A PILOT STUDY OF SHORT-TERM CHANGES IN OCULAR COMPONENTS IN MYOPIC AND NON-MYOPIC YOUNG ADULTS AFTER LIGHT THERAPY

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

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December, 2016

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Laura Chan

New England College of Optometry, 2016

PURPOSE

The purpose of this study is to investigate the effect of varying lux during a reading task on short term changes in axial length and choroid thickness in human eyes.

METHODS

A total of thirty-nine young adults (mean age ± SD; 24.26 ± 1.33 years) participated in this study. Non-cycloplegic distance refractive error was measured using the Grand Seiko WR-5100K. Twenty were myopes (mean Rx = -3.19 D) and nineteen were non-myopes (mean Rx = +0.15 D). The Haag-Streit Lenstar LS 900 was used to measure axial length (AL) at baseline, and at 0, 5, and 10 minutes following a 20 minute reading task, in room light (300-500 lux) and bright light (~10 000 lux via a Seasonal Affective Disorder (SAD) lamp). Choroid thickness (ChT) was manually determined by two independent experimenters from the Lenstar data. For data analysis, repeated measures analysis of variance (ANOVA) was used, with change in AL and ChT over time, lighting condition, and refractive group as the main factors.

RESULTS

With data from all subjects combined, there was an interaction between time and lighting that approached significance ($p = 0.064$). No significant differences in axial length were found between room light and bright light at any time point. There were no significant differences between refractive groups, though there was a suggestion that following the bright light condition, AL decreased in myopes and increased in non-myopes. For all subjects with usable choroid data ($n = 31$), there was no significant interaction between time and lighting condition. For the hour prior to testing, the majority of subjects performed near tasks (61.6%), compared to intermediate/far tasks (38.4%). However, there were no significant differences in axial length changes in room light based on near vs. intermediate/far viewing before testing ($p > 0.05$).

CONCLUSIONS

Based on our results, we cannot yet recommend increased indoor lighting using SAD lamps as a viable therapy to protect against myopia. Future research in children using SAD lamps for a longer duration is needed to determine their efficacy in the prevention of myopia.

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INTRODUCTION

1.1. Importance of Myopia

Myopia is the result of a discrepancy between the power of the refractive ocular surfaces and the axial length of the eye, resulting in blurred distance vision. Myopia typically begins around 8-10 years of age and progresses at an average rate of 0.5 D per year, with slowing and eventual stabilization around 15 or 16 years of age (The COMET group, 2013; Thorn et al., 2005; Goss et al., 1983). Treatment for myopia involves presenting a clear image to the retina via spectacle or contact lens correction, or laser refractive surgery. However, these methods do not slow the growth of the eye and the myopia may continue to progress.

Globally, a sixth of the world's population is myopic with the prevalence increasing markedly over time (Holden et al., 2015). The highest prevalence (80-90%) is found in urban East Asian populations (Pan et al., 2011; Rudnicka et al., 2016). The prevalence of myopia has also been increasing in the United States., with one third of the U.S. population being myopic (Vitale et al., 2009). An estimated $3.8 billion dollars was spent annually in 2000 to correct for myopia in the U.S. (Vitale et al., 2006).

Myopia, especially later in life, is often accompanied by sight threatening conditions (e.g. retinal detachments, glaucoma, myopic macular degeneration), and may contribute to impaired ocular health and compromised functional quality of life (Saw et al., 2005; Holden et al, 2015; Wang et al., 1998; Davidson et al., 2011; Rudnicka et al., 2016). Therefore, it is important to identify a way to slow the progression or to prevent the development of myopia.

1.2. Myopia Risk Factors – Genetic versus Environmental

Although the precise mechanism of myopia is unknown, potential factors involve both genetic and environmental components (Morgan et al., 2005; Morgan et al., 2012; Wang et al., 2015). Studies investigating myopia in twins have shown refractive error is well correlated in monozygotic twins, with significantly smaller correlations in dizygotic twins (Hammond et al., 2001; Dirani et al., 2006; Tsai et al., 2009; Lopes et al., 2009; Hysi et al., 2010; He et al., 2008). The risk of becoming myopic is greater in children with one or two myopic parents compared to no myopic parents (Mutti et al., 2002; Saw et al, 2006; Pacella et al., 1999; Zadnik et al., 1994; Lyhne et al., 2001). Several genetic loci have been reported to be associated with high myopia (Tang et al., 2014; Farbrother et al., 2004). However, myopia is a complex trait, associated with multiple genetic loci and various environmental factors.

Currently, the two most studied environmental risk factors for myopia are near work and time spent outdoors. School children spend a large proportion of their day performing near activities. Many studies have investigated excessive near work as a contributor to myopia development and progression. However, its role is still debated (Ip et al., 2008; Mutti et al., 2002; Saw et al., 2002). Studies in adults have shown transient increases in axial length during sustained accommodation (Woodman et al., 2012; Woodman et al., 2015, Mallen et al., 2006; Read et al., 2010), which if found in children could be related to subsequent development of myopia (Gao et al., 2002).

Studies using questionnaires have found that myopes spend less time outside than non-myopes, suggesting that increased time spent outdoors may protect against myopia (Rose et al., 2008; Guggenheim et al., 2012). A few intervention trials have shown that more time spent outdoors decreases the risk of development of myopia in children (Wu et al., 2013; Jin et al.,

2015; He et al., 2015). Overall, more studies show significant associations with time outdoors and myopia, than with near work and myopia.

On the contrary, the first study to show an interaction between genetic and environmental factors found that near work rather than outdoor activity was the key factor. Tkatchenko et al. (2015) reported that the expression of the APLP2 gene was significantly associated with an increased susceptibility for myopia in children with a high number of hours of reading ($p = 4.0 \times 10^{-3}$). No significant interaction was found between this gene and time spent outdoors. Two previous studies showed a high risk of developing myopia in children with two myopic parents in combination with few hours of outdoor activity (Jones-Jordan et al., 2010; Zhang et al., 2015). Fourteen hours per week of outdoor activity decreased the risk of myopia to that equal to a child with one or no myopic parents (Jones, et al., 2007). Thus, it appears that environmental factors may alter the risk of myopia despite the presence of non-modifiable genetic and familial risk factors.

1.3. Myopia and Time Spent Outdoors

As mentioned above, recent research has identified limited outdoor activity as an environmental risk factor related to myopia development in children (Deng et al., 2010; Rose et al., 2008; Dharani et al., 2012; Wu et al., 2013; Sherwin et al., 2012; Guggenheim et al, 2012; Mutti et al., 2002; Read, 2015). Myopic children report less time spent outdoors than non-myopic children, especially during the school year (Deng et al., 2010). Being outdoors rather than physical activity was associated with decreased myopia risk, suggesting that light intensity may be a key factor (Rose et al, 2008).

Another line of research may relate time outdoors to myopia. Seasonal differences in myopia progression and axial elongation have been reported, with less myopic shift and slowed

eye growth in the summer compared to winter months (Gwiazda et al, 2014; Fulk et al., 2002; Donovan et al, 2012). Gwiazda et al. (2014) suggested that increased time outdoors and/or decreased near work during the summer months may contribute to the seasonal changes in myopic progression.

Many factors have been proposed to account for the slowed eye growth and less myopia found with time spent outdoors, including increased depth of focus, greater viewing of distant targets, increases in dopamine, and high light intensity (Ashby et al., 2010; Karouta et al., 2015; French et al., 2013; Flitcroft, 2012; Norton et al., 2016). Average outdoor light intensity ranges from 10,000 to 100,000 lux on a cloudy to sunny day, respectively, whereas typical indoor light may range from 100 to 500 lux for visual tasks and office work (The Engineering Toolbox, 2016). Indoor lighting can be increased to approximately 10,000 to 20,000 lux, but it never reaches the levels found outside (The Engineering Toolbox, 2016).

1.4. Support for Using Light Interventions during the School Year

Light interventions for myopia control in children may be most beneficial during the time of year that children are in school, given that myopia progression is twice as fast during the school year compared to the summer (Gwiazda et al., 2014; Fulk et al., 2002; Donovan et al., 2012). Recently, a few studies have tested light interventions during school time in China.

