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BRIGHT COMPUTER MONITORS SLOW EYE GROWTH AND THICKEN CHOROIDS IN CHICKENS

A thesis presented to the graduate faculty of
New England College of Optometry in partial fulfillment of the requirements
for the degree of Master of Science

Matthew Barnes

January, 2022

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This manuscript has been read and accepted by the
Thesis Committee in satisfaction of the
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Abstract:

BRIGHT COMPUTER MONITORS SLOW EYE GROWTH AND THICKEN CHOROIDS IN CHICKENS

Matthew Barnes

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Purpose

The aim of this study is to understand how light from computer displays influences eye growth, and to determine whether displays can protect against myopia development. Previous experiments have shown that blue-rich, white LED light conditions reduce axial growth in chicks and red-rich LED light conditions promoted choroidal thickening. In this experiment, computer displays were tuned closely to the brightness and color levels of LED light to establish whether a similar effect on eye growth was achievable. Conventional computer displays are typically dim, particularly in the blue spectral range, which makes matching to LED light difficult, so extra bright displays were also tested.

Methods

135 White leghorn chicks were hatched in the lab and at age 19 days were exposed for 3 days (8am- 8pm) to one of two flickering light (0.2 Hz) conditions that were colored white/black (LUM) or blue/yellow (B/Y) (alternating, counter-phase). These conditions were presented on one of five sources. Three sources were at a low intensity of 120 lux including 1) a conventional monitor (Mon), 2) LED lights cone-matched to the monitor (CLED) and 3) blue rich LED lights (LED). The other two sources were at a high intensity of 550 lux on 4) a

high brightness monitor (HMon) and 5) LED matched to the monitor (HLED). Ocular components were measured using a Lenstar biometer (Lenstar LS 900) on Day 0 and Day 3. ANOVAs were performed on each data set followed by Tukey's HSD tests if the ANOVA showed significance ($p<0.05$).

Results

Light source and illuminance affected axial elongation in the LUM and B/Y conditions ($F_{(4,133)} = 3.71$; $p < 0.01$). The choroid was only affected in the LUM condition ($F_{(4,133)} = 4.499$; $p < 0.01$).

White/black (LUM): At 120 lux, axial elongation increased with both blue deficient Mon and CLED sources compared to the blue-rich LED condition ($p < 0.001$, $p < 0.01$). The 120 lux Mon source increased axial elongation compared to the 550 lux HMon source ($p = 0.028$). Choroid thickness increased less with blue-rich LED and HLED, and more with Mon and HMon. LED and the HLED both had less choroidal thickening compared to all other conditions (Mon ($p = 0.019$, $p = 0.001$); CLED ($p = 0.041$, $p = 0.022$); HMon ($p = 0.005$, $p = 0.009$).

Blue/yellow (B/Y): Axial elongation decreased with blue rich HMon ($p < 0.05$) and HLED ($p < 0.01$) compared to blue deficient CLED.

Conclusions

Low intensity computer monitors with a dim blue light and bright red light component induce significant axial elongation with significant choroid thickening. High intensity monitors, with a bright blue light and bright red light component, slow axial

elongation with significant choroidal thickening. Novel computer monitor-based therapies that protect against myopia development may be viable with high brightness, high blue monitors.

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Chapter 1: General Introduction

1.0 Prevalence of Myopia

Approximately one in five American adults has myopia (SE < -0.5 D) as reported by several studies across the United States (Katz et al., 1997; Tarczy-Hornoch et al., 2006; Wang et al., 1994). This figure increases dramatically in parts of Asia to approximately 95% in some parts of the population (Sun et al., 2012), and incidence rates are said to be increasing in both Asia and the US (Holden et al., 2016). In 2009, the WHO estimated the worldwide productivity loss caused by refractive error to be 202 billion US dollars per year (Smith et al., 2009). On top of the economic factors, there are significant health risks associated with myopia. Individuals with myopia are at a much higher risk for retinopathy and glaucoma, which can ultimately lead to permanent vision loss. For example, a study of 3654 patients

aged 49-94 in Australia showed that myopic patients with refractions of at least -1.00 D were 2.3 times more likely to have glaucoma than those who were not myopic (Mitchell et al., 1999). Thus, the impact of myopia on global health and the economy is significant, and preventative measures are key to stopping the physical and financial damage caused by myopia.

1.1. Preventative Measures in Humans

One of the methods for slowing myopia progression in humans includes prescription of Atropine eye drops. A study was conducted in which 400 children, ages 6-12, were given atropine in varying concentrations: low (0.01%), medium (0.5%) and high (1%). The results showed that control patients progressed -1.20 D over a year, while patients with 1% atropine progressed only -0.29 D over the same period (Chia et al., 2012). After the initial year of treatment, the progression of myopia was recorded over the following two years. No atropine was given to patients during year two, and if refractive error progressed more than - 0.5 D over the year, a maintenance dose of 0.01% atropine was prescribed during year three. The 0.01% group progressed a total of -1.38 D, whereas the 0.5% group progressed -1.98 D over the same time. Patients prescribed 0.01% Atropine presented with fewer side effects. The 0.01% Atropine patients had smaller pupils, greater accommodative ability, better near visual acuity, and slower progression of myopia relative to all other doses (Chia et al., 2016).

Other methods of myopia control include the use of Ortho-K contact lenses. Ortho-K acts by reshaping the central cornea with rigid lenses at night, which results in clear central vision during the day. Ortho-K has been shown to significantly slow the progression of myopia, as shown by a 12-year retrospective study of 66 Ortho-K patients, ages 7-16. The control group of 36 patients changed by about -0.37 D to -0.52 D per year, whereas the experimental group progressed -0.17 D to -0.32 D per year (Lee et al., 2017). This method is convenient for patients who do not want to wear eyeglasses, but it requires custom fitting, which can lead to higher costs.

Other studies have used multifocal lenses (Aller et al., 2016; Anstice and Phillips, 2011; Sankaridurg et al., 2011; Walline et al., 2013). One study prescribed multifocal contacts with +2.00 D addition to 40 children ages 8-11 over two years. Subjects were included in the study if the spherical component of their refraction was between -1.00 and -6.00 and the cylinder less than -1.00 D. The 40 control patients with single vision soft contacts on average progressed -1.03 D over two years, while the experimental patients progressed -0.51 D on average over the same time period (Walline et al., 2013). These methods are all options for slowing progression of myopia, but they are costly and often require excellent compliance from young patients and their parents, which can be challenging.

In these cases, myopia can be managed with some caveats, and a low cost, low effort method of myopia control would allow for a much broader patient population to be reached,

earlier in the development of myopia. If the treatment is effective, it could be used as a preventative measure against myopia development.

Research into methods of preventing or slowing myopia development is typically performed in the laboratory on animal models of myopia such as the chick, tree shrew and guinea pig. Advantages of using the chick as an experimental model include their large eyes, rapid growth, high sensitivity to retinal image quality and focus, excellent optics, friendliness, and inexpensiveness (Schaeffel and Feldkaemper, 2015; Wisely et al., 2017). Experiments can be performed on the scale of a few days and return significant results that may prove useful for future human studies.

1.2. Full Time Defocus Studies

Emmetropization of the chick eye is highly adaptive, and a wide variety of stimuli can accelerate or inhibit growth of the eye. Previous studies have shown that positive and negative lens stimuli affect eye growth in a temporally sensitive manner (Irving et al., 1992; Schmid and Wildsoet, 1996; Zhu and Wallman, 2009). A study by Schmid and Wildsoet examined the effects of lens wear on refractive error and eye growth in chicks and found significant differences in the effects of +10.00 D and -10.00 D lenses. Chicks that wore the +10.00 D lens uninterrupted for a 12-hour day had an average refraction of +7.00, while chicks that wore the -10.00 lens in otherwise similar conditions had an average refraction of -8.4 D. Lens wear can induce rapid changes in refraction, as indicated by this study(Schmid

and Wildsoet, 1996). Mammals do not adapt as rapidly or as strongly to lens stimuli, but similar effects are seen in both marmosets, tree shrews and guinea pigs (Howlett and McFadden, 2009; Metlapally and McBrien, 2008).

Tree shrews are mammals that have been extensively studied in the lens wear paradigm. A 2008 study by Metlapally and McBrien compared the eye growth during uninterrupted lens wear of 4-6 shrews with sequentially more powerful positive lenses, from +2.00 D to +9.50 D, attached every one to two weeks, against shrews wearing plano lenses for 8 weeks. The shrews wore goggles with replaceable lenses, and were kept in a cage for 12/12 hour light dark cycles. The shrews with sequentially increasing positive lenses were refracted at +10.90 D, while the plano shrews were refracted at +5.3 D. If the shrews were given the +9.50 D lens for the whole 8 weeks, hyperopia was not induced because the eyes could not detect the sign of blur due to its magnitude (Metlapally and McBrien, 2008). The results may indicate that tree shrews are less sensitive to myopic blur than chicks, which is an important difference to note in understanding how results from our experiments might translate to the human model.

Spectacle lens compensation was also observed in guinea pigs (Howlett and McFadden, 2009). Constant negative lens wear induced myopia while positive lenses induced hyperopia. Full compensation took longer for negative lenses than positive lenses. A +4.00 D lens took 5 days for the eyes to adapt, while a -4.00 D lens took 10 days to adapt. These experiments focused on light manipulation by lenses and again highlight the differences between animal species.

1.3. Interrupted Defocus Studies

Interrupted lens studies are important for understanding the temporal sensitivity of chicks in environments with different signs of blur. Negative and positive lenses cause opposing axial and choroidal changes in chicks. Given a controlled timeframe, the magnitude of those changes is not equal, and this feature can be used to control refraction. Experiments that have used periods of interrupted lens wear have shown significant results in many animal models.

After Schmid and Wildsoet (1996) completed their uninterrupted lens study, a follow up experiment presented chicks with 3 hours of normal vision and 9 hours of lens wear. The +10.00 D lens birds had an average refraction of +7.4 D, and birds wearing the -10.00 D lens had an average refraction of -0.8 D (Schmid and Wildsoet, 1996). These results indicate that the positive lens stimuli had more robust effects than negative lens stimuli. In addition, it was noted that significant changes in eye length, choroidal thickness, and corneal curvature can occur within hours. This study theorizes the chick eye to be evolutionarily adapted to positive defocus, which ensures eyes do not grow too long.

Another study in chicks investigated the effect of brief periods of alternating myopic and hyperopic defocus on eye growth (Winawer et al., 2005). 7-day-old chicks with a +6 D lens on one eye and an occluder on the other were placed in a drum for three days with alternating myopic and hyperopic defocus stimuli. To create the defocused stimuli, the drum

had two walls which were alternately illuminated, and the far point was positioned between the two walls using the +6D lens: a semi-transparent inner wall inside the far point created hyperopic defocus and the outer wall outside the far point created myopic defocus. When the stimuli were presented for equal durations, the chicks developed hyperopia, indicating that myopic defocus had a stronger effect. To have no net effect, it was found that the inner wall illumination must be presented for 2.5 seconds for every 0.5 seconds of outer wall illumination. The rate of alternation also affected the results. It was noted that with 25 minutes and 5 minutes of the respective stimuli (inner wall/outer wall), the chicks became 2.4 D more hyperopic. This inequality in weighting of the responses indicates that the emmetropization response is not the equally weighted sum of the two defocus stimuli (Winawer et al., 2005).

