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Interactions of chromatic and lens-induced defocus during visual control of eye growth in guinea pigs (*Cavia porcellus*)

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ABSTRACT

It was recently demonstrated that chromaticity could affect eye growth and refractive development in guinea pigs but it remained unclear whether correction with spectacle lenses could balance these effects and how retinal responses change with different spectral compositions of light. Three illumination conditions were tested: blue, red and white light. Animals were raised without or with monocular spectacle lenses from three to seven weeks of age. Luminance electroretinograms (ERGs) were recorded to explore retinal responses with the different spectral compositions. In our special colony of pigmented guinea pigs, characterized by residual hyperopia, spontaneous myopia and poor emmetropization, red light induced early thinning of the choroid and relative myopia, compared to white light. Effects of red light could not be suppressed if positive spectacle lenses were worn. ERGs showed that red light failed to elicit robust retinal responses. Blue light inhibited axial eye growth, even when animals were reared with negative lenses. Intensity-matched blue and white light elicited similar a-waves but different b-waves, suggesting that the wavelength of light affects visual control of eye growth through different processing in the inner retina. We hypothesize that blue light might stimulate preferentially the ON pathway to inhibit myopia induced by negative lenses, at least in guinea pigs.

1. Introduction

Visual control of eye growth has been extensively investigated and abundant evidence shows that the axial eye growth and refractive state are altered not only by visual deprivation and lenses rearing but also by the alteration of specific visual cues, such as spatial frequency composition (Schmid & Wildsoet, 1997), ambient illuminance (Ashby & Schaeffel, 2010), and spectral composition of light (Kroger & Wagner, 1996; Rucker & Wallman, 2008; Seidemann & Schaeffel, 2002). As a result of the longitudinal chromatic aberration (LCA), light with shorter wavelengths is focused more anteriorly compared to light with longer wavelengths. As a consequence, eyes of African cichlid fishes that were raised under red light were larger than those raised under blue light (Kroger & Wagner, 1996); in chicks, the eyes compensated for chromatic defocus imposed by LCA (Rucker & Wallman, 2009) and among mammals, guinea pigs were found to become more myopic when they were reared under red (769 nm) or green light (530 nm), compared to those raised under white light or blue light (430 nm). However, illuminance was not controlled in those studies (Liu et al., 2011; Long, Chen, & Chu, 2009).

Kroger and Binder (2000) proposed that children could become less myopic if they read in blue light or from paper that reflects preferentially at short wavelengths. However, a more recent study (Graef & Schaeffel, 2012) found that over-accommodation occurs in deep blue light below 430 nm. Furthermore, defocus imposed by the LCA affects accommodation. At shorter wavelengths, the accommodation response is reduced compared to longer wavelengths (Kruger et al., 1995; Seidemann & Schaeffel, 2002).

A striking observation by Rucker and Wallman (2008) in chicks was that cones sensitive to short wavelengths guide lenses compensation preferentially by modulating scleral growth, whereas cones sensitive to long wavelengths modulate choroidal thickness. That different fundal tissues are targets for emmetropization was an unexpected observation. But there is still little known as to how LCA affects the underlying retinal processing.

Beyond LCA and accommodation, an interaction has been reported between the ON and OFF retinal responses and refractive compensation in chicks (Crewther & Crewther, 2002). It is possible

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that ON and OFF channels are differentially affected by the spectral composition of light. Under photopic conditions, the b-wave is dominated by the ON pathway (Stockton & Slaughter, 1989). Therefore, we have recorded the luminance electroretinogram (L-ERG) b-wave to explore the possible mechanisms under monochromatic light stimulation.

Until now, there have been no experiments in guinea pigs to describe eye growth in blue light above 430 nm. In the current study, we selected a blue light source, LEDs with a narrow emission spectrum (λ_{max} = 470 ± 5 nm), and compared it to the effects of red light (λ_{max} = 600 ± 5 nm). Furthermore, a white light source was used, without or with monocular spectacle lenses treatment. Although guinea pig retinas contain rods with peak sensitivity around 494 nm and two classes of cones with peak sensitivities at 429 nm and 529 nm (Jacobs & Deegan, 1994), we used also red light to learn whether the retina can still respond to LCA using the broad band absorption of their 529 nm cone.

Different from chickens which have powerful accommodation, guinea pigs (at least in our colony) do not seem to accommodate at all since they never changed their refractions when accommodation targets, like a pencil, were presented in front of their eyes (Jiang et al., 2009). Also when the experimentator moved a fellow animal towards them, they never accommodated. Accommodation was monitored by eccentric infrared photoretinoscopy, as it was previously done in the chicken (Schaeffel, Howland, & Farkas, 1986). Frozen sections of the eyes show that the crystalline lens is thick and large (Howlett & McFadden, 2007; Fig. 7), making it unlikely that their small ciliary muscle could significantly deform or move it.