Three studies added extra outdoor time to the school day. One study found that an intervention of 80 minutes per day of extra outdoor recess time produced a significant decrease in the prevalence of new onset myopia in the intervention group (8.4%) compared to the control group (17.7%, $p = 0.001$) (Wu et al., 2013). There was no effect on the progression of myopia in children who were already myopic. A study on 6-year old children added 40 minutes of outdoor activity at school compared with usual activity, and showed a reduced incidence of myopia in the

intervention group (30.4%) compared to the controls (39.5%; $p < 0.001$) across 3 years (He et al., 2015). Another study found that an intervention of an additional two 20-minute recess programs in children 6-14 years old resulted in a significantly lower incidence of myopia onset and slowed axial elongation, compared to controls (standard program: two 10-minute outdoor recesses) (Jin et al., 2015). These studies suggest that implementation of light therapy prior to the onset of myopia in children may be beneficial.

1.5. Indoor Light Therapy

The effect of increased indoor light levels on eye growth and myopia has been mainly studied in animal models. The animal study that is most relevant to human myopia (because of the species studied and the type of myopia induced) found that increasing lux did not alter the degree of lens-induced myopia in rhesus monkeys, a species that is evolutionarily similar to humans (Smith et al., 2013). Unlike the several studies in animals, the protective effect of light on eye growth and myopia has been shown to a limited extent in humans.

One study compared higher intensity versus standard lighting in schools (Hua et al., 2015). Results showed significantly decreased development of new onset myopia in children in the high light schools (4%) compared to the standard schools (10%, $p = 0.03$), with no effect on progression of myopia. Given weather and seasonal differences, it may be easier to implement indoor light therapy for myopia control.

Apart from Hua et al. (2015) cited above, the effect of increased lux using indoor light on the development of myopia in humans remains largely unexplored. However, bright indoor light has been used as a therapy for other conditions. The use of bright indoor lighting of 10,000 lux has been most widely used as an accepted treatment for Seasonal Affective Disorder (SAD), a type of depression experienced seasonally especially during the winter months (Meesters et al.,

2011; Wileman et al., 2001). Unlike the effect on mood, the effect of bright indoor lighting on eye growth in human eyes is not well studied. Indoor light therapy and/or the use of outdoor sunlight may offer a competitively lower cost for myopia prevention therapy compared to the yearly cost for spectacles, specialty contact lenses, or drug therapy (Ramamurthy et al., 2015). The current study was designed as a pilot to investigate the effect of bright indoor lighting on ocular components.

1.6. Purpose & Hypothesis

The purpose of this study is to investigate the effect of varying indoor light intensity on short term changes in ocular components, specifically axial length and choroid thickness, in myopic and non-myopic young adult eyes after reading. Our hypothesis is that reading in room light will induce a transient increase in axial length and that reading in bright light will result in smaller or no increases in axial length.

MATERIALS AND METHODOLOGY

2.1. Subjects

Thirty-nine young adults (mean ± SD age, 24.2 years ± 1.5 years) were tested, with 25 females and 14 males. Ethnicity was determined through self-reported questionnaire: 21 subjects identified as Caucasians, 12 as Asians, 3 as Indian, 1 as American Indian or Alaskan Native, and 2 subjects identified as other ethnicity. The mean spherical equivalent refraction (SER) of both eyes was -1.56 D ± 2.22 D for all subjects. There were 19 myopes with a mean SER of both eyes of -3.19 D ± 2.01 D, and 20 emmetropes with a mean SER of both eyes of +0.15 D ± 0.30 D. Myopia was defined as a SER of both eyes of at least – 0.50 D.

Subject recruitment was conducted at the New England College of Optometry via electronic advertisement. Eligibility requirements included a refractive error between +2.00 D and -8.00 D inclusive, astigmatism ≤ 1.50 D and anisometropia ≤ 1.00 D, no remarkable ocular history or surgery, and no history of light-induced seizures.

2.2. Apparatus

Autorefraction was performed using the Grand Seiko Co., Ltd, *Binocular Autorefractor/Keratometer WR-5100K* to determine the distance refractive error. The manufacturer's manual states that the measurement capabilities of the WR-5100K range from +22.00 D to - 22.00 D inclusive. Davies et al. (2003) reported that this autorefractor had an average intra-session repeatability of 0.11 D for the spherical component and 0.13 D for the cylindrical component.

Ocular biometric parameters were measured using the Haag-Streit *Lenstar LS 900*. The Haag-Streit Lenstar LS 900 is a noncontact optical reflectometer and keratometer that has been

available since 2009. The Lenstar uses optical low-coherence reflectometry to measure ocular biometry (Shammas et al., 2012). The manufacturing specification states that the Lenstar's axial length measurement range is 14-32mm. A recent study reported an in vivo repeatability of +/- 0.013mm (Read et al., 2011). Choroidal thickness can be calculated using the data provided by the Lenstar, and the method of calculation in this study is provided in the Data Analysis section below.

Indoor lighting was obtained using a floor lamp for the room light condition, with the addition of a DL930 Day-Light Seasonal Affective Disorder (SAD) Lamp in the bright light condition. According to the manufacturer, the lamp emits 7,000-10,000 lux of light via three fluorescent light tubes. It is advertised as ultraviolet-filtered, glare-free and flicker-free. The manufacturer's recommendations for treating seasonal affective disorder are 20 minutes per day for 2 weeks. Parameters for the experimental and control conditions in the current study are summarized below.

Indoor light levels were measured lateral to each of the subject's eyes using the *LX1010B* lux meter. This meter is commercially available with a sampling rate of 0.4 seconds and a measurement range of 0-50,000 lux ± 5% (Chu, 2015). Room lighting was between 300 and 500 lux and for the bright light condition, obtained using the SAD lamp in addition to the normal room lighting, lighting was between 9,000 and 10,000 lux.

2.3. Procedure

The study received approval from the Institutional Review Board at the New England College of Optometry. Prior to beginning the study, each subject was required to read and sign a written informed consent form in order to participate in the study. Subjects were required to abstain from contact lens use for 24 hours prior to and throughout the duration of the experiment.

A Clinical Data Questionnaire was used to gather demographic and health history information via self-report from each subject (Appendix 1), followed by a 24 Hour Activity Log that listed self-reported activities of work/school, reading/writing, computer use, television or movie, other indoor activity, driving, outdoor activity, or sleep (Appendix 2).

The non-cycloplegic spherical equivalent refraction (SER), calculated from measurements of sphere and cylinder taken from the Grand Seiko Autorefractor, was used to determine the power of the lens placed in the trial frame for each eye. This was worn by the subject throughout the experiment, including during each reading condition. Near Log MAR visual acuity using the SER in the trial frame was measured in room lighting at 33 centimeters to ensure a binocular visual acuity Snellen equivalent of 20/25 or better. All axial length measurements were obtained using the Haag-Streit Lenstar on the right eye only with the left eye unpatched and looking in the distance.

Figure 1 shows the experimental setup for the (a) room lighting condition, (b) bright lighting condition, and (c) the proximity of the Lenstar to the experimental testing area where subjects were asked to sit and read. The subjects maintained a 30 cm distance from the lamp using a string attached to the trial frame. This also ensured a constant reading distance with the reading material placed at a 45 degree angle on a stand situated beneath the lamp base. Personal reading material was allowed if it consisted of black text with white background and was of standard 12-font size text, with no pictures. Otherwise, appropriate reading material was provided. Baseline ocular measurements were obtained using the Lenstar, followed by a 20 minute reading condition in room lighting (Figure 2). Subjects were asked to read continuously for 20 minutes, maintain a constant distance from the lamp, and were instructed to refrain from looking away from the reading material. Immediately after completion of the reading condition,

ocular measurements were taken using the Lenstar (at 0 minutes), as well as 5 and 10 minutes after reading. Subjects were then given a 10 minute break, when the subject was instructed to avoid looking at near targets. This was followed by baseline measurements for the bright light condition. The subjects then read in the bright light condition, using the room lighting with the addition of the 10,000 lux SAD lamp, and following the same instructions as in the room light condition. Measurements at time = 0, 5, and 10 minutes following the bright light condition were taken in the same manner as following the room light condition.