Amedo and Norton (2012) performed an interrupted lens wear study on tree shrews. Juvenile shrews were placed in a brooder with a 14h/10h light/dark cycle and had normal visual stimulus for 16 days. A -5 D lens was then placed on one eye for 11 days, and for the next 35 days the lens was replaced by a -2 D lens, Plano lens, +2 D lens, or the lenses were removed for two hours each day. The control group had the lens removed completely after 11 days, and their eyes emmetropized after an average of 20 days after removing the lens. By the end of recovery, the treated eyes were measured relative to the untreated eye. The Plano group was -1.1 D, the -2 D group was -2.5 D, the +2 D group was +1 D, and the 2 hour interrupted group was -0.4 D. Continuing to use the -5 D lens and removing it for two hours

each day allowed for the most significant recovery relative to the control group (Amedo and Norton, 2012).

Leotta et al. used an interrupted lens wear paradigm. -5 D lenses were put on guinea pigs at age 4 or 5 days and kept on for 7 days, animals were kept in the same cage as the mother and littermates. Lenses were kept in place overnight, and during the 12-hour day the lens was removed for as little as 5 minutes or as much as 9 hours of each day. At 30 minutes of free vision per day, axial length was significantly shorter relative to full-time lens wear, and 9 hours of free vision per day completely emmetropized the eye (Leotta et al., 2013).

Across the above studies, a variety of vertebrates had opposing and rapid responses to different signs of defocus, and emmetropizing factors or hyperopic stimuli have more robust effects on refraction, axial length, and choroid thickness. These models of lens wear are an important step towards understanding the mechanisms for myopia development, and they are the foundation of the current experiment. As discussed below, light stimuli (without the use of lenses) can have emmetropizing or myopia inducing effects, and it is our hypothesis that light stimuli will affect eye growth similar to the lens studies.

1.4. Role of Spatial Contrast

Spatial contrast is also an important factor in emmetropization (Diether and Wildsoet, 2005; Schmid et al., 2006). In a form-deprivation study (Schmid and Wildsoet, 1997), one-day-old chicks had monocular occlusion with white diffusers for 10 days. Chicks were

given 20 minutes of interrupted vision to view targets of different contrast. They were either presented with normal vision, or stimuli at contrast levels of 9%, 38%, 72%, or a mix of all three. All the test conditions equally reduced form-deprivation myopia relative to normal cage lighting (Schmid and Wildsoe, 1997). The conclusion was that contrasts between 9% and 72% prevented form-deprivation myopia equally. A subsequent study by Schmid et al examined the role of contrast in more detail. 8-day-old chicks had a cone-shaped imaging system attached monocularly to the chicks' right eyes. A target was placed at 3.3 cm from the eye, and a +30 D lens focused the image on the retina. The image had a spatial frequency of 1.6 c/deg, and the contrast was varied in each trial. 11 different contrast levels were used from 0% to 95%, and measurements were taken after 4.5 days of stimulus wear. It was found that contrast levels 4.2% and below produced relative myopia, between 4.2% and 47.5% produced moderate myopia, and 47.5% or above produced isometropia.

In all our experiments, contrast was set at maximum (for our lighting systems) to reduce any increase in eye growth due to low contrast. In future studies, contrast may be manipulated to induce myopia.

1.5. Role of Temporal Contrast

Different temporal waveforms, sinusoidal and non-sinusoidal, can have different effects on emmetropization. Square-wave temporal modulation contains other frequencies that stimulate the retina at higher frequencies than the fundamental. Square waves and pulsed

stimuli contain a broad range of temporal frequency information, and this extra information is difficult to take into account. Sinusoidally modulated stimuli do not have these issues; very little noise is present, so the sinusoidal flickering induces a linear retinal response (Shapley, 2009) for both horizontal cells (Tranchina et al., 1981) and midget ganglion cells, but parasol cells show non-linear responses (Shapley and Victor, 1978). The sinusoidal light used in our experiment is optimized for linear responses.

Previous experiments have used a variety of light sources, many of which had different waveforms. Schwahn and Schaeffel (1997) used a square-wave Xenon light source (Schwahn and Schaeffel, 1997), Crewther et al. (2006) used a halogen light source with a pulse profile of 250 ms (Crewther et al., 2006), and Di et al. (2013), used a square-wave monochromatic, green light of 505 nm (Di et al., 2013). Rucker et al. (2015) used sinusoidally modulated white and yellow LED lights (Rucker et al., 2015). Different light sources may have unique effects on emmetropization, and an understanding of the temporal effects of the stimulus is important for understanding how the eye develops under different environmental lighting conditions. For the purposes of this experiment, LCD monitors (Foris FS2735, Orion Images 32RTCS; Orion Images 32RTCSR 32” Sunlight Readable LCD Monitor) with a refresh rate of 60 Hz will produce a sinusoidal wave of 0.2 Hz.

Using sinusoidal temporal modulation, a study by Rucker et al (2017) compared the growth of chick eyes over a range from 16% to 80% contrast, with flicker modulation of 0.2 Hz or 10 Hz, in white or yellow light. 10-day-old chicks were placed in a cage with top-mounted LED bulbs and exposed to the light during the day. When chicks were presented

with white or yellow luminance stimuli at 10 Hz with 80% contrast, eye growth was inhibited, increasing only 0.179 mm and 0.171 mm, respectively. At 0.2 Hz, only the white light inhibited eye growth, increasing only 0.205 mm relative to 0.277 mm for yellow light in otherwise similar conditions. When the stimuli were replaced with red/green or blue/yellow 0.2 Hz color modulation, eye growth was least with blue/yellow modulation (Rucker et al., 2017). These results demonstrate a dependence on contrast, color, and temporal frequency of the light source.

This experiment used computer monitor generated sine-wave modulation similar to that of Rucker et al (2015, 2017), with a white/black light and a yellow/blue alternating light at 0.2 Hz.

1.6. Role of Color

While lens wear clearly affects eye growth in chick, tree shrew, and guinea pigs, more recent experiments have shown that the color of light (and the effects of longitudinal chromatic aberration on its focus) also influences eye growth in chicks (Foulds et al., 2013; Rohrer et al., 1992; Rucker and Wallman, 2008; Seidemann and Schaeffel, 2002) and a number of other animals (Gawne et al., 2017; Kröger and Wagner, 1996; Liu et al., 2011; Smith et al., 2015). Rohrer et al placed 4 day-old chicks in a white dome with a light source and a filter of either 383 nm or 665 nm at the top of the cage. No significant difference was discovered between the two experimental conditions, which initially led to the conclusion

that longitudinal chromatic aberration did not affect emmetropization (Rohrer et al., 1992). It is now acknowledged that the light intensity was too low (max 66 mWm^{-2}) for an effect to be seen.

Later experiments led to testing of different wavelengths. Seidemann and Schaeffel attempted a similar experiment in 2002 with filters at 430 nm and 615 nm, with measurements every two days. Animals in red light were 1.41 D more myopic than those in blue light after two days (Seidemann and Schaeffel, 2002). Rucker and Wallman (2008) isolated the different cone responses to red and blue illumination by reducing the illumination of the undesired cone below the threshold for emmetropization. Defocus produced by LCA was corrected and lenses of +6 D or -8 D were placed on chicks in combination with filtered chromatic light of either 460 nm or 620 nm or white light. Under both negative and positive lens test conditions, long-wavelength light (L-cone excitation) caused choroidal changes, and short-wavelength light (S-cone excitation) affected axial length. Note that globally, lenses had their typical effect on growth. Negative lenses increased eye growth while positive lenses decreased eye growth. Neither of the colored light conditions produced as accurate emmetropization as the white light condition indicating that LCA provides a signal for emmetropization (Rucker and Wallman, 2008).

Testing the effect of exposing chicks for long periods in monochromatic light, Foulds et al placed chicks from birth in either 477 nm light or 641 nm light for 14-42 days. At 28 days, chicks in the long wavelength condition had an average refraction of – 2.83 D, while chicks in the short wavelength condition had an average refraction of +4.55 D. In a later

experiment, it was found that 21 days of one light condition could be reversed by 21 days of the opposite light condition. The conclusion was that the amount of refraction change exceeded the defocus caused by LCA (Foulds et al., 2013). However, caution should be taken in interpreting these results since the light level in the blue condition may have induced hyperopia as a result of dim light rearing and stated eye length changes do not correspond to known changes in refraction.

Changes in color and luminance contrast may guide emmetropization (Rucker and Wallman, 2012). A study by Rucker and Wallman (2012) used chicks 5-7 days old and placed them in a cage with a modulated light source for three days, then allowed them to recover in normal diurnal lighting for 4 days, then the entire process was repeated for a second week. There were two illumination conditions: luminance flicker and a red-green color flicker. The luminance flicker condition was constructed with white light composed of red (615 nm), green (515 nm), and blue (465 nm) LEDs modulated at 2 Hz, and the red-green color flicker condition was constructed with only the red and green LEDs that fluctuated in counterphase at 2 Hz. The chicks were measured at the end of three days, and it was noted that luminance flicker caused a hyperopic shift of +2.01 D, while color flicker caused a myopic shift of -2.25 D. By day 10, the hyperopic shift of luminance flicker was maintained at +1.20 D, while the red-green condition led to a myopic shift and emmetropization at +0.09 D. The opposing effects color and luminance contrast may be important in guiding emmetropization, and have been adapted for our study.

In a subsequent experiment, Rucker et al. (2015, 2018) tested the effect of the rate of temporal modulation on eye growth (Rucker et al., 2015, 2018). This experiment showed that luminance flicker only produces a reduction in eye growth at higher temporal frequencies at which the eye is most sensitive to luminance changes. Meanwhile red/green color flicker produced an increase in growth at low temporal frequencies, at which the eye is most sensitive to color flicker. However, blue/yellow flicker actually reduced growth indicating that the presence of blue light was important in preventing excessive eye growth. Temporal frequency and color of the light source was more important than whether the modulation was luminance or color. Five-day-old chicks were exposed to blue-inclusive (white), blue-exclusive (yellow) light, and red/green or blue/yellow color flicker at 80% contrast, mean illumination of 680 lux, and a temporal frequency of either 0, 0.2, 1, 2, 5, or 10 Hz for three days. When chicks were presented with white light or blue/yellow light, their axial length did not change with frequency, while those chicks exposed to low frequency stimuli of yellow luminance flicker or red/green color flicker had significant myopic shifts. Chicks exposed to all high frequency conditions had a hyperopic shift.

1.7. Hypothesis and Future Experiments

The aim of this study is to understand how light from computer monitors influences emmetropization, and to determine if certain modifications to screen lighting can protect against myopia development. Our hypothesis is that by increasing the intensity of the blue

component of the light source, we will be able to slow axial growth, and by increased the intensity of red component of the light source, we will be able to increase choroidal thickness. Both of these factors are considered vital markers in myopia control.

The conventional computer monitor has a fairly low intensity blue light component. A high brightness computer monitor with a higher intensity blue component, similar to that of the LED bulbs in Rucker et al. (2015, 2018), should produce a reduction in axial eye growth with blue-yellow modulation. To test this hypothesis, experiments were run on a conventional computer monitor at the mean light settings, and on a high brightness computer monitor (Orion Images 32RTCSR 32" Sunlight Readable LCD Monitor) with spectral and brightness profiles matched to high and low brightness LED lights. This experiment will provide a more direct comparison between both light modalities and may address whether a computer monitor stimulus can be used to slow eye growth and the development and progression of myopia.