Guinea pigs, like most non-primate mammaliam species, have dichromatic color vision (Parry & Bowmaker, 2002). The current study was undertaken to provide a better understanding of the effects of LCA on eye growth in a dichromatic mammalian model.

2. Methods

2.1. Animals

Three-week-old pigmented guinea pigs (*Cavia porcellus*, the English short hair stock, n = 81) were involved in this study. Animals were maintained in temperature-controlled rooms in the animal facilities at the Wenzhou Medical School. All guinea pigs had free access to standard food and water, and fresh vegetables were provided twice a day. The procedures used were approved by the Institutional Animal Care and Ethics Committee at Wenzhou Medical College, Wenzhou, China, and were in agreement with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

2.2. Experimental design

All guinea pigs were kept in cages measuring 65 × 45 × 23 cm. Each cage accomodated up to five animals. Daylight was simulated by fluorescent light (36 W, PHILIPS lifemax TLD, Shenzhen, China) on the ceiling. Lamps were operating at a 12–12-h light–dark cycle. Illuminance at cage floor was about 300 lux. Experimental groups were raised under illumination by colored LEDs (Dianfei Ltd., Shenzhen, China), fixed on the inside top of the cages. The cages were covered inside by silvered paper to ensure homogenous illumination.

2.2.1. Experiment A

From three weeks of age, guinea pigs were raised for four weeks with unobstructed vision under either red light (RL, λ_{max} = 600 ± 5 nm; n = 13) or blue light (BL, λ_{max} = 470 ± 5 nm; n = 13) using LEDs (Dianfei Ltd., Shenzhen, China), or white light (WL, fluorescent lamp, color temperature 6500 K, n = 14) as a control. The illuminance at cage level was 50 (human) lux under BL, 300 (human) lux under RL, and 350 (human) lux under WL on the cage floor respectively. Refractive error, lens thickness, vitreous chamber depth, and axial length were measured on days 0, 6, 14, and 28, and choroid thickness was measured on days 0, 1, 2, 4, 6, 10, 14, and 28 of treatment.

2.2.2. Experiment B

Three-week-old guinea pigs were monocularly treated with either both kind of lenses (+4.0 D or −4.0 D) under RL (+4.0 D lenses: n = 10; −4.0 D lenses: n = 11) or minus lenseses under BL (−4.0 D, n = 7) for 4 weeks. No positive lenses were tested in blue light because calculations showed that the focal plane would then be even further in front of the retina than with blue light alone. Guinea pigs with plus lenses (+4.0 D, n = 7) or minus lenses (−4.0 D, n = 6) under white ambient light served as control. Lens-rearing was continued for four weeks. Lenses were attached via a facemask with two hole openings for the eyes as described earlier (Lu et al., 2009). In short, lenses, made of polymethylmethacrylate were attached to the right side hole of the facemask, with the distance from the cornea to the lenses apex of about 3 mm. The left eye served as control. Lenses were cleaned daily. Measurements of the ocular parameters were performed one day before the lens-wearing began, and on days 14 and 28 while wearing the lenses.

2.3. Calculations of imposed defocus by LCA and by the spectacle lenses, including the effects of the small eye artifact

Based on the dispersion of the ocular media and the schematic eye model of the guinea pig (Howlett & McFadden, 2007; detailed in Table 1a), ZEMAX (EE version February 3, 2005, ZEMAX Development Corporation) was used to evaluate the paraxial defocus of guinea pig eyes at different wavelengths. No adjustments were made for the spectral sensitivity function. Calculated refractions were normalized to the refraction at 530 nm. The distance in micrometers between the photoreceptor layer and the focal plane with different spectacle lenses in front of the eye was also calculated.

Table 1
(a) Detailed parameters of the schematic eye and (b) detailed parameters of the attached lenses.

Parameters of the guinea pig schematic eye	
Cornea front surface radii	3.28 mm
Cornea thickness	0.25 mm
Cornea refractive index	1.376
Cornea back surface radii	3.28 mm
Anterior chamber depth	0.90 mm
Aqueous humor refractive index	1.335
Lens front surface radii	2.94 mm
Lens thickness	3.50 mm
Lens refractive index	1.539
Lens back surface radii	−2.18 mm
Vitreous refractive index	1.335
Vitreous chamber depth	3.15 mm
Retina refractive index	1.357
Retina thickness	0.129 mm
Parameters of attached lenses	
−4.0 D lens front surface radii	18.60 mm
−4.0 D lens thickness	0.18 mm
−4.0 D lens back surface radii	16.00 mm
+4.0 D lens front surface radii	10.98 mm
+4.0 D lens thickness	0.30 mm
+4.0 D lens back surface radii	12.00 mm
The lens-to corneal vertex distance	3 mm
Material of lens	PMMA