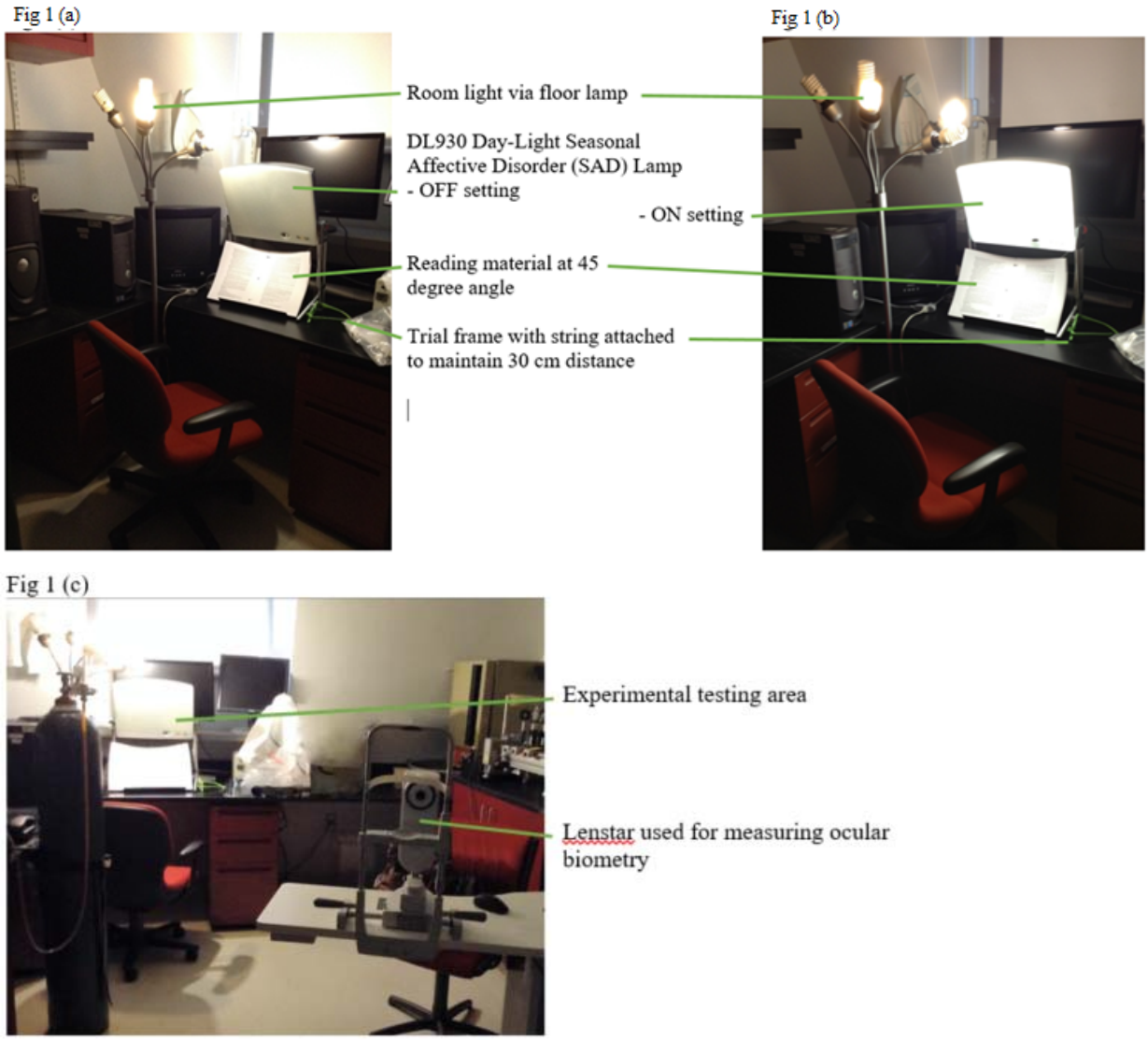


Figure 1: Experimental Set-up: (a) room light condition, (b) bright light condition, (c) testing room showing proximity of experimental testing area to Lenstar for biometry measurements.

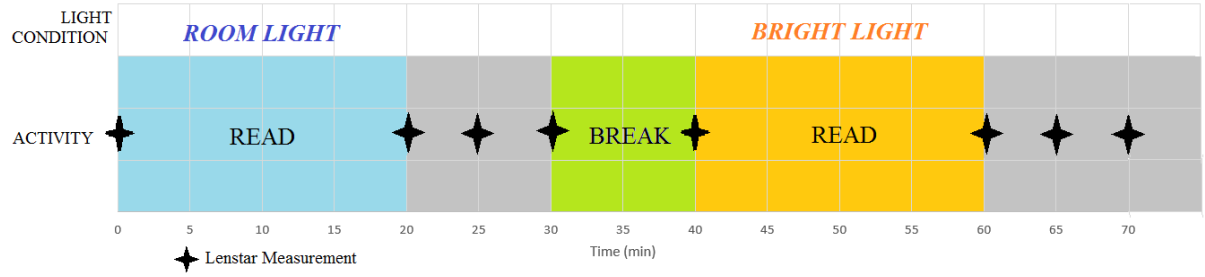


Figure 2: Schematic diagram of the experimental procedure.

2.4. Outcome Measures

The primary outcomes investigated in this study were changes in axial length and choroid thickness, relative to baseline, after reading with room and bright lighting.

2.5. Data Analysis

Subject Demographics

Subject demographic information (e.g. gender, age, and ethnicity) was collected via questionnaire prior to beginning the study. Baseline means and standard deviations (SD) were calculated for age, spherical equivalent, axial length and choroid thickness for all subjects and within refractive groups. The percentages of subjects by gender and ethnicity were also presented, overall and by refractive group. The subject demographics were analyzed by refractive group (non-myopic or myopic) using an unpaired student t-test or chi-square test, depending on whether the data were continuous or categorical.

Axial Length

Axial length from the Lenstar was defined as the distance from the anterior corneal epithelium to the retinal pigment epithelium (RPE), and in the current study we measured the right eye of each subject (Figure 3). Unreliable measurements from the Lenstar (e.g. blinks, eye movements), and any measurements that were more than 0.05 mm from the majority of the measurements, were manually excluded to calculate the average axial length. The limit of 0.05 mm was chosen because the repeatability of the Lenstar measurements is reported to be ± 0.013 mm (Read et al., 2011). Repeated measures analysis of variance (ANOVA) was used, with change in axial length over time, lighting condition, and refractive group as the main factors.

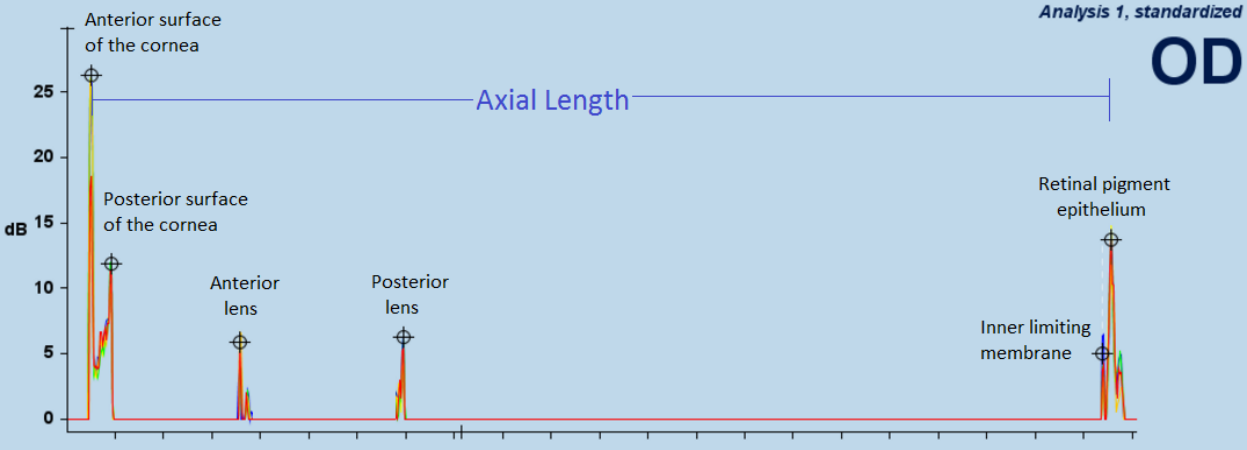


Figure 3: A-scan signal peaks from the Lenstar biometer for the entire eye. Axial length is measured from the anterior surface of the cornea to the RPE.