Chapter 2: Methods

2.0. Animals

135 White leghorn chicks (Gallus gallus domesticus, Cornell K strain; Cornell University, Ithaca, NY) were hatched in the lab. Before the experiments, the birds were kept in brooders in an animal room on a 12-hour light/12-hour dark cycle. Animals were raised

under fluorescent lighting (Sylvania Soctron XP 4100K 30 W; Philips LED 8.5T8/24 3500 K) at an intensity of approximately 300 lux. The birds were supplied with food and water ad libitum. In these experiments, chicks were 19 days of age at the start of the experiment. Use of animals in this study was in compliance with the ARVO statement for the Use of Animals in Ophthalmic and Vision Research and was approved by the NECO Institutional Animal Care and Use Committee.

2.1 Experimental Conditions

Conditions	Illuminance	L-cone	M-cone	S-cone	UV	Double	L+M
Low Brightness LED (LED)	120 lux	0.004	0.022	0.039	0.021	0.029	0.026
Low Brightness Monitor (Mon)	120 lux	0.012	0.014	0.013	0.021	0.021	0.026
Low Brightness Cone Matched LED (CLED)	120 lux	0.010	0.016	0.020	0.011	0.021	0.026
High Brightness Cone Matched LED (HLED)	550 lux	0.018	0.104	0.183	0.098	0.136	0.122
High Brightness Monitor (HMon)	550 lux	0.037	0.085	0.162	0.172	0.124	0.122

Table 1. Mean illuminance and cone excitation for each source.

2.1.0 Light Sources

Low Brightness Conditions

1) Mon: A conventional LCD computer monitor (Foris FS2735 27") was attached to a laptop computer (Thinkpad T450) running Ubuntu 16.04 with a stimulus created on MATLAB/Psychtoolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997). The average luminance was 88 cd/m^2 for all conditions. Mean Illuminance was 120 lux.

2) LED: This condition used LEDs that were matched in illuminance with that of the MON condition using a neutral density filter with a flat absorption spectrum. Since the conditions were matched only in illuminance and not spectral characteristics, the intensity of the blue light component of the LED was greater than in MON. Mean illuminance was 120 lux.

3) CLED: This condition matched the illuminance *and* cone excitation of the LEDs with that of the MON condition. Since the LEDs used in prior experiments only consisted of 3 primaries (RGB), we were unable to precisely match the cone excitation for all cone types in chick. This condition is notably different from the LED condition because the amount of blue light, and S-cone excitation was reduced to a level similar to the MON condition. Mean illuminance was 120 lux.

High Brightness Conditions

4) HLED: In this condition, cone excitation and illuminance were matched with the HMON condition creating a blue rich stimulus in both. As in **CLED**, cone excitations could not be matched precisely due to the limitations of our light source. As a result, HLED had less L-cone excitation than HMON. Mean illuminance was 550 lux.

5) HMon: In this condition, a high intensity LCD monitor (Orion Images 32RTCSR 32" Sunlight Readable LCD Monitor) was used. The average luminance was 392 cd/m^2 for all conditions. Mean illuminance was 550 lux. Stimuli were created with laptop computer (Thinkpad T450) running Ubuntu 16.04 with a stimulus created on MATLAB/Psychtoolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997).

LED, CLED, and **HLED** Stimuli were created with Lamina Titans RGB LED (Lamina Ceramics) driven by an eight channel, 12-bit Access I/O, USB-DA12-8A digital to analog converter with waveform generator functionality connected to BuckPucks (LuxDrive: 3021 D-E-500) that provides a linear current output over a range of 1.6 – 4.3 V.

2.1.1 Illumination Conditions

For each light source, chicks were randomly assigned to one of two flicker conditions:

1) LUM: White (RGB) in-phase sinusoidal flicker at 0.2 Hz

2) B/Y: Blue/yellow counter-phase sinusoidal flicker at 0.2 Hz

2.2 Lab Setup

For the experiments using a computer monitor, chicks were placed in a 29" x 16" x 16" (l/w/h) cage with a Plexiglas side facing a monitor. The monitor light output was

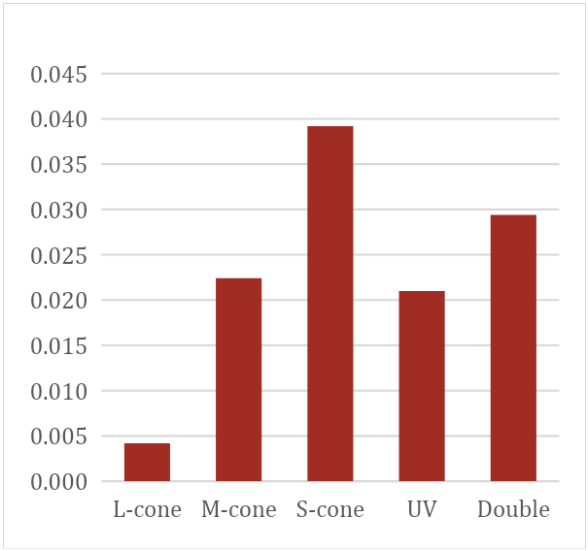
characterized with a PhotoResearch PR-670. The stimuli were displayed on a full-screen computer monitor producing a plain screen that modulated in brightness over time. The monitor stimulus ran from 8 AM to 8 PM daily and chicks were kept in darkness overnight. No lenses were placed on the chicks, and both eyes were exposed to the stimulus. Chickens were able to move around the cage at all times of day and night, except during measurements.

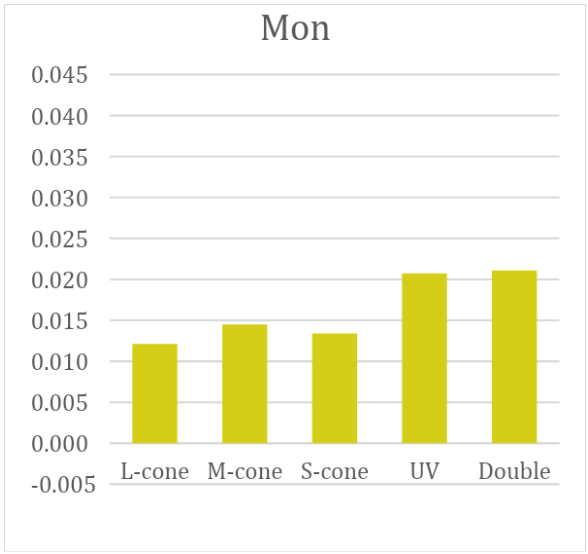
For the LED experiments, chicks were placed in a 29” x 16” x 16” (l/w/h) wire cage beneath the light source. Light output was further controlled with the use of neutral density filters to match the light intensity of the monitor with the LEDs. Calibration and sinusoidal output were produced digitally using lookup tables, and illuminance output was confirmed (Newport Model 818-SL serial number: 6915). The temporal contrast for achromatic was 83%, and contrast for Blue-Yellow was 74%.

2.3 Cone Excitation Calculation

To compare the monitors against LED light stimuli, chick cone excitation values were calculated in the following steps. Light bulbs were positioned 16 inches above the cage floor and computer monitors were placed directly against the cage side. A spectroradiometer (Photo-Research PR-670) was used to determine the radiance at each wavelength from 380 to 704 nm. Next, the output values of the spectroradiometer were used to calculate the long- (L-), middle- (M-), short- (S-), ultraviolet (UV) and double (D-) cone excitation values of the chick (Rucker & Wallman, 2008). Radiance of the source was normalized to the peak

intensity before multiplication with the chick cone spectral sensitivity function, so as to obtain the relative cone excitation caused by the source irrespective of intensity. Since all conditions in the low intensity or high intensity conditions were illuminance matched, the sum of the L-and M-cone excitation was matched within these conditions.





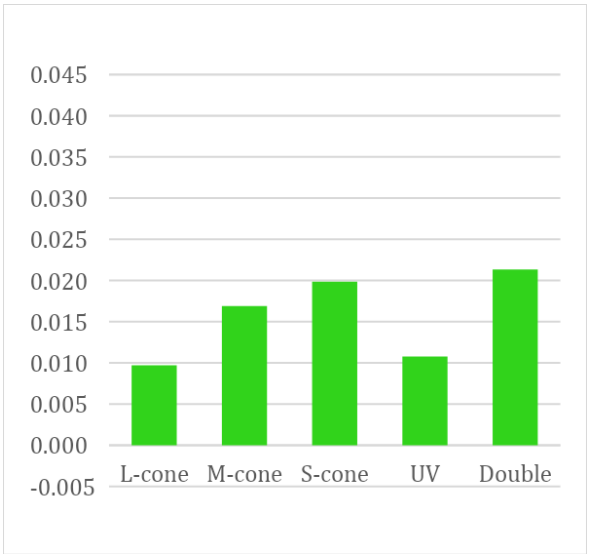


Figure 0a. Relative differences in S, M, L, UV, and Double cone excitations for Low Brightness Conditions (LED, Mon, CLED). LED condition has relatively higher S-cone stimulation and lower L-cone stimulation compared to the two other low brightness conditions, Mon and CLED. With only 3 primaries, it was not possible to match cone excitation exactly, as a result CLED had lower UV-cone stimulation than Mon. D-cone excitation was similar in all conditions, though slightly higher in LED. Since the conditions were equi-illuminant, all conditions were normalized to the sum of the L-cone and M-cone excitation.

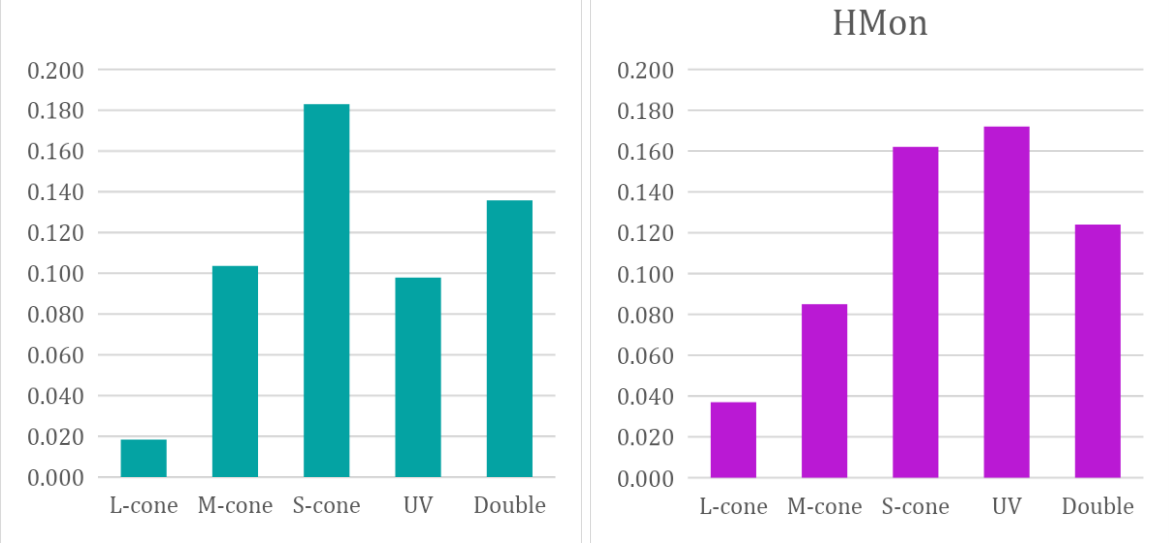


Figure 0b. Relative differences in S, M, L, UV and Double cone excitations for High Brightness Conditions (HLED and HMon). HLED condition has a higher L-cone stimulation compared to the HMon condition and lower UV-cone stimulation. With only 3 primaries, it was not possible to match cone excitation exactly. D-cone excitation was similar in all

conditions. Since the conditions were equi-illuminant, all conditions were normalized to the sum of the L-cone and M-cone excitation.

