antagonist and SCH39166 on the refractive development of normal vision and FDM (NL or BL) were stimulating and interesting. Compared with the enhanced myopia shifts in the FDM (both NL and BL) group, SCH39166 did not alter refraction and axial length in the normal vision group (both NL and BL). A previous study found that another D1R antagonist, SCH23390, promoted excessive eye growth and myopia development naturally. It also could inhibit the protective effects of intermittent periods of clear vision on lens-induced myopia. The nonsignificant changes in axial length may be due to the optical coherence tomography insensitivity, as the authors explained. However, the possible reason for unchanged refractive error under normal vision (NL and BL) should be discussed. Why did BL have effects on FDM but no influence on normal vision compared with the corresponding NL condition? This may be because retinal DA normally oscillates in a diurnal pattern with storage levels and releases at higher rates during daytime than nighttime. Moreover, wearing an image-diffusing goggle induces myopia and reduces the daytime increase in DA metabolism. Is there any difference regarding the function of D1R receptors in the natural and FDM processes of refractive development? Does the light intensity play a different role in nature than in FDM?

The conclusion of this study described that the increased D1R activity in the ON pathway contributed to the BL suppression of FDM development in mice. We are looking forward to further studies about the D2R receptors, the balance of D1R and D2R receptors, and the contribution of the OFF pathway in myopia development. Last, it would be helpful to explore the relationship among light, DA, and myopia, which might provide deep and valuable perceptions about the etiology of myopia and protection against it.

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