Choroid Thickness

The choroid measurements from the Lenstar were independently measured by two experimenters using the A-scan data by manually determining the distance between peaks representing the RPE and the junction between the choroid and sclera (Figure 4). Thus, axial length and choroid thickness measurements were not completely independent when measured with the Lenstar. Consensus between the two investigators was necessary to resolve discrepant choroid measurements. Measurements lacking a peak corresponding to the RPE or choroid-scleral junction were excluded from choroid calculations. Repeated measures ANOVA was used, with change in the choroid thickness over time, lighting conditions, and refractive groups as the main factors. A total of three myopic subjects and five non-myopic subjects were excluded from statistical calculations for choroid thickness due to unreliable or missing RPE and/or choroid-scleral junction peaks.

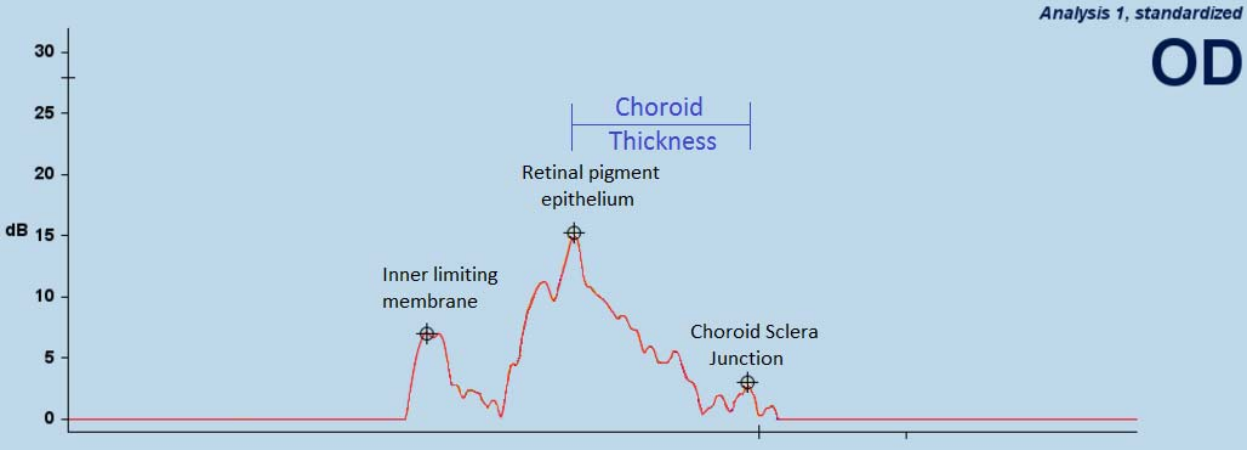


Figure 4: Magnified portion of the posterior eye showing individual A-scan signal from the Lenstar biometer. Choroid thickness is measured from the RPE to the choroid-scleral junction.

Activity Log

The 24-Hour Activity Log (Appendix 2) was used to determine the activities performed one hour prior to testing. Subjects were asked to report activities using ten categories; reading, writing, computer use, school, work, television/movie, other indoor, driving, outdoor activity, and sleep. These categories were further combined into four general categories; 1) indoor activity (near viewing), 2) indoor activity (mostly intermediate and far viewing), 3) outdoor activity, 4) sleep.

Other Analyses

Correlations between changes in axial length and changes in choroid thickness were analyzed using linear regression and shown on a scatter plot to observe trends at each time point after reading compared to baseline, for the two lighting conditions separately.

RESULTS

3.1. Subject Demographics

The subject demographics for all subjects overall and by refractive group are summarized in Table 1. Thirty-nine young adults with a mean ± SD age of 24.26 ± 1.33 years were tested, as shown in Table 1. Myopia was defined as having an SER of < -0.50 D. There was no significant difference in gender ($p = 0.43$) or age ($p = 0.83$) between refractive groups. The majority of the subjects in the non-myopic group were Caucasian (65%), whereas the majority of the subjects in the myopic group were Asian (57.89%), resulting in a significant ethnic difference ($p = 0.01$).

The mean SER of all subjects was -1.56 ± 2.22 D; 19 non-myopes had a mean SER of +0.15 D ± 0.30 D, and 20 myopes had a mean SER of -3.19 D ± 2.01 D. As expected, there was a significant difference in the SER between refractive groups ($p < 0.001$).

There also was a significant difference in the baseline axial length measurements between refractive groups ($p < 0.001$); the mean axial length of the myopes (25.21 mm ± 0.96 mm) was significantly longer ($p < 0.001$) than the mean of the non-myopes (23.52 mm ± 0.71 mm) (Table 1).

The mean baseline choroid thickness for all subjects ($n = 31$) was 297.29 ± 71.21 um. The difference in baseline choroid thickness approached significance when comparing refractive groups at baseline ($p = 0.055$), with the choroid in the myopic group ($n = 17$) slightly thicker (304.49 um ± 67.93 um) than the non-myopic group ($n = 14$) (288.54 um ± 76.63 um) (Table 1).

Table 1: Subject demographics at baseline prior to testing.

	Total n = 39	Non-Myopes n = 19	Myopes n = 20	P-value
Gender [n (%)]				
Female	25 (64.10%)	11 (57.90%)	14 (70.00%)	0.43 [C]
Male	14 (35.90%)	8 (42.11%)	6 (30.00%)	
Age (years) mean (SD)	24.26 (1.33)	24.30 (1.30)	24.21 (1.40)	0.83 [T]
Ethnicity [n (%)]				
Caucasian	21 (53.85%)	13 (65.00%)	8 (42.11%)	0.01 [C]
Asian	13 (33.33%)	2 (10.00%)	11 (57.89%)	
Other	5 (12.82%)	4 (20.00%)	1 (5.26%)	
Spherical equivalent refraction (D) (OU) *Mean (SD)*	-1.56 (2.22)	+0.15 (0.30)	-3.19 (2.01)	$P < 0.001$ [T]
Axial Length (mm)				
Mean (SD)	24.39 (1.18)	23.52 (0.71)	25.21 (0.96)	$P < 0.001$ [T]
Choroid Thickness (um)	n = 31	n = 14	n = 17	
Mean (SD)	297.29 (71.21)	288.54 (76.63)	304.49 (67.93)	0.055 [T]

C: Chi-square test

T: T-test

3.2. Axial Length

With all subjects combined, there was an interaction between time and lighting that approached significance ($p = 0.064$). The axial length for all subjects decreased after reading in room lighting, and was most apparent at 5 minutes following reading (Figure 5). In bright lighting, an increase in axial length was most apparent at 0 minutes followed by return to baseline. In other words, there was a suggestion that axial length was affected by the level of lighting and varied depending on the time. There were no significant differences between room and bright light conditions at any time point. Furthermore, there was no significant difference between room baseline and bright baseline axial length measurements.