2.4 Measurements

At the beginning and end of the stimulus presentation, refraction and ocular biometry were measured at 12:00 PM of day zero and day three. Pre- and post-measurements were commenced at the same time of day for both pre- and post-measures to avoid timing effects on eye growth. For the duration of the measurements, birds were placed under anesthesia using 1.5% isoflurane in oxygen with a 2.5 L/min oxygen flow rate.

Measurements of the ocular components were made using a Lenstar biometer (Lenstar LS 900: Haag-Streit AG, Konig, Switzerland). For each bird, the Lenstar data was averaged over five measurements. Measurements were excluded if clear peaks corresponding to each of the ocular components could not be recorded. Lid retractors were used to keep the eyes open during measurements.

An infrared optometer (Schaeffel et al., 1987) was used to measure the refractive error. Measurements were taken over 15 seconds in each meridian, and they were averaged over that period. Lid retractors were used to keep the eyes open. Measurements were excluded if the refraction was not between +4.00 D and -4.00 D in any meridian because of the limited accuracy at those powers (unpublished comparison of data from the Lenstar and

Hartinger refractometer), or if the measurements were not stable due to either blinking, tear film inconsistencies, or if the software could not locate the Purkinje Image.

2.5 Analysis

The effects of the illumination conditions on the dimensions of the refraction, axial length, vitreous depth, and choroidal thickness were calculated as the mean change between pre- and post-measurements. Measurements were made in both eyes and the average change in the two eyes was used in analysis.

Eye length was calculated as the distance from the anterior cornea to the posterior surface of the posterior sclera. Choroid thickness was calculated as the distance from the retinal pigment epithelium to the posterior choroid. Vitreous depth was calculated as the distance from the back of the lens to the anterior retina.

To compare intra-source data, a one-way ANOVA was completed on each data set, and Tukey's HSD tests were performed if the ANOVA showed significance ($p < 0.05$). To compare intra-stimulus data, a one-way ANOVA was completed on each data set, and Tukey's HSD tests were performed if the ANOVA showed significance ($p < 0.05$). To compare interactions between source and stimulus, a two-way ANOVA was completed, and Tukey's HSD tests were performed if the ANOVA showed significance ($p < 0.05$).

Chapter 3: Results

3.0 Axial Length

Figures 1a-c show the change in axial length in each of two conditions (Figure 1a: LUM, BY) over a 3-day period run on each of the five sources (Figure 1b: LED, Mon, CLED, HLED, HMon) and their interaction (Figure 1c). One-way ANOVAs were performed on the data by source ($F_{(4,133)} = 8.91$; $p < 0.001$) and by stimulus ($F_{(1,133)} = 2.47$; $p = 0.119$). A two-way ANOVA was performed by source and stimulus ($F_{(4,133)} = 3.71$; $p = 0.0068$).

3.0.0 Inter-Stimulus Comparisons

There were no significant inter-stimulus interactions found when the data from the different sources were pooled. Axial growth across the B/Y stimulus was 0.340 ± 0.055 mm compared to the Lum stimulus at 0.352 ± 0.055 mm ($p = 0.119$). This indicates that when the stimuli were presented from mixed sources they did not differentially affect axial growth.

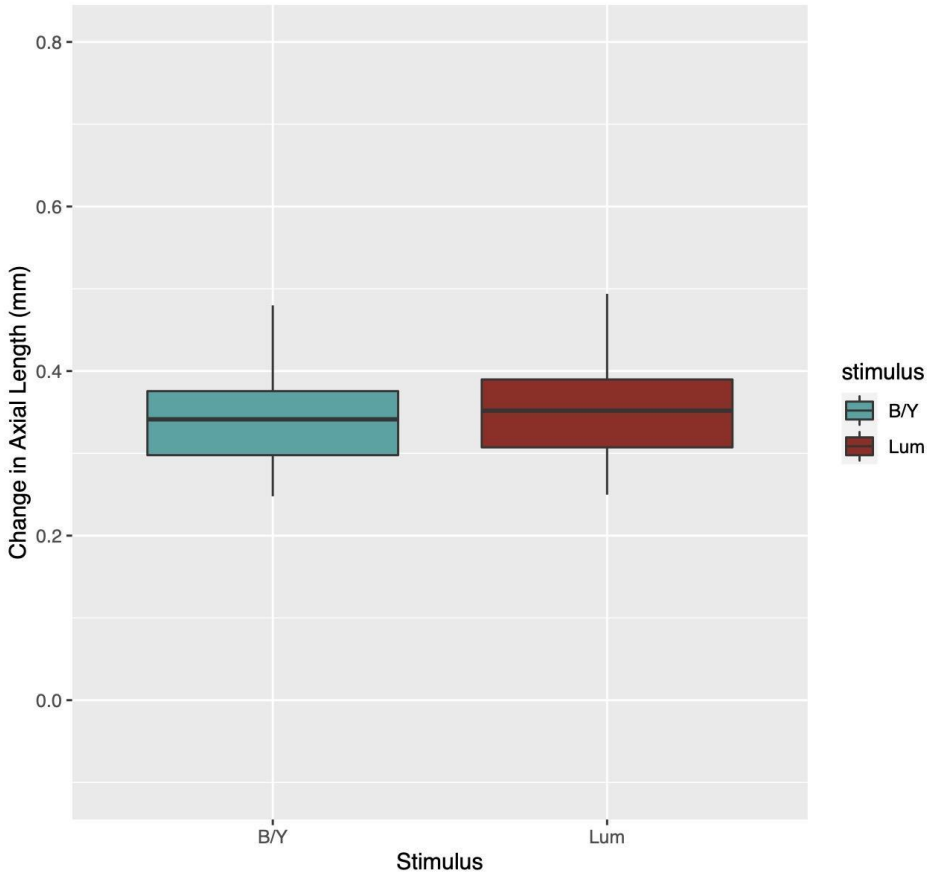


Figure 1a. Change in Axial Length in each of two stimulus conditions (B/Y, Lum) over a 3-day period when source data was pooled. No significant difference was seen between conditions (p=0.119).

3.0.1 Inter-Source Comparisons

Sources that were low intensity and blue-poor produced excess axial growth. When data for each source were compared without considering the stimuli, the axial growth in the Mon and CLED condition was greater than that in LED, HLED, and HMon conditions. In the Mon condition, the presence of a lower intensity blue light increased eye growth relative to

LED, causing axial lengthening of 0.370 ± 0.061 mm compared to the LED source at 0.330 ± 0.047 ($p < 0.05$). The Mon condition also increased eye growth compared to the HLED condition with growth of 0.328 ± 0.046 ($p < 0.05$) and the HMon condition with growth of 0.321 ± 0.047 mm ($p < 0.01$). In the CLED condition, the presence of a lower intensity blue light increased eye growth relative to LED, causing axial lengthening of 0.379 ± 0.047 mm compared to the LED source at 0.330 ± 0.047 mm ($p < 0.001$). The CLED condition also increased eye growth compared to the HLED condition and HMon condition with axial lengthening of 0.328 ± 0.046 mm ($p < 0.001$) and 0.321 ± 0.047 mm ($p < 0.001$), respectively.

As anticipated, with similar color, intensity and cone excitation in Mon and CLED, there was no significant difference in axial growth between the Mon condition and the CLED condition. Axial growth in the Mon condition was 0.370 ± 0.061 mm compared to 0.379 ± 0.047 mm in the CLED condition ($p = 0.965$). In a mixed stimulus environment, the axial changes were dependent on the source. Sources without sufficient blue light intensity, or S-cone and UV-cone stimulation, had significant axial growth.

There were no significant differences between the LED, HLED, and HMon conditions. Axial growth in the LED condition was 0.330 ± 0.047 mm compared to 0.328 ± 0.046 mm in the HLED condition ($p = 1.000$) and 0.321 ± 0.047 mm in the HMon condition ($p = 0.459$). The LED condition was approximately 20% the brightness of the HLED and

HMon condition, yet all these conditions had relatively high S-cone and UV-cone stimulation compared to the Mon and CLED conditions.

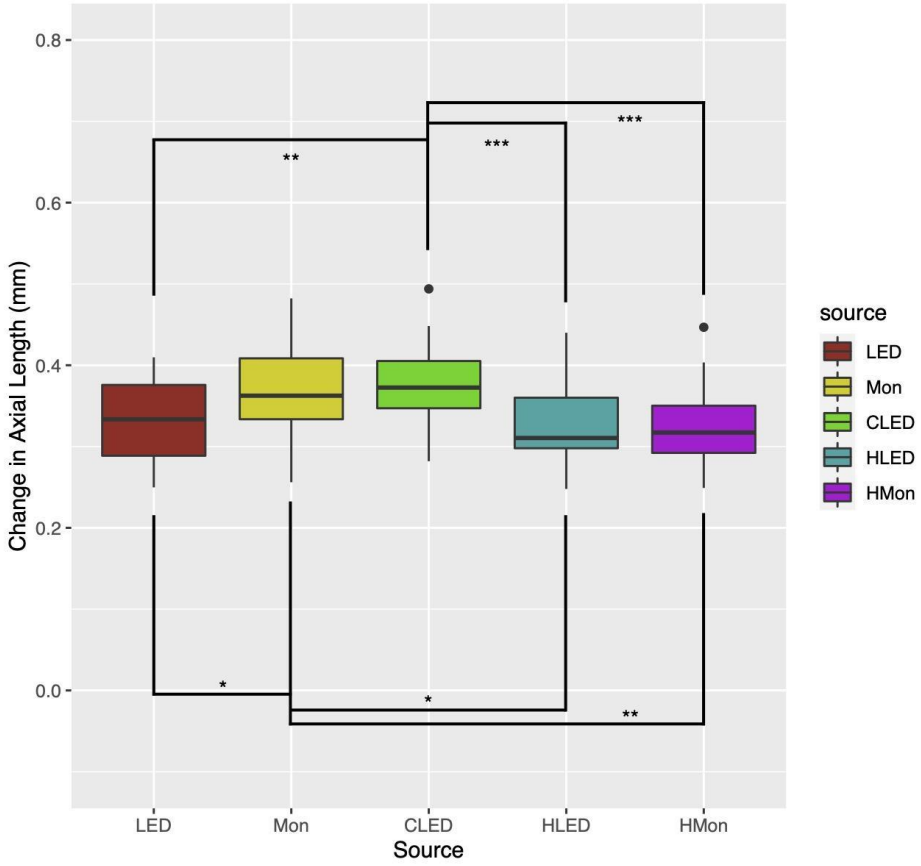


Figure 1b. Change in Axial Length in each of five sources (Low Brightness Monitor = Mon, Cone Matched LED = CLED, Low Brightness LED = LED, High Brightness Cone Matched LED = HLED, High Brightness Monitor = HMon) over a 3-day period. p < 0.05 represented by *, p < 0.01 represented by **, p < 0.001 represented by *. When comparing between the sources of light, blue-poor environments promoted axial growth.**

3.0.2 Source and Stimulus Interactions

B/Y stimulus

The low intensity CLED B/Y stimulus, with low intensity blue light, produced increased axial growth relative to the higher intensity conditions. The CLED B/Y stimulus had significant growth at 0.379 ± 0.038 mm compared to the high intensity HLED B/Y and HMon B/Y stimuli, at 0.304 ± 0.027 mm ($p = 0.003$) and 0.315 ± 0.062 ($p = 0.028$), respectively. There was no difference in axial length changes between all the low intensity conditions. This included the CLED and Mon conditions ($p = 0.823$), the CLED and LED conditions ($p = 0.803$), as well as the Mon and LED conditions ($p = 1.00$). With the low intensity B/Y color stimulus all sources promoted axial growth, while high intensity sources promoted a reduction in axial growth compared to CLED.

