

# Constant light rearing disrupts compensation to imposed- but not induced-hyperopia and facilitates compensation to imposed myopia in chicks

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## Abstract

**Purpose:** While rearing chicks in constant light (CL) inhibits anterior segment growth, these conditions also induce excessive enlargement of the vitreous chamber. The mechanisms underlying these effects are poorly understood although it has been speculated that the enlarged vitreous chambers are a product of emmetropization, a compensatory response to the altered anterior segments. We examined the ability of eyes to compensate to defocusing lenses in CL as a direct test of their ability to emmetropize. We also studied recovery responses, i.e. from lens-induced changes in CL as well as CL-induced changes alone or combined with lens-induced changes in eyes returned to normal diurnal lighting (NL).

**Methods:** Hatching White-Leghorn chicks were reared in either CL or NL (control) lighting conditions ( $n = 36$ ) for 2 weeks, with lenses of either +10 or -10 D power fitted to one eye of all chicks at the beginning of the second week. The lenses were removed at the end of the same week, at which time some CL chicks ( $n = 14$ ) were shifted to NL, the rest of the chicks remaining in their respective original lighting conditions. Retinoscopy, IR photo-keratometry and high-frequency A-scan ultrasonography were used to track refractions, corneal radii of curvature and ocular axial dimensions, respectively; data were collected on experimental days 0, 7, 9, 14 and 21.

**Results:** Under CL, eyes showed near normal, albeit slightly exaggerated responses to +10 D lenses while the response to -10 D lenses was disrupted. With +10 D lenses, lens-wearing eyes became more hyperopic (RE), and had shorter vitreous chambers (VC) and optical axial lengths (OL) relative to their fellows by the end of the lens period [RE:  $+10.5 \pm 1.5$  D, CL,  $+8.25 \pm 2.5$  D, NL; VC:  $-0.363 \pm 0.129$  mm, CL;  $-0.306 \pm 0.110$  mm, NL; OL:  $-0.493 \pm 0.115$  mm, CL,  $-0.379 \pm 0.106$  mm, NL (mean interocular difference  $\pm$  SD)]. With -10 D lenses, the NL group showed a myopic shift in RE and increased elongation of both VC depth and OL (RE:  $-10.75 \pm 2.0$  D; VC depth:  $0.554 \pm 0.097$  mm; OL:  $0.746 \pm 0.166$  mm), while the CL group showed a small hyperopic shift in RE ( $+4.0 \pm 6.0$  D). Nonetheless, CL eyes were able to recover from lens-induced hyperopia, whether they were left in CL or returned to NL. One week of exposure to NL was sufficient to reverse the effects of 2 weeks of CL on anterior and vitreous chamber dimensions.

**Conclusion:** CL impairs emmetropization. Specifically, it disrupts compensation to lens-imposed hyperopia but not imposed myopia. However, CL eyes are able to recover from lens-induced hyperopia, suggesting that the mechanisms underlying the compensatory responses to defocusing lenses are different from those involved in recovery responses. The ocular growth effects of CL on young eyes are reversible under NL.

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## 1. Introduction

The epidemic levels of myopia in some Asian countries (Au Eong, Tay, & Lim, 1993), the potentially sight-threatening complications associated with myopia (Curtin, 1985) and the possibility that myopia might occur as a product of

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emmetropization have stimulated renewed interest in the mechanisms underlying the latter.

The term, emmetropization, describes the process by which neonatal refractive errors are corrected through adjustments to eye growth. Although emmetropization has a passive component, an optical artifact of normal eye growth (Edwards, 1992; Hofstetter, 1969; Wallman, Gottlieb, Rajaram, & Fugate-Wentzek, 1987; Wildsoet, 1997), animal studies have provided convincing evidence for an active component as well. For example, when lenses are used to impose focusing errors on the eyes of young animals, compensatory growth changes involving both the choroid and sclera follow. Chicks, the most widely used model for this research, are able to compensate for a wide range of imposed myopia and hyperopia (Irving, Sivak, & Callender, 1992; Nevin, Schmid, & Wildsoet, 1998; Schaeffel, Glasser, & Howland, 1988; Wildsoet & Wallman, 1995). The bidirectional nature of these responses and their rapid onset points to an active regulatory mechanism; that young chicks are able to recover from experimentally induced refractive errors, e.g. seen when lenses are removed after compensation has occurred, has been interpreted as further evidence for active emmetropization (Irving, Callender, & Sivak, 1995; Wildsoet & Wallman, 1995).