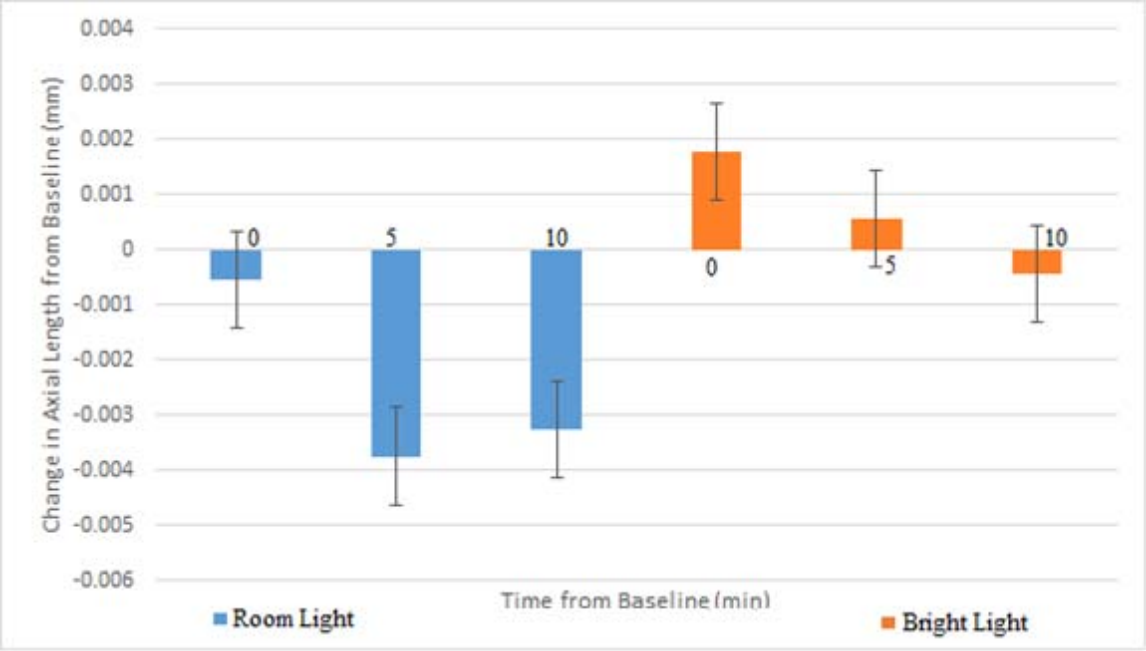


Figure 5: Mean axial length change (mm) compared to baseline at different time intervals following reading under room (blue bars) and bright lighting (orange bars) conditions for all subjects (n=39). Error bars show standard errors.

There were no significant differences between refractive groups. Figure 6 shows the change in axial length for myopes and non-myopes in room and bright light conditions. Axial length decreased for both myopes and non-myopes in room light. In bright light axial length in the myopes decreased and increased in the non-myopes. However, these changes were small and did not reach statistical significance

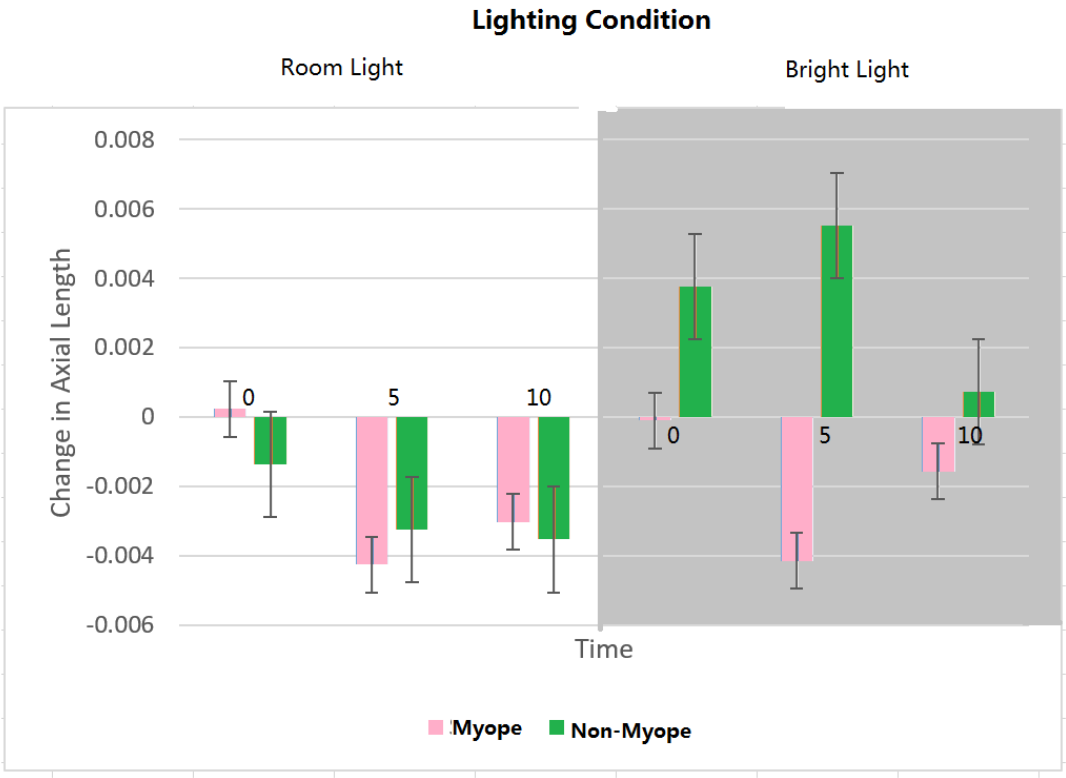


Figure 6: Mean axial length change (mm) compared to baseline at different time intervals following reading under room (green bars) and bright lighting (pink bars) conditions for myopes (n = 20), and non-myopes (n = 19). Error bars show standard errors.

Table 2 shows mean axial length in millimeters for all subjects and by refractive group for each time point in the room and bright light conditions. Non-myopic eyes were significantly shorter than myopic eyes, overall and at all time points ($p < 0.001$).

Table 2: Mean axial length (mm) at baseline and timed measurements after reading in room light and bright light for non-myopes (n = 19) and myopes (n = 20).

Lighting Condition	Refractive Group	Time			
		Baseline	0 min after reading	5 min after reading	10 min after reading
Room Light Mean ± SD	All Subjects	24.3878 ±1.1830	24.3872 ±1.1837	24.3840 ±1.1837	24.3845 ±1.1853
	Non-Myope	23.5197 ±0.7114	23.5183 ±0.7110	23.5164 ±0.7101	23.5161 ±0.7123
	Myope	25.2125 ±0.9609	25.2127 ±0.9616	25.2082 ±0.9645	25.2095 ±0.9658
Bright Light Mean ± SD	All Subjects	24.3826 ±1.1841	23.3843 ±1.182	24.3831 ±1.1802	24.3821 ±1.1822
	Non-Myope	23.5145 ±0.7122	23.5183 ±0.7127	23.5200 ±0.7106	23.5153 ±0.7105
	Myope	25.2072 ±0.9634	25.2071 ±0.9603	25.2030 ±0.9635	25.2056 ±0.9619

3.3. Choroid Thickness

For all subjects with usable choroid data (n = 31), there was no significant interaction between time and lighting. Although changes were not significant, there appeared to be a delayed increase in choroid thickness after reading in room lighting, and a delayed decrease in choroid thickness after reading in bright light (Figure 7). There was no significant difference between room baseline and bright baseline measurements.