LUM stimulus

As with B/Y, axial growth increased with the low intensity/blue-poor sources including Mon and CLED compared to blue rich sources, LED and HMon. Axial growth was significantly greater with the low intensity Mon_Lum stimulus at 0.394 ± 0.046 mm compared to LED_Lum and high intensity HMon_Lum stimuli at 0.311 ± 0.047 mm ($p = 0.014$) and 0.327 ± 0.031 mm ($p = 0.026$) respectively. Axial growth was also significantly greater with the CLED_Lum stimulus at 0.378 ± 0.055 mm compared to the LED_Lum

condition at 0.311 ± 0.047 mm ($p < 0.001$). The LED condition, with the same illuminance as CLED and Mon but with higher blue light intensity, protected against an increase in axial growth at the lower light level.

There were no other significant interactions between source and stimulus.

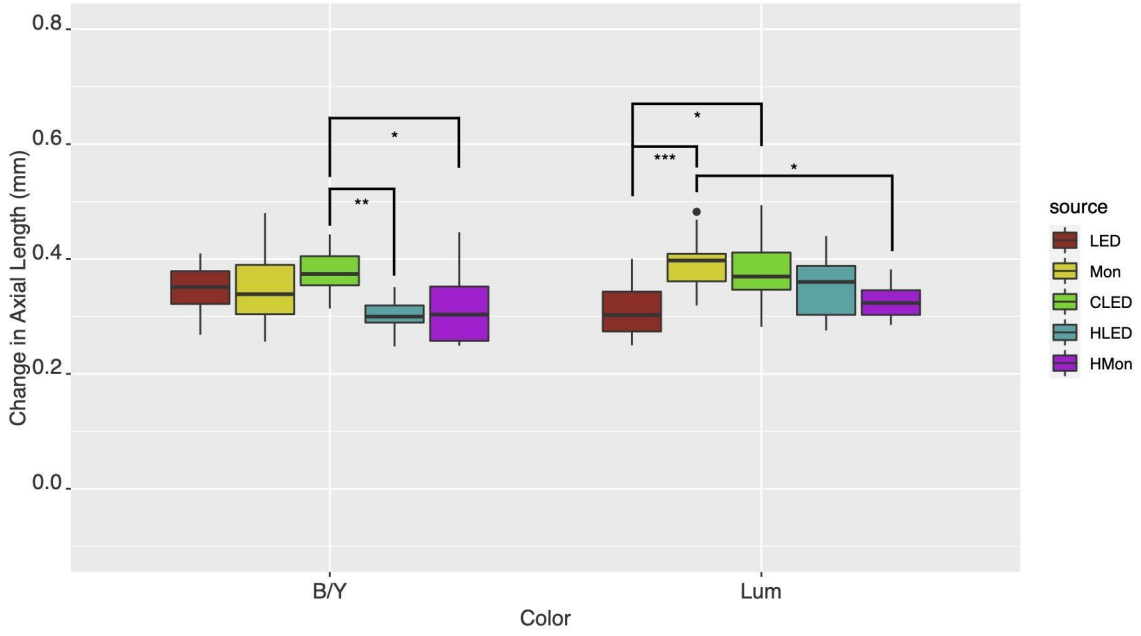


Figure 1c. Change in Axial Length in each of two stimulus conditions (B/Y, Lum) in each of the five sources (Low Brightness Monitor = Mon, Cone Matched LED = CLED, Low Brightness LED = LED, High Brightness Cone Matched LED = HLED, High Brightness Monitor = HMon) over a 3-day period. $p < 0.05$ represented by *, $p < 0.01$ represented by **, $p < 0.001$ represented by *. Blue-poor, dim sources produced increased axial growth.**

3.1 Choroid Thickness

Figures 2a-c show the change in choroid thickness in each of two conditions over a 3-day period run on each of the five sources. ANOVAs were performed on the data by source ($F_{(4,133)} = 6.163$; $p < 0.001$), by stimulus ($F_{(1,133)} = 27.537$; $p < 0.001$), and by the interaction of source and stimulus ($F_{(4,133)} = 4.499$; $p = 0.002$).

3.1.0 Inter-Stimulus Comparisons

When data for the five sources was pooled, it was found that the Lum stimulus caused significant choroidal thickening at 0.044 ± 0.033 mm compared to B/Y at 0.020 ± 0.028 mm ($p < 0.001$).

This indicates that in a mixed source environment, choroidal thickening is stimulus dependent. The main difference between the stimuli is that the Lum condition stimulates all cones at once in an on/off sinusoidal manner, whereas the B/Y stimulus alternates in a sinusoidal manner between strong S-cone stimulation to strong M-cone and L-cone stimulation. The alternating stimulation of cones in the B/Y stimulus slows choroidal thickening.

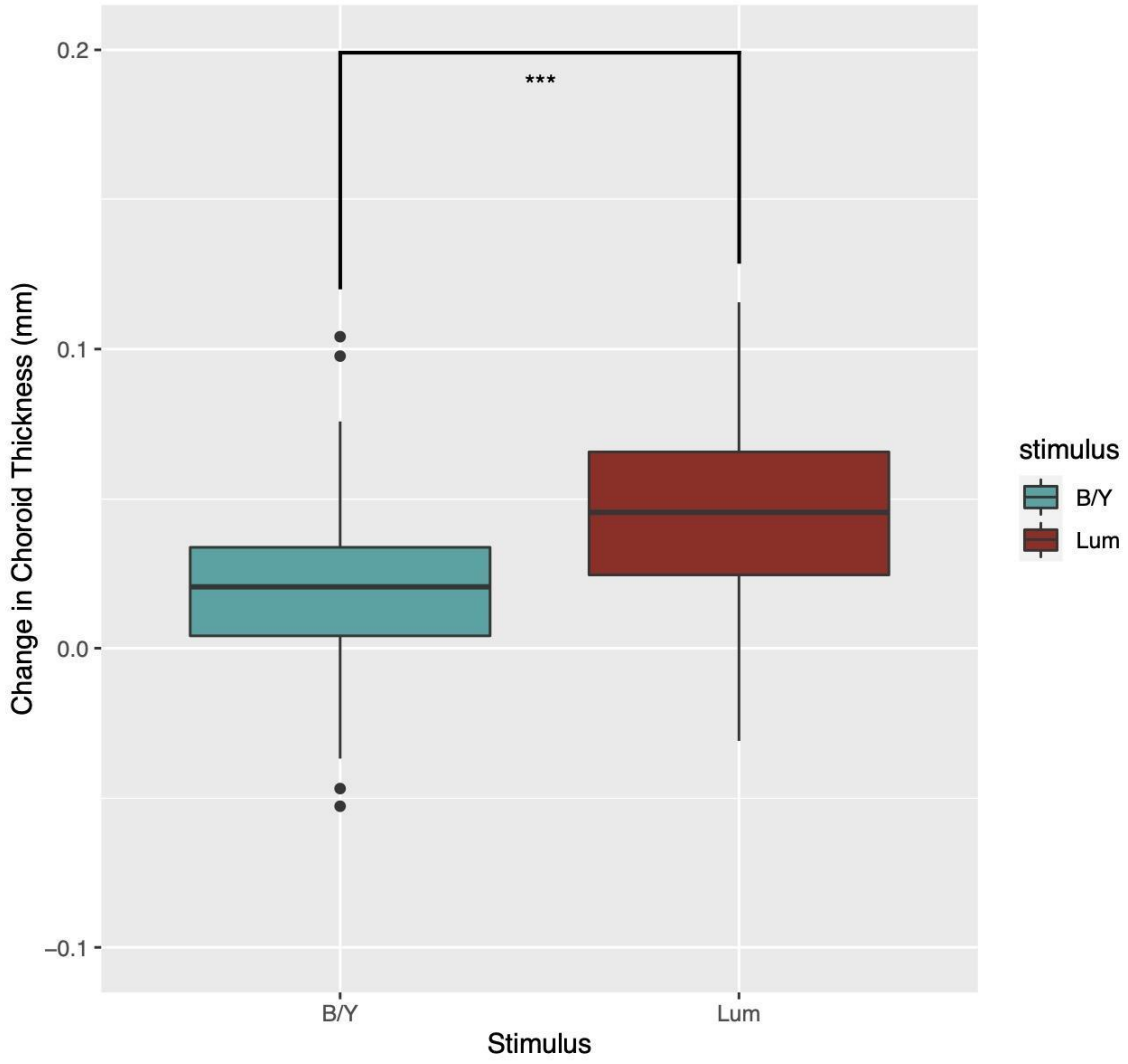


Figure 2a. Change in Choroid Thickness over a three-day period in each of two conditions (B/Y, Lum) over a 3-day period. $p < 0.001$ represented by *. Alternating cone stimulation in the B/Y condition slowed choroidal thickening.**

3.1.1 Source and Stimulus Interactions

Lum comparisons

The red rich Mon, CLED, and HMon sources produced significant choroidal thickening compared to the blue rich HLED and LED sources. The HLED source was associated with significantly less choroidal thickening (0.020 ± 0.025 mm) compared to the red rich CLED source (0.057 ± 0.028 mm; p = 0.022), Mon source (0.059 ± 0.038 mm; p = 0.001) and HMon source (0.063 ± 0.014; p = 0.009).

Similarly, the blue rich LED source was associated with significantly less choroidal thickening (0.021 ± 0.027 mm) compared to the CLED source (0.057 ± 0.028 mm; p = 0.041), Mon source (0.059 ± 0.038 mm; p = 0.019) and HMon source (0.063 ± 0.014; p = 0.009).

