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Effects of different monochromatic lights on refractive development and eye growth in guinea pigs

Rui Liu [a,b,1], Yi-Feng Qian [a,b,1], Ji C. He [c], Min Hu [d], Xing-Tao Zhou [a,b], Jin-Hui Dai [a,b], Xiao-Mei Qu [a,b], Ren-Yuan Chu [a,b,*]

[a] Department of Ophthalmology, Eye & ENT Hospital, Fudan University, 83 FengYang Road, Shanghai 200031, China
[b] Key Laboratory of Myopia, Ministry of Health PR China, 83 FengYang Road, Shanghai 200031, China
[c] New England College of Optometry, 424 Beacon Street, Boston, MA 02115, USA
[d] Department of Ophthalmology, The Second People's Hospital of Yunan Province, 176 QinNian Road, Kunming, Yunnan 650021, China

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ABSTRACT

We investigated whether different monochromatic lights with similar luminance or identical light quantum number produce predictable changes in refractive state and eye growth in early eye development in guinea pigs. In experiment I, three groups of guinea pigs (two weeks of age, $n = 18$ in each group) were reared for 12 weeks under LED lighting of 430 nm (short-wavelength light, SL), 530 nm (middle-wavelength light, ML), and broad-band light (BL). The lighting conditions were set to provide equal levels of luminance. All animals underwent refraction and biometric measurements every 2 weeks. In experiment II, the lighting conditions were set at equal quantum number and another three groups of guinea pigs were raised and tested for 20 weeks. In experiment I, compared to the BL group, refraction of the ML group was less hyperopic ($P < 0.001$) with a faster vitreous extension ($P < 0.001$), while the SL group was more hyperopic with a slower vitreous elongation ($P < 0.001$). The mean difference in refraction between the SL and ML groups reached about 4.5 D at maximum. The refractive changes and eye growth in experiment II were very similar to experiment I during the first 12 weeks, but the difference in refraction between the SL and ML groups reached 6.05 D after 20 weeks of treatment, which was greater than the longitudinal chromatic aberration (approximately 1.5 D) in the guinea pigs eyes. The results suggest that the guinea pigs' eyes overcompensated in response to narrow-band light, which resulted in an exaggerated and inaccurate refractive growth.

1. Introduction

Elimination of refractive error during postnatal development is achieved by regulating elongation of the axial length of the eye through a process called emmetropization. Visual experience has been found to play an important role in emmetropization during early life, implying that a visual-feedback mechanism is involved (Norton, 1999; Rabin et al., 1981; Schaeffel and Howland, 1991; Wildsoet, 1997). A wavelength-dependent refractive error, called longitudinal chromatic aberration (LCA), can also affect emmetropization, and this has been investigated in fish and chickens by exposing animals to monochromatic lights or chromatic simulations of hyperopic and myopic defocus (Kroger and Fernald, 1994; Kroger and Wagner, 1996; Rohrer et al., 1992; Rucker et al., 2007; Rucker and Wallman, 2008, 2009; Schaeffel and Howland, 1991; Seidemann and Schaeffel, 2002; Wildsoet et al., 1993). It was found that the difference in eye size and refraction for the animal reared under different wavelengths matches the difference in focal length determined by LCA. Accumulating evidence implies that the chromatic cues of LCA may vary with accommodation state and lead to choroidal or ocular length compensatory responses, which may guide eye growth (Rucker et al., 2007; Rucker and Kruger, 2006; Rucker and Wallman, 2008, 2009; Seidemann and Schaeffel, 2002). In human studies, it has long been known that an important relationship exists between chromatic aberration and the accommodative reflex (Fincham, 1951; Flitcroft, 1990), and it has been suggested that the luminance pathway (L + M channel) and chromatic pathway (L/M and L + M/S channels) contribute to the accommodation response and relate to refraction error

* Correspondence to: Ren-Yuan Chu, Department of Ophthalmology, Eye & ENT Hospital, Fudan University, 83 FengYang Road, Shanghai 200031, China. Tel.: +86 13641696313; fax: +86 2164377151.
E-mail address: churenyuan@hotmail.com (R.-Y. Chu).
[1] These authors contributed equally to the work present here and should therefore be regarded as equivalent authors.