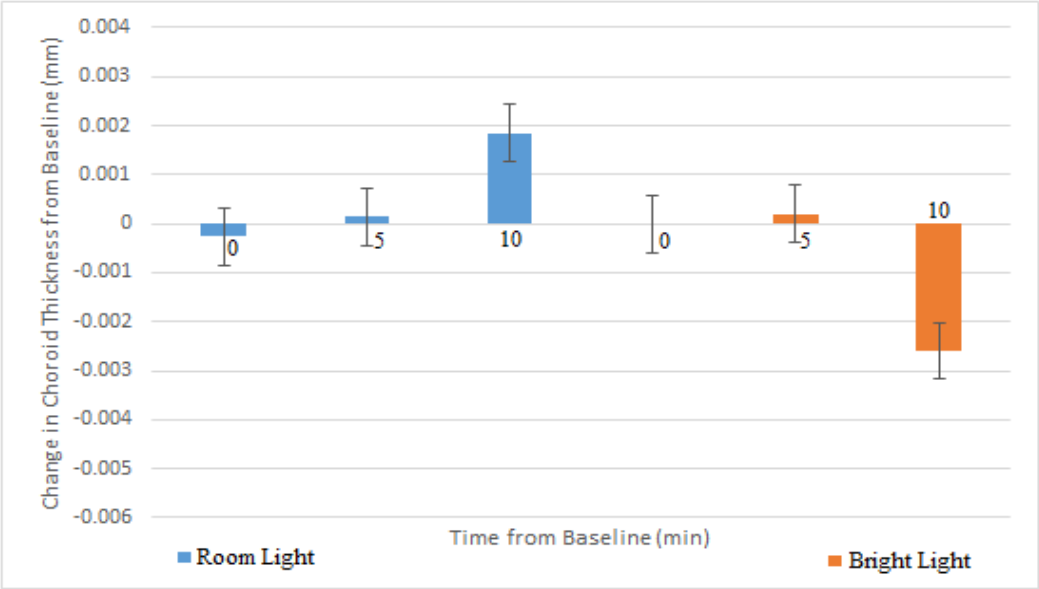


Figure 7: Mean choroid thickness change (mm) compared to baseline at different time intervals following reading under room (blue bars) and bright lighting (orange bars) conditions for all subjects (n=31). Error bars show standard errors.

Table 3 shows the mean choroid thickness in microns for all subjects, and by refractive group for each time point in the room and bright light conditions. Myopic subjects had thicker choroids than non-myopic subjects at all time points.

Table 3: Choroid thickness (um) for baseline and timed measurements after reading in room and bright light conditions for non-myopes (n = 14) and myopes (n = 17).

Lighting Condition	Refractive Group	Time			
		Baseline	0 min after reading	5 min after reading	10 min after reading
Room Light Mean ± SD	All Subjects	297.29 ±71.21	297.02 ±73.46	297.42 ±77.65	299.13 ±75.40
	Non-Myope	228.54 ±76.63	289.20 ±82.55	292.61 ±78.87	297.35 ±83.00
	Myope	304.49 ±67.93	303.46 ±66.97	301.39 ±78.83	300.60 ±71.10
Bright Light Mean ± SD	All Subjects	300.19 ±74.40	300.39 ±74.19	297.60 ±74.81	297.12 ±78.67
	Non-Myope	294.91 ±82.50	294.27 ±79.74	292.72 ±74.49	296.95 ±79.99
	Myope	304.54 ±68.31	305.42 ±71.37	301.61 ±77.13	297.27 ±80.03

3.4. Correlation between Changes in Axial Length and Changes in Choroid Thickness

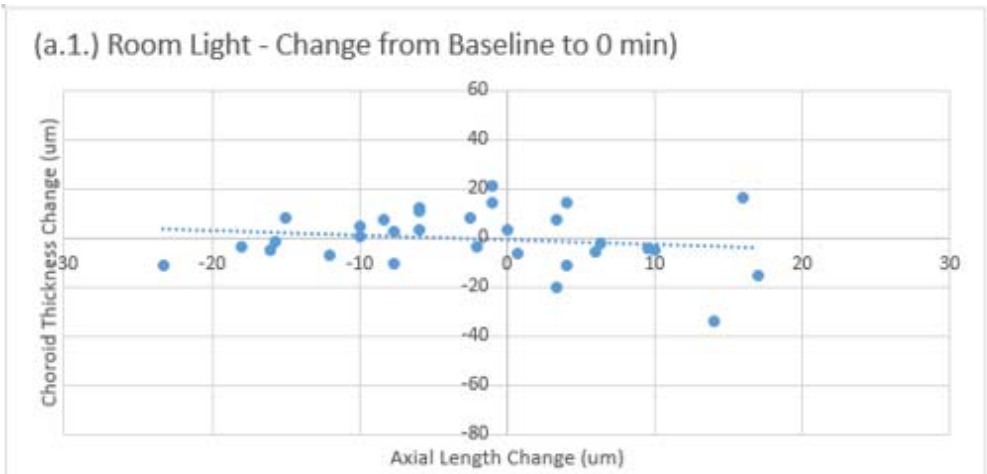
Changes in mean axial length and choroid thickness at each time point are summarized for all subjects with paired usable data (n = 31) for room and bright light in Table 4. To facilitate comparison between choroid thickness and axial length values, axial length is presented in microns. An increase in axial length or choroid thickness is represented by a positive number, whereas a decrease in either parameter is represented by a negative number. In three of the six comparisons the mean change in axial length and choroid thickness was in the opposite direction, whereas in the other three the changes were in the same direction, all by small amounts.

Table 4: Changes in axial length (AL) and choroid thickness (ChT) in room and bright light conditions for all subjects (n = 31).

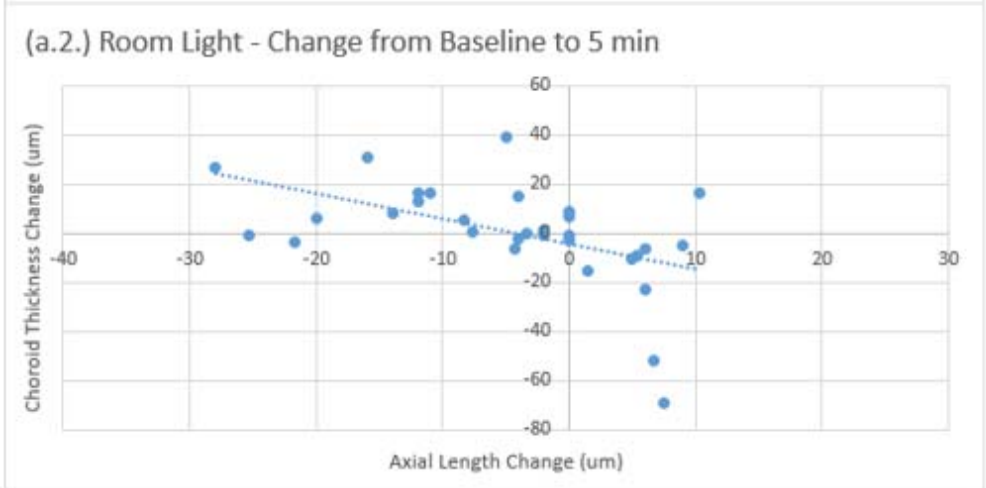
Lighting Condition	Ocular Parameter	Time		
		0 min after reading	5 min after reading	10 min after reading
Room Light	AL (um)	-0.6	-3.8	-3.3
	ChT (um)	-0.3	0.1	1.8
Bright Light	AL (um)	1.8	0.6	-0.4
	ChT(um)	0.2	-2.6	-3.1

Figure 8 presents scatter plots of axial length and choroid thickness changes in microns in the room light (a.1., a.2., a.3.) and in the bright light (b.1., b.2., b.3.) conditions at each time point for all subjects. All of the correlations were in the negative direction, suggesting that changes in axial length and choroid thickness were in the opposite direction. However, axial length and choroid thickness are not completely independent with the given Lenstar measurements, due to the measurement of axial length to the RPE and not to the posterior sclera.