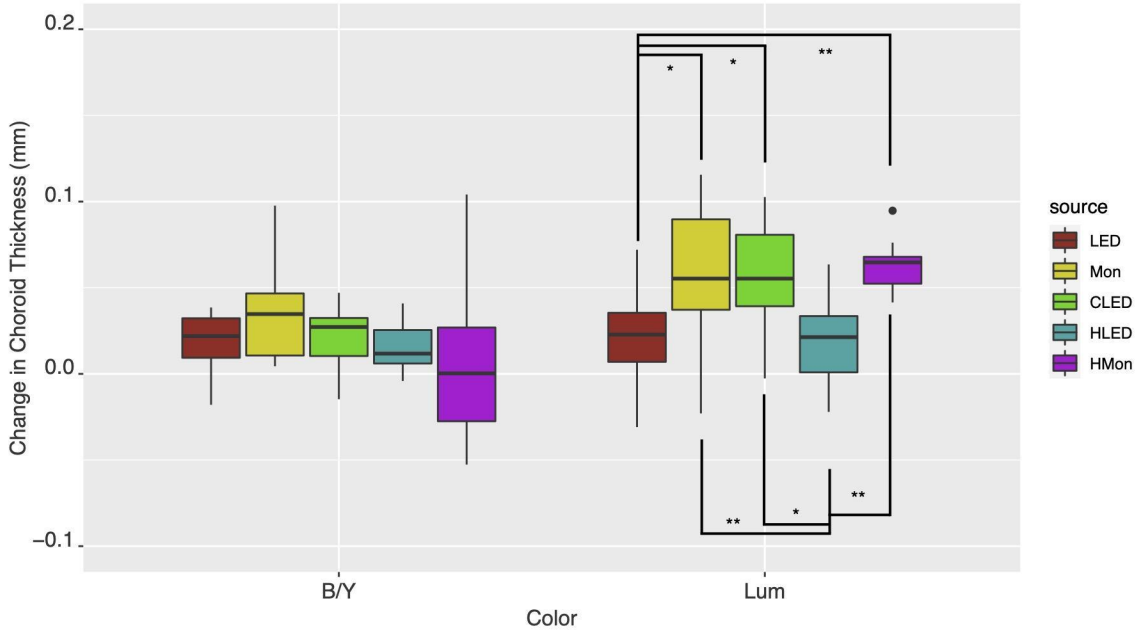


Figure 2b. Change in Choroid Thickness in each of two conditions (B/Y, Lum) over a 3-day period on each of the five sources (Low Brightness Monitor = MON, Low Brightness Low Blue LED = CLED, Low Brightness High Blue LED = LED, High Brightness Low Blue LED = HLED, High Brightness Monitor = HMon). $p < 0.05$ represented by *, $p < 0.01$ represented by **, $p < 0.001$ represented by *. Red rich sources, in combination with the Lum stimulus, caused choroidal thickening.**

3.2 Vitreous Chamber Depth

Figures 3a-c. show the vitreous expansion in each of two conditions over a 3-day period run on each of the five sources. ANOVAs were performed on the data by stimulus

($F_{(1,133)}$ = 17.16; $p < 0.001$), by source ($F_{(4,133)}$ = 0.803; $p = 0.525$), and the interaction between stimulus and source ($F_{(4,133)}$ = 12.10; $p < 0.001$).

3.2.0 Inter-Stimulus Comparisons

When data for the five sources was pooled, the vitreous expansion in the Lum condition was less than in B/Y. The Lum stimulus across sources was associated with less vitreous expansion of 0.161 ± 0.040 mm compared to the B/Y stimulus of 0.186 ± 0.043 mm ($p < 0.001$). The Lum stimulus caused choroidal thickening, therefore the vitreous depth expanded less.

No other significant inter-stimulus interactions were found.

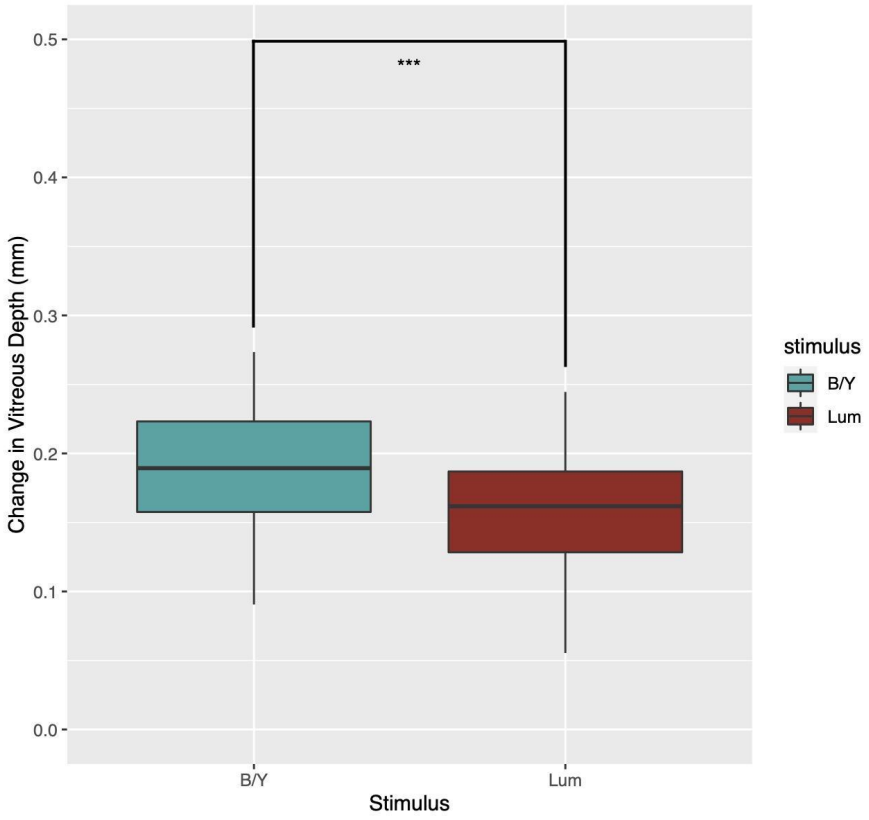


Figure 3a. Change in Vitreous Depth in each of two conditions (B/Y, Lum) over a 3-day period. $p < 0.001$ represented by *. Vitreous depth is dependent upon the axial length and choroid thickness. Since there were no differences between axial measures, all changes in the vitreous opposed the changes in choroid thickness.**

3.2.1 Inter-Source Comparisons

When data for the stimulus conditions was pooled, there were no significant differences between any of the sources. As described above, the choroid thickens with red rich environments, specifically with the Lum stimulus, and the axial growth slows in blue rich

environments, independent of the stimulus. As a result, there are no significant differences in the vitreous chamber depth between any conditions when the stimulus conditions are pooled.

No other significant inter-source interactions were found.

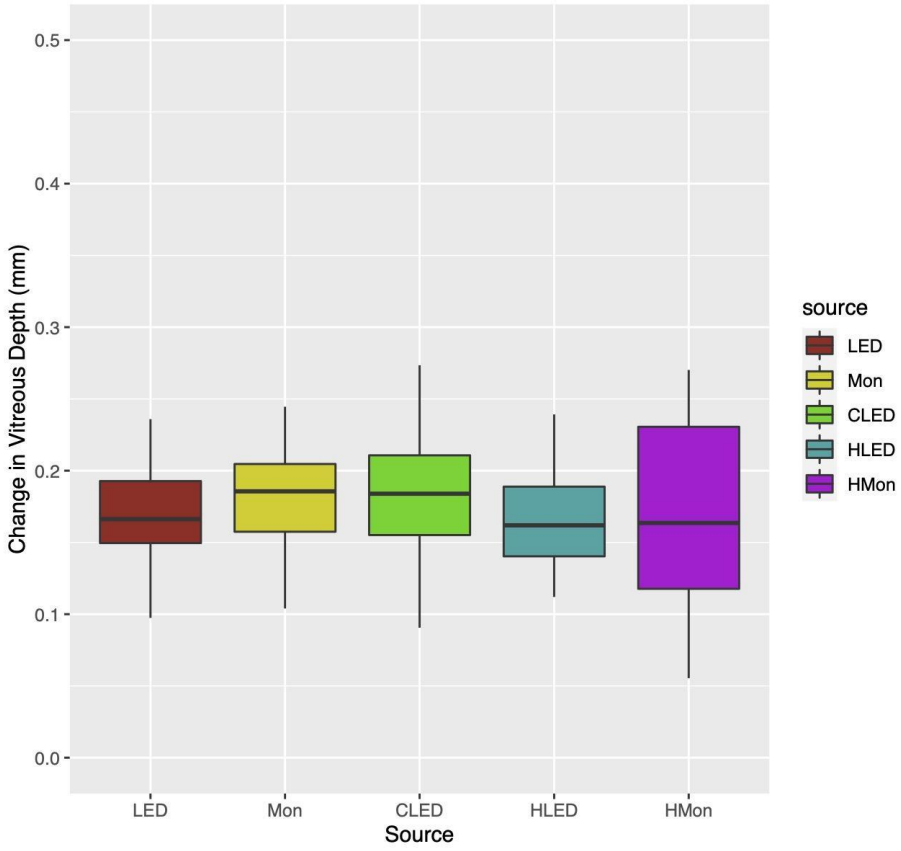


Figure 3b. Change in Vitreous Depth over a 3-day period in each of the five sources (Low Brightness Monitor = Mon, Low Brightness Low Blue LED = CLED, Low Brightness High Blue LED = LED, High Brightness Low Blue LED = HLED, High Brightness Monitor = HMon).

3.2.2 Source and Stimulus Interactions

When the sources and the stimuli are analyzed in depth, we found that one condition slows axial growth while thickening the choroid, effectively slowing vitreous expansion. This condition must have sufficient blue light to slow axial growth and enough red light to increase choroidal thickening.

B/Y stimulus

The HMon B/Y stimulus produced significantly *greater* vitreous expansion of 0.214 ± 0.039 mm compared to the HLED B/Y of 0.152 ± 0.028 mm ($p = 0.0022$). While there were no significant differences between the axial length and choroid thickness in these two conditions, the combined differences may have led to a significant difference in vitreous depth.

LUM stimulus

The HMon_Lum stimulus created significantly *less* vitreous expansion at 0.121 ± 0.034 mm compared to the HLED_Lum and Mon_Lum stimuli at 0.183 ± 0.037 mm ($p < 0.01$) and 0.183 ± 0.037 mm ($p < 0.01$) respectively.

This relationship is due to significantly thicker choroid in the HMon_Lum condition at 0.063 ± 0.014 mm compared to the HLED_Lum condition at 0.020 ± 0.025 mm ($p < 0.01$). The HMon and HLED sources produced similar axial length changes since both conditions produced bright blue light, but the HMon condition produced significantly more red light

compared to the HLED condition, which led to choroidal thickening. The increased choroidal thickening paired with reduced axial growth in the HMon_Lum condition produced relatively less vitreous expansion.

No significant differences in vitreous depth were found between the other conditions.

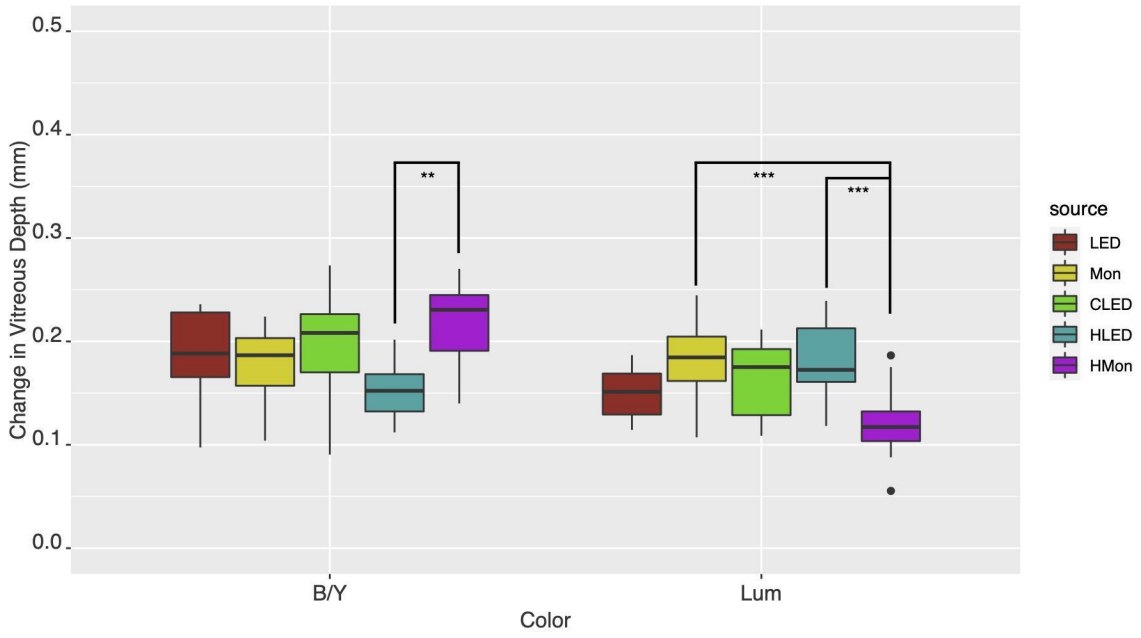


Figure 3c. Change in Vitreous Depth in each of two conditions (B/Y, Lum) over a 3-day period on each of the five sources (Low Brightness Monitor = Mon, Low Brightness Low Blue LED = CLED, Low Brightness High Blue LED = LED, High Brightness Low Blue LED = HLED, HMon = High Brightness Monitor). $p < 0.05$ represented by *. The HMon_Lum condition decreased vitreous expansion compared to the HLED and Mon conditions due to the increased choroidal thickening paired with reduced axial growth.