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(Aggarwala et al., 1995; Kruger et al., 2005; Rucker and Kruger, 2004a, 2006). Our recent work also suggested that the prevalence of myopia and myopic refraction among individuals with red-green color vision deficiency was significantly lower than that among individuals with normal color vision (Qian et al., 2009). However, it remains unclear to what extent refractive regulation is influenced by chromatic or other cues in different species.

The guinea pig represents an interesting additional animal model to study the development of emmetropization. Long et al. found that guinea pigs raised in long-wavelength light (760 nm) developed significant myopia after 4 weeks of illumination (about 3.5 D and 2.0 D compared to the normal light or mixed light groups, respectively) (Long et al., 2009). However, only the refraction change under long-wavelength illumination was examined in that study. To complete the investigation into the effects of illumination with light of different wavelengths on emmetropization, we raised guinea pigs under two different conditions of shorter wavelength monochromatic light with spectra that matched the spectral sensitivity of the cones and examined longitudinal changes in both refraction and eye growth.

2. Materials and methods

2.1. Animals

Pigmented guinea pigs (Cavia porcellus, approximately 2 weeks of age) were obtained from the laboratory of Fudan University. The animal research was approved by the Animal Care and Ethics Committee at Eye & ENT Hospital of Fudan University, Shanghai, China. The treatment and care of the animals was conducted according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision research.

2.2. Illuminative conditions and housing

The guinea pigs were raised in specially designed enclosures covered with white paint on the interior walls to produce homogenous illumination (Fig. 1). Four to six LED light tubes (RuiGaoXiang Light & Electronic Co. Shanghai, China) were installed on the inner walls, ceiling, and bottom of the enclosures. Light directly entered the wire mesh cage (cage dimension: $80.0 \times 50.0 \times 40.0\ cm^3$, mesh size: $1.5 \times 5.0\ cm^2$) inside the enclosure. A removable transparent plastic box was set between the lights on the floor and bottom of the cage to collect the waste. These were cleaned six times per day to maintain the transillumination of light.

The spectral composition was controlled with three different types of LEDs: short-wavelength ($\lambda_{max} = 430$ nm, half-bandwidth of 20 nm), middle-wavelength ($\lambda_{max} = 530$ nm, half-bandwidth of 30 nm), and broad-band (color temperature 5000 K). Intensities were controlled by modulating the voltage of the LEDs. The irradiance in the cage was calibrated by an IL1700 Research Radiometer (International Light Inc, USA). Animals were kept under a 12/12 h light/dark cycle (light: 8 a.m.–8 p.m.) at temperatures of 22–26 °C and a relative humidity of 55–65%.

2.3. Optical and biometric measurements

All measurements were performed by two researchers who were blinded with regard to the treatment groups. Refractive status was examined by streak retinoscopy with trial lenses in a dark room. One hour before retinoscopy, one drop of 1% cyclopentolate hydrochloride (ALCON, Belgium) was topically administered every 5 min for four times to achieve a completely dilated pupil. Refractive states were recorded as the mean refractions of the horizontal and vertical meridians. A refractive accuracy of 0.25 D has been determined previously by Zhou et al. (2007).

The corneal radius of curvature was measured by keratometry (Topcon OM-4, Japan). A plus 8.0-D lens was attached onto the anterior surface of the keratometer, so the keratometry could be performed on the steep cornea of the guinea pig. A group of stainless-steel balls with diameters ranging from 5.5 to 11.0 mm were used for calibration. Three readings were recorded for each measurement. The corneal radius of curvature in the guinea pigs was then derived from the mean of three readings of the balls with known radii (Norton and McBrien, 1992; Zhou et al., 2006).

A-scan ultrasonography (11 MHz; Optikon Hiscan A/B) was used to measure the axial length of the eye, which consists of the anterior segment length (depth of the anterior chamber and the corneal thickness), thickness of the crystalline lens, and vitreous chamber length. The conducting velocity was 1540 m/s for measurement of both the anterior segment and vitreous chamber and 1645 m/s for measurement of the crystalline lens (Howlett and McFadden, 2006; Zhou et al., 2006). Corneal anesthesia was achieved by topical application of 0.4% oxybuprocaine hydrochloride (Santen, Japan) before the ultrasound measurement. The ultrasound probe was in direct contact with the cornea during the axial measurement. The tip of the probe had a red light that was used to

Fig. 1. Picture of the cages used for guinea pig growth illuminated by middle-wavelength (A), short-wavelength (B), and broad-band (C) LED tubes.