Apart from optical defocus, the light cycle used in rearing also can influence early eye growth. Of relevance to the study reported here is the observation in chicks that constant light (CL) inhibits anterior segment growth while enhancing vitreous chamber elongation (Jensen & Matson, 1957; Kinnear, Lauber, & Boyd, 1974; Li, Troilo, Glasser, & Howland, 1995), although there are strain-related differences with the Cornell strain of White-Leghorn showing exaggerated anterior segment changes (Li et al., 1995; Stone, Lin, Desai, & Capehart, 1995; Troilo, Li, et al., 1995). These ocular effects of CL are reversible, provided chicks are returned to diurnal lighting cycle (NL) at a sufficiently early age (Li, Wahl, & Howland, 2002; Li, Wahl, & Howland, 2004).

Understanding the influence of CL rearing on emmetropization in the chick may go part way to resolving the on-going debate over the possible causal relationship between altered light exposure and myopia in humans. For example, there is a study linking exposure to light at night in infancy and childhood myopia (Quinn, Shin, Maguire, & Stone, 1999), and another linking myopia in college students with reduced hours of sleep (darkness) (Loman et al., 2002). However, other related studies have questioned this link (Guggenheim, Hill, & Yam, 2003; Gwiazda, Ong, Held, & Thorn, 2000; Saw et al., 2001; Saw et al., 2002; Zadnik et al., 2000).

In relation to the effects of CL on emmetropization in chicks, there are two studies of direct relevance although their findings are inconclusive. One study by Bartmann, Schaeffel, Hagel, and Zrenner (1994) reports normal compensation to both plus and minus lenses, although it is not possible to rule out sign-related changes in these responses due to the use of bilateral lenses of opposite sign.

A second study by Guo, Sivak, Callender, and Herbert (1996) avoided this problem by using monocular lenses fitted to hatchling chicks. However, while only partial compensation to both minus and plus lenses was observed, these data are confounded by the lack of a pre-lens CL adaptation period as included in the Bartmann and Schaeffel study. Light is known to be an important Zeitgeber for biological rhythms, among them, ocular growth rhythms that are known to be perturbed by CL (Weiss & Schaeffel, 1993). Because other experimental manipulations that alter ocular growth also appear to alter ocular growth rhythms (Nickla, Wildsoet, & Wallman, 1998; Schmid, Papastergiou, Riva, Stone, & Laties, 1997; Weiss & Schaeffel, 1993), it is important that such rhythms be allowed time to first stabilize (free-run) under CL in testing the eye's ability to actively emmetropize under CL.

In the study reported here, we re-examined the effect of CL on active emmetropization. We asked three questions: (1) is lens compensation in CL similar to that in NL, i.e. is the emmetropization process altered in chicks reared in CL, (2) can chicks reared in CL recover from lens-induced changes while still in CL and/or when returned in NL, and (3) does CL affect choroidal thickness and/or other components that contribute to eye length and if so, how reversible are these effects in chicks returned to NL. Thus we studied the ability of eyes to compensate for defocus imposed with spectacle lenses and also followed both lens-treated eyes and their fellows after lenses were removed, to see if they were able to recover from induced changes, in either CL, in relation to the lens effects, or in NL, in relation to lens- and CL-effects. The high resolution offered by high frequency A-scan ultrasonography (approximately 10  $\mu\text{m}$ ) (Nickla, Wildsoet, & Wallman, 1997), also allowed us to characterize the effects of CL on ocular dimensions more completely than in already published studies, which employed lower resolution methods.

Aspects of this work have been published in abstract form (Padmanabhan & Wildsoet, 2004).

## 2. Methods

### 2.1. Animals and treatments

A total of 36 four- to six-day-old White-Leghorn chicks obtained from a commercial hatchery (Privett Hatchery, New Mexico) were used in this study. Food and water were available ad libitum. The chicks were allocated to one of three groups, based on the lighting conditions to which they were exposed over the course of the study. On arrival, chicks were allocated to either normal diurnal lighting conditions and open cages (NL; 12 h light/2 h dark cycle) or constant light (CL) and special sound- and light-proof chambers. Lighting levels in the chambers were similar to the levels in open cages, ranging from 331 to 385 lux. Chicks remained in their allocated lighting environment for a 7-day period before the start of the lens-wearing period that lasted another 7 days (days 7–14). The pre-lens period of 7 days allowed all light-dependent body rhythms to become either entrained (NL) or become free-running (CL). At the end of the lens-wearing period, the CL chicks either remained in CL (rCL) or were placed in diurnal lighting conditions (rNL) where they remained for another 7 days. In total, there were three different rearing conditions: NLRNL (normal lighting throughout), CLrCL (constant lighting throughout) and

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