3.3 Axial Length Versus Choroid Thickness

The correlation between axial length and choroid thickness was calculated due to its importance as an end-goal in myopia control. In the Lum condition, with data from all sources, axial length and choroid were positively correlated ($p < 0.001$, $R^2 = 0.399$). All conditions generally exist along the best-fit line except for the HMon condition, which groups below the line, in the area with low axial growth and high choroidal expansion. The high S-cone and L-cone stimulation was ideal in this condition to promote choroidal expansion while also slowing axial growth.

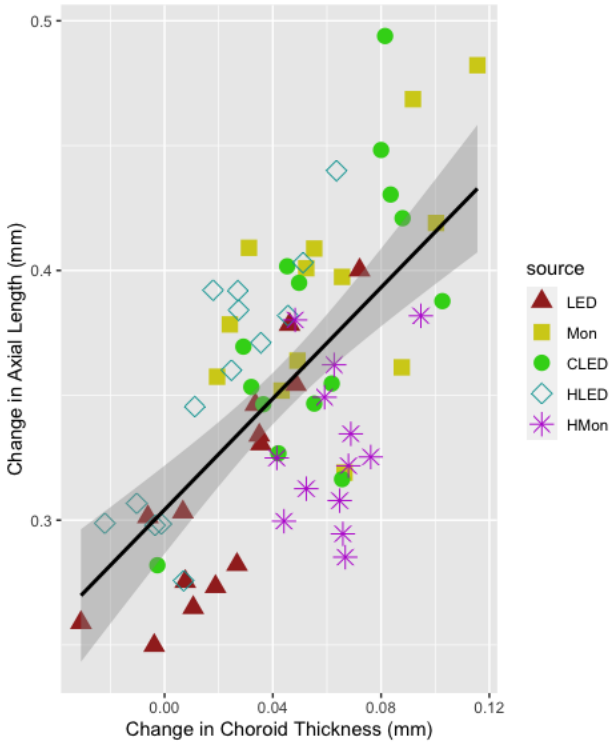


Figure 3c. Change in Choroid Thickness vs Change in Axial Length in the Lum condition over a 3-day period on each of the five sources (Low Brightness Monitor = Mon, Low Brightness Low Blue LED = CLED, Low Brightness High Blue LED = LED, High Brightness Low Blue LED = HLED, HMon = High Brightness Monitor). 95% confidence interval is represented by the area in gray. The HMon condition uniquely increased choroidal expansion while it reduced axial growth.

3.4 Refraction

ANOVAs were performed on the data by source ($F_{(4,133)} = 1.81$; $p = 0.13$), by stimulus ($F_{(1,133)} = 0.012$; $p = 0.91$), and by the interaction of source and stimulus ($F_{(4,133)} = 2.29$; $p = 0.063$). There were no significant comparisons for any of the sources or stimuli.

Chapter 4: Discussion

4.0 Effects on Ocular Components

This experiment examined the achromatic and chromatic components of computer stimuli on eye growth. The hypothesis was that blue light emitted from computer monitors would be protective against axial growth and red light emitted from computer monitors would promote choroidal expansion as had been observed in LED experiments (Khanal et al., 2021; Lin et al., 2020; Rucker et al., 2015, 2018, 2020).

4.0.1 Choroidal Changes

Choroidal expansion occurred in red rich conditions, while standard LED sources with blue rich light slowed choroidal expansion. This finding is supported by previous research that suggests that choroidal thickening is L-cone dependent (Gawne et al., 2017; Khanal et al., 2021; Lin et al., 2020; Rucker et al., 2015, 2018, 2020; Rucker and Wallman, 2008). All significant changes to choroid thickness occurred with the Lum stimulus, where in-phase cone stimulation light led to choroidal thickening. The B/Y counterphase stimulus halted choroidal expansion on all sources. The Lum condition had a steady ratio of S-cone/L-cone stimulation, while the B/Y stimulus fluctuated between high S-cone and high L-cone stimulation in a sinusoidal manner. Drops in L-cone stimulation, or competing short- and long-wavelength signals, even for a short period may be the guiding factor in halting choroidal expansion. Previous research at 0.2 Hz and 10 Hz, with graduated levels of exposure to blue and red light, with in-phase and counterphase stimuli, demonstrated choroidal thinning in the presence of a blue component (S- and UV-cone stimulation) and choroidal thickening with L-cone stimulation (Rucker et al 2020).

4.0.2 Vitreous Changes

The vitreous change was dependent upon the combined effects of axial growth and choroidal changes. Choroidal thickening, caused by high intensity L-cone stimulation caused the vitreous to expand *less* in the HMon_Lum condition. However, the reduction in vitreous chamber depth in HMon_Lum condition differs from the results of the other conditions tested and from those in previous experiments (Rucker et al., 2015, 2018). In Rucker et al., 2015, the effect of modulating a blue rich, white, LED light at a low temporal frequency was compared with that of a blue poor LED light. In the blue rich condition, there was a greater reduction in axial growth, and vitreous chamber depth, but it was associated with choroidal thinning, particularly with a B/Y stimulus. Similarly, in Rucker et al., 2018 stimulation of the eye with a 0.2 Hz B/Y modulated stimulus produced a reduction in axial growth and choroidal thinning. (Rucker et al., 2015, 2018; Rucker and Wallman, 2012). The disparity in the HMon_Lum condition is most likely due to the difference in spectral ranges of LED lights and computer monitors, where computer monitors induce much stronger L-cone excitation than LED lights and thereby cause greater choroidal thickening.

These results are in agreement with earlier studies where lenses were used to manipulate emmetropization, and reduced axial lengthening was associated with choroidal thickening (Schmid and Wildsoet, 1996). They are also in agreement with the proposed "STOP" signal suggested in Rucker et al. (2020) that arises with both S-cone and L-cone stimulation. The difference in the results in lens experiments and the HMon_Lum condition on one hand, and the LED lighting experiments and low brightness monitor conditions on the other, appears to arise because of the relative combination of a high intensity blue *and* red

component in the light source. When the intensity of the blue *and* red component is increased, as in the higher intensity conditions, the results match closely with previous lens experiments due to the choroidal thickening associated with the red rich environment and reduced axial growth associated with the blue rich environment. The Mon source was not bright enough nor did it have enough blue light to stimulate reduced axial growth effectively compared to the LED and HLED conditions. The CLED source and the Mon source produced similar results because of their similar color and intensity characteristics. The LED and HLED conditions both had much greater blue light intensity, lower L-cone stimulation, and the results were consistent with those found in Rucker et al. (2015, 2018) where axial length was shorter, vitreous depth was shorter, and the choroid was thinner compared to conditions with high intensity red light. The HMon source was unique because of its high brightness, high L-cone stimulation, and high S-cone stimulation. In this regard, high brightness monitors may be better than low brightness monitors for slowing growth of the developing eye, as the S-cone component of the monitor slows axial elongation while the significant L-cone stimulation increases choroidal thickening.

4.1 Radiance and Relative Cone Stimulation in Lum Condition

With equi-illuminant stimuli, the radiance of each source differed, so the effects of cone stimulation and radiance on the axial length and choroid thickness must be separated. In previous chicken experiments, it has been found that spectral content, and inadvertently

radiance, impacts eye growth (Lin et al., 2020; Rucker et al., 2015, 2017, 2018, 2020; Rucker and Wallman, 2008, 2012; Yoon et al., 2018).

Axial growth was correlated with S-cone stimulation ($p < 0.001$, $R^2 = 0.11$) as well as radiance ($p < 0.001$, $R^2 = 0.07$), which indicates that axial growth is dependent upon each of these variables. When S-cone stimulation is expressed as a ratio against radiance, the correlation persists ($p < 0.001$, $R^2 = 0.17$). These correlations suggest that S-cone stimulation as a proportion of the overall radiance is important in controlling axial growth, with reduced axial growth being seen in the low intensity LED condition as well as in the high intensity conditions.

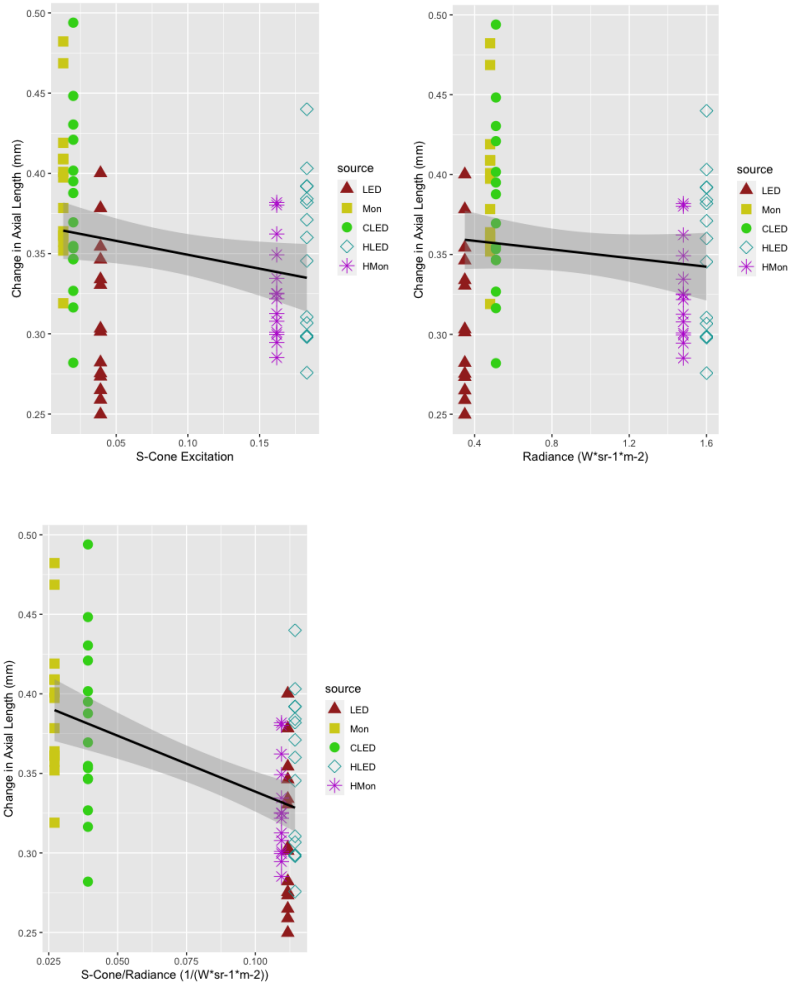


Figure 4a. Change in Axial Length vs S-cone stimulation, Radiance ($W \cdot sr^{-1} \cdot m^{-2}$), and S-cone stimulation/Radiance ($1/W \cdot sr^{-1} \cdot m^{-2}$) in the Lum condition over a 3-day period on each of the five sources (Low Brightness Monitor = Mon, Low Brightness Low Blue LED = CLED, Low Brightness High Blue LED = LED, High Brightness Low Blue LED = HLED, HMon = High Brightness Monitor). 95% confidence interval is represented by the area in gray. Conditions with high S-cone/Radiance ratios exhibited slower axial growth, while those with low S-cone/Radiance ratios exhibited significant

axial growth. These results indicate that the S-cone stimulation as a proportion of the overall radiance is important in controlling axial growth.