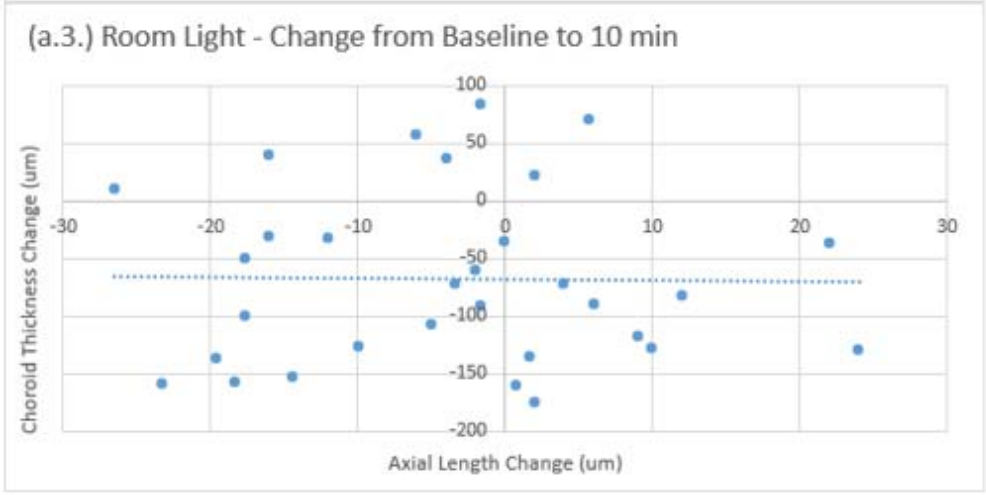
Out of the six scatter plots, only one (Figure 8 – a.2.) showed a moderately strong correlation (r = -0.500). Decreases in axial length were accompanied by increases in choroidal thickness for most subjects.



r = -0.152



r = -0.500



r = -0.014

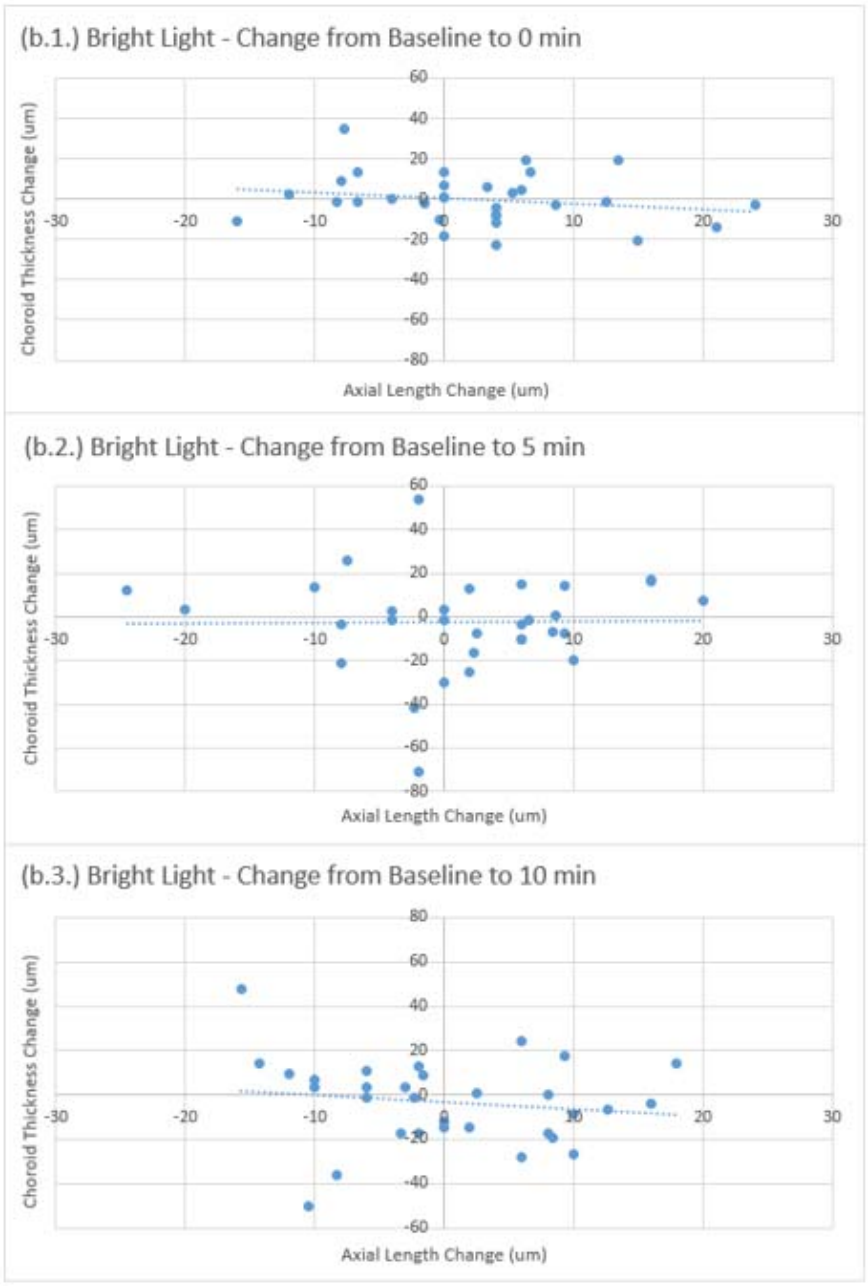


Figure 8: Axial length change versus choroid thickness change for all subjects (n = 31): (a) following room light condition compared to baseline , at (a.1.) 0 min, r = -0.152, (a.2.) 5 min, r = -0.500, (a.3.) 10 min, r = -0.014; (b) following reading in bright light compared to baseline, at (b.1.) 0 min, r = -0.006, (b.2.) 5 min, r = -0.014, (b.3.) 10 min, r = -0.153.

3.5. Activity Log

For the hour prior to testing, the majority of subjects performed near tasks (61.6%), compared to intermediate/far tasks (38.4%). No significant change in axial length was found between near and far viewing activities at any time point for the room light condition, which was first, suggesting that prior activity did not affect the results of the experiment.

3.6. Pupil Sizes

Data from a random sample of 5 myopes and 5 non-myopes were reviewed to see if lighting affected pupil size. According to the User Manual, the Lenstar LS 900 measures pupils from 2 to 13 mm, with a display resolution of 0.01 mm. Pupil diameters in this sample ranged from x to y, with a mean of z, and more importantly, did not vary by lighting condition. Thus, axial length and choroid measurements were unlikely to have been affected by pupil size.

DISCUSSION

4.1. Summary

Our study investigated the effect of bright light (10,000 lux) compared to standard room light intensity (350 lux) on short term changes in ocular parameters in young adults after reading. An analysis of axial length changes for all subjects (n = 39) showed an interaction between time and lighting that approached significance ($p = 0.064$). Axial length decreased over time after reading in room light, while in the bright light condition, it showed an initial increase before returning to baseline. However, this effect was not found when analyzing the refractive groups separately, nor were there significant differences over time when comparing changes in axial length between refractive groups. Therefore, the discussion will focus on the analyses from all subjects. None of the changes in choroid thickness were significant.

4.2. Axial Length

Only a few studies have investigated short term changes in axial length in human eyes, and they showed increases in axial length after reading (Woodman et al., 2012; Mallen et al., 2006; Read et al., 2010). Of these studies, only Woodman et al. (2012) reported the light intensity that was used (237 lux, similar to our room light of 350 lux). Contrary to these findings, our study found that reading in room light resulted in a small decrease in axial length. Woodman et al. (2012) controlled for the effect of previous activities by implementing a 20 minute distance-viewing activity prior to commencement of the study. Based on the activity log in the current study, during the hour prior to testing the majority of activity was spent on near indoor tasks. However, it was shown that the prior activity had no effect on the subsequent

measurements in axial length. Woodman et al. (2012) found no significant differences in changes in axial length between refractive groups, similar to our results.

The effect of controlled indoor light levels on slowing myopia and eye growth has been studied more extensively in animals than in human eyes. Although several studies have supported the protective effect of indoor light on axial myopia in animal models, many of these studies have used form-deprivation myopia in non-primate eyes (Norton et al., 2013; Smith et al., 2012; Smith et al., 2013; Ashby et al., 2010; Feldkaemper et al., 2013; Wang et al., 2015). For example, the eyes of form-deprived chicks exposed to varying light levels (500, 15 000, or 30 000 lux) had decreased axial length and lower myopic refractions with increasing light levels (Ashby et al., 2009). This disagrees with the findings from our study, where the lower rather than the higher light level was associated with a small decrease in axial length. However, these findings and others using form-deprivation myopia are less applicable to our study, since form-deprivation myopia is less common in humans and may be governed by a different mechanism. Contrary to the above-mentioned studies, a study on lens-induced myopia, which is more relevant to human myopia, (Smith et al. 2013) found no significant refractive error changes in infant monkeys when using lighting conditions ranging from 350 lux to 25,000 lux, consistent with the current results.