Choroidal expansion was correlated with L-cone stimulation ($p < 0.05$, $R^2 = 0.04$), but there was no correlation found to radiance ($p = 0.54$, $R^2 = -0.01$), which indicates choroid thickness is dependent upon L-cone stimulation. Choroidal expansion was also dependent on the stimulus type rather than on the source. When L-cone stimulation is represented as a ratio against radiance, the correlation is moderate ($p < 0.001$, $R^2 = 0.31$). This suggests that L-cone stimulation as a proportion of overall radiance is important in inducing choroidal expansion.

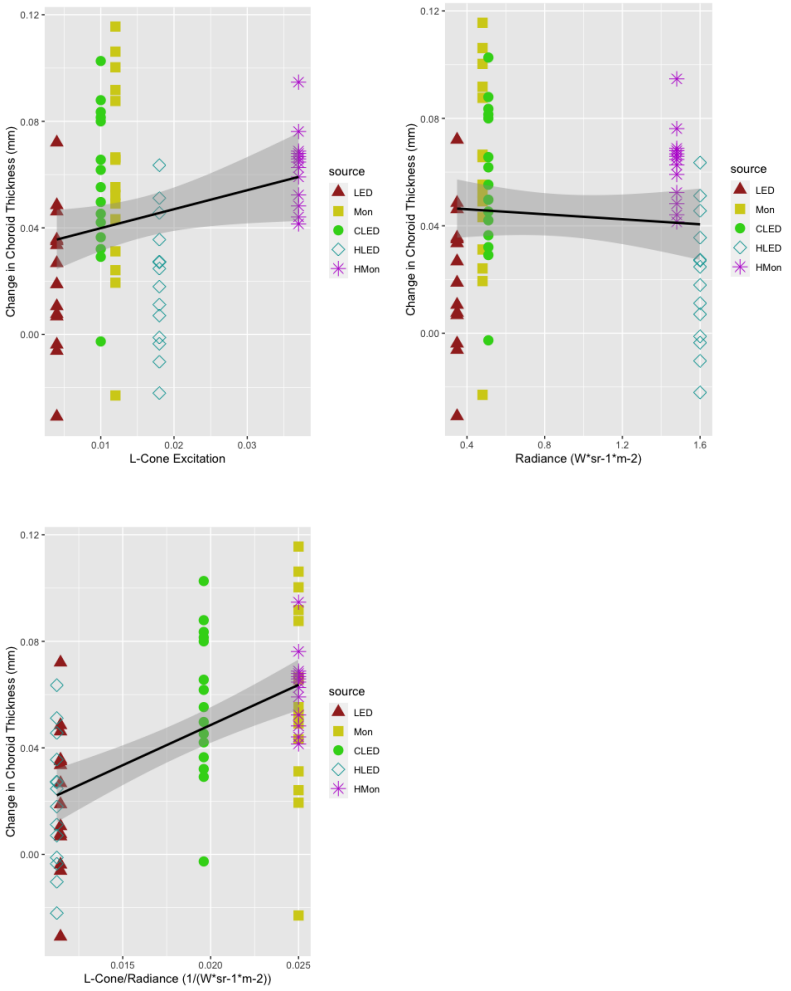


Figure 4b. Change in Choroid Thickness vs L-cone stimulation, Radiance ($W \cdot sr^{-1} \cdot m^{-2}$), and L-cone stimulation/Radiance ($1/W \cdot sr^{-1} \cdot m^{-2}$) in the Lum condition over a 3-day period on each of the five sources (Low Brightness Monitor = Mon, Low Brightness Low Blue LED = CLED, Low Brightness High Blue LED = LED, High Brightness Low Blue LED = HLED, HMon = High Brightness Monitor). 95% confidence interval is represented by the area in gray. Conditions with high

L-cone/Radiance ratios exhibited significant choroidal expansion, while those with low L-cone/Radiance ratios exhibited little choroidal expansion. L-cone stimulation as a proportion of overall radiance is important in inducing choroidal expansion.

Radiance is the common basis for comparing axial growth and choroid thickness in the above plots, and may be useful in creating novel stimuli for myopia control treatments in monitor and LED models. The minimum ratio of S-cone stimulation/Radiance required to slow axial growth in chick was 0.11/($W \cdot sr^{-1} \cdot m^{-2}$). The minimum ratio of L-cone stimulation/Radiance required to increase choroidal expansion in chick was 0.02/($W \cdot sr^{-1} \cdot m^{-2}$).

Results from the LED condition indicate that axial growth can be slowed in low radiance conditions as long as there is sufficient S-cone stimulation. A high radiance, low S-cone stimulation condition was not tested, though this would be achieved with red monochromatic light and the data from earlier experiments can be compared. As the data stands, S-cone stimulation can slow axial growth even with low radiance, but it cannot be determined if radiance alone impacts axial growth.

4.2 Comparison to LED Model

The foundational study for this experiment, Rucker et al. (2018), examined stimuli in an LED stand-alone model. Our experiments were based around the spectral profile of the

computer monitor, which produced significantly less blue light across all sources compared to the LED model.

As seen in Rucker et al. (2015, 2018), the high brightness LED source reduced axial growth in the B/Y condition, which had a significant blue light component. Rucker et al. (2018) indicated that a Yellow condition which lacked a blue component caused an increase in axial length and more myopia relative to the blue rich, B/Y stimulus. In our experiments, the B/Y stimulus produced less growth in the HMon and HLED conditions, where the illuminance and cone excitation were similar to that of the prior Rucker experiments. When data from all the monitors and LEDs was combined, the B/Y stimulus alone did not significantly impact axial length changes. This is likely due to the low intensity blue component in the Mon and CLED conditions compared to experiments by Rucker et al (2015, 2018). These results suggest that a low intensity B/Y stimulus is insufficient to reduce axial growth, and the source of the light must have a significantly bright blue component. The Mon source, which was a conventional computer monitor at average brightness, was not able to slow axial growth despite using a B/Y stimulus.

In Rucker et al. (2018), with light modulated at 0.2 Hz, the choroid expanded least in the B/Y condition, and thickened most in the Lum condition. Our experiments showed similar results; the Lum stimulus caused the greatest increase in choroidal thickness, and the B/Y conditions slowed choroidal expansion. In Lin et al. (2020), with a steady light source, choroid expanded least in blue light and expanded most in red light. In tree shrew experiments using bright amber light with significant L-cone stimulation, choroid expanded

significantly compared to a blue flicker condition (Khanal et al., 2021). In all these experiments, the choroid expanded in response to strong L-cone stimulation. While we observed a relationship between choroid thickness and the ratio of L-cone stimulation to radiance, the experiments above did not study radiance effects.

4.3 Clinical Implications

These experiments were performed in chick and further research is needed to determine if they can be translated to humans. From a clinical perspective, there are some challenges in recommending bright displays with a significant blue light component to children, especially with the current climate surrounding blue-blocking glasses. The current literature suggests there are no real health benefits regarding eye health or sleep rhythm from wearing blue-blocking lenses in a variety of lens wear situations. While some patients report subjective benefits, the glasses performed no better than the control groups (Lawrenson et al., 2017). Due to the fact that current computer monitors provide little blue light in general, blue-blocking lenses are currently unlikely to impact myopia development in regard to computer use. The use of blue-blocking lenses with high intensity computer monitors is likely to negate the potential advantage of these monitors in children and adolescents.

4.4 Limitations

The basis for this experiment was the LED model in Rucker et al (2015, 2018), and there were challenges in creating a similar environment with computer monitors. One of the greatest hurdles was matching the illuminance and cone excitation of the monitor to the LED

lights. The maximum brightness of the conventional monitor was about 20% that of the LED lights in previous experiments, and the blue light from computer monitors has the weakest output of the RGB components relative to that of the LEDs. As a result, we were limited in the conclusions we could draw from the differences in cone excitation. However, since the conditions are matched for intensity (low and high), temporal frequency, and contrast, it is clear that the color of the light source matters, particularly with regard to the intensity of the blue component and the S-cone excitation it induces relative to the L-cone excitation.

The D-cone and UV-cone further complicate the comparison between conditions. The D-cone has a broad spectral sensitivity that spans that of the L-cones and M-cones, where the D-cone excitation tends to be similar to that of the sum of the L- and M-cones. The D-cone is not involved in color processing, and is only involved in detecting luminance changes (Osorio et al., 1999) . All the low brightness conditions and high brightness conditions were matched within groups by illuminance, so it is unlikely the D-cone contributed to differences within groups.

The HMon condition had much higher UV-cone stimulation than the HLED condition, which may have affected emmetropization. Previous research has indicated that the UV-cone can impact emmetropization in chick when compensating for hyperopic lenses of +10 D or +20 D (Hammond and Wildsoet, 2012) under illumination conditions of 200 lux. Our experiments did not use lens compensation as a mechanism, so while it is unclear whether the UV-cone affected emmetropization, it is a possible confounding factor. The

results should be interpreted as being potentially due to an increase in UV-cone excitation as well as S-cone excitation.

The computer monitors were side-mounted to the cage, whereas the LED lights were top-mounted. The directionality of the light could have had an impact on the overall light exposure of the chickens.

The refresh rate of the monitors was at 60 Hz, and while that is above the critical flicker frequency of chickens, there is the possibility that it had a physiological effect. All these limitations may be remedied with new computer monitor technology, which has become widely available in consumer electronics in the last few years. Higher brightness levels, especially in the S-cone range, higher refresh rates, as well as top-mounting of the monitor would give a more even comparison between the LED and the monitor conditions.

This experiment was only run at 0.2 Hz, and as we have seen in prior experiments temporal frequency has a big impact on choroidal and axial responses.

4.5 Summary

The majority of consumer electronics currently available have displays that are most similar to the monitor in the low brightness Mon condition. It had the lowest brightness and S-cone and UV-cone stimulation of any source, (excluding CLED), and caused increased eye growth. The high brightness monitor slowed axial elongation and increased choroidal thickening. The main difference between HMon and HLED was that the HMon condition had

a relatively higher L-cone activation, but other factors such as the refresh rate or the direction of the incident light have not been accounted for. New display technology entering the consumer market has higher brightness and higher blue intensity levels, and if these results are translatable to humans, then the high brightness monitor may have the ability to slow myopia development. Novel computer monitor-based therapies that protect against myopia development may be viable with high brightness, high blue monitors but research in other animal models is necessary before this becomes a reality.

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