The mechanisms underlying the protective effect of light in slowing axial elongation have been explored mostly in animal models. Light levels have been shown to modulate axial elongation and refractive error via retinal neurotransmitters and peptides that increase or retard axial elongation (George et al., 2005; Rada et al., 2006; Vessey et al., 2005). The neurotransmitter dopamine is released with increasing light levels and has been shown to result in slower axial elongation, whereas decreased dopamine release has been associated with greater

elongation (Cohen et al., 2012; Morgan et al., 1996). However, in a recent study retinal dopamine metabolism did not account for the limited decrease in myopia in chicks reared outdoors (Stone et al, 2016).

4.3. Choroid Thickness

The present study found no significant changes in choroid thickness after reading in room or bright lighting conditions. However, short-term changes in choroid thickness after accommodation have been reported in other studies (Woodman et al., 2012; Woodman-Pieterse et al., 2015). Significant thinning of the choroid was found following a 30 minute accommodation task in myopic subjects ($p < 0.05$), but not in non-myopic subjects (Woodman et al., 2012). However, over all subjects there were significant changes. Furthermore, the greatest thinning has been shown to occur in the temporal and inferotemporal parafoveal regions of the choroid, and to a lesser extent at the fovea ($p<0.05$) (Woodman Pieterse et al., 2015). Possible differences between other studies and our results may have been due to the shorter duration of accommodation activity in our study, or the measurement of choroid thickness at the fovea, which is not the area shown to have the most significant changes following accommodation.

One study investigated short term changes in choroid thickness in schoolchildren following a period of optical defocus under cycloplegia while viewing a distant target for 2 hours (Wang et al., 2016). This study differed from our study due to the use of optical defocus, and the longer measurement times, 1 and 2 hours after the defocus condition. Results were similar to our study in that there were no significant changes in choroid thickness after 1 hour, though changes after 2 hours were significant ($p < 0.05$). These results suggest that changes in the choroid may depend on the task and its duration. Although the effects of indoor light on choroid thickness in

human eyes are not yet known, longer durations may be necessary before changes in the choroid are observed.

Several mechanisms underlying transient changes in choroid thickness associated with accommodation have been hypothesized. These include mechanical forces resulting from contraction of the ciliary muscle, alterations in blood flow, changes in the tone of non-vascular smooth muscle, or increase in parasympathetic input causing contraction of non-vascular smooth muscles cells and choroid thinning (Woodman et al., 2012; Tamm et al., 1991; Lutjen-Drecoll, 2006; Nickla et al., 2010). Other mechanisms that are not be related to the choroid may also be contributing, including changes in lens thickness with accommodation. Due to the short time period used in our study, it is not surprising that we did not find transient choroid changes.

4.4. Benefits of the Potential Use of Light Therapy for Myopia Risk Reduction

The benefit of light as a modifiable risk factor lies in its potential to be an affordable prophylactic treatment for children at risk of myopia. Outdoor lighting is free and, in most urban areas with high populations of children at risk for myopia, it is available in varying proportions throughout all seasons of the year (Rudnicka et al., 2016). Light therapy also provides a favorable risk to benefit ratio. The benefits of light therapy include minimal costs, minimal risks and a high safety profile, and general accessibility regardless of geographic or seasonal differences. Compared to other myopia prevention modalities, exposure to outdoor light yields minimal side effects other than a potential increased risk of skin cancer (Young, 2009). The concern from outdoor exposure to sunlight stems from an increased exposure to ultra-violet radiation, which has known chronic carcinogenic effects including skin melanoma and cancer. Long-term ocular effects are diverse, including photokeratoconjunctivitis, squamous neoplasia,

pterygium, limbal stem cell deficiency and cataracts (Yam et al., 2014). Fortunately, the protective use of topical skin lotion with Sun Protection Factor (SPF) and sunglasses with ultra-violet coatings may reduce the risk of ultra-violet damage to the skin and eyes, and thus may decrease the risk of side effects from any light therapy (Jean et al., 2001).

4.5. Light in Schools

Recent studies have supported the use of elevated light levels to protect against the development of myopia in children. The most relevant study to ours investigated controlled indoor lighting levels and found that elevated lighting in schools (a minimum of 300 lux on desks, 500 lux on the blackboard) resulted in a significant reduction in the onset of myopia after 1 year in 317 children (Hua et al., 2015). There was a significantly lower incidence of new onset myopia (4% versus 10%, $p = 0.029$), less myopic shift in non-myopic students (-0.25 D versus -0.47 D, $p = 0.001$), and less growth in axial length in non-myopic compared to myopic students ($p = 0.0001$). The slightly elevated light levels in this one study were similar to our room lighting rather than bright lighting condition.

A few studies on the effect of time outdoors on myopia were conducted in Asian schools and support the use of light to protect against myopia (Table 6). These studies implemented interventions of extra-outdoor time at school and found a significant decrease in the onset of new myopia, in the treatment group compared to the control group (regular school schedules) (Wu et al., 2013; He et al., 2015; Jin et al., 2015). However, there was no effect of light on progression in already myopic children, a finding that may be applicable to the myopic adult subjects tested in our study. The intervention of extra-outdoor time during the school day would be a simple low-cost method to prevent myopia in school-age children. However, given that it is not always feasible to be outdoors, further studies into the use of elevated light levels in schools are needed.

Table 5: Summary table of studies using light in schools.

Author	Study Design: Prospective school-based intervention (location)	Subject Characteristics			Methods	Main Findings For New Onset Myopia
		N	Age (y) [Range (y)]	Mean Refractive Error (D)		
Outdoors						
Wu et al. (2013)	(Taiwan)	571	8.94 ± 1.36 [7-11]	-0.85 ± 1.83	I = Recess Outside Classroom (80 min/day) I & C = 2 hrs/week physical education TD = 1 year	I = 8.41% C = 17.65% $p < 0.001$
Jin et al. (2015)	(China)	3051	8.47 ± 1.54 [6-14]	-0.61 ± 1.30	I = Two extra 20-min outdoor recess per day I & C = Standard two 10-min recess per day TD = 1 year	I = 3.70% C = 8.50% $p = 0.048$
He et al. (2015)	(China)	1903	6.59 ± 0.34 [6-7]	1.28 ± 0.89	I = One extra 40-min outdoor activity per day I & C = Regular TD = 3 years	I = 30.4% C = 39.5% $p < 0.001$
Indoors						
Hua et al. (2015)	(China)	317	10.61 ± 2.36 [6-14]	0.58 ± 0.49	I = 300 lux on desks and 500 lux on blackboard C = No change in classroom lighting TD = 1 year	I = 4% C = 10% $p = 0.029$

y = years, D = Diopters, I = Intervention, C = Control, TD = Total Duration

4.6. Strengths and Weaknesses

A major strength of our study is that we were able to directly measure short term changes in axial length and calculate choroid thickness in human eyes, and under different light intensity conditions. Our study also used repeated measures and tested both conditions around the same time of day to limit confounding factors including diurnal fluctuations in axial length and choroid thickness (Nickla et al., 2002; Nickla et al., 1998; Chakraborty et al., 2011).

Study limitations included the use of a small sample of adult subjects. Given that myopia stops progressing around the age of 15 or 16 years (The COMET group, 2013; Thorn et al, 2005; Goss et al., 1983), the majority of our subjects likely had stable myopia. Changes may be more easily observed in younger eyes with progressing myopia. Also, a larger sample size would increase the statistical power.

4.7. Clinical Implications

Many treatments have been tried to slow the progression of myopia, including spectacles, contact lenses, and pharmaceutical agents. However, many of these treatments only work for a short period of time and are accompanied by adverse side effects, and/or are costly (Smith et al., 2015; Ramamurthy et al., 2015; Wang et al, 2015). While light therapy with SAD lamps is convenient and not as costly as these other therapies, based on the current findings it is premature to make clinical recommendations for its use. Even though we cannot now recommend the use of SAD lamps for slowing axial elongation, clinical recommendations based on other studies can be made to use outdoor light and increased classroom lighting to help protect against the development of myopia.

4.8. Conclusion

This study found an interaction between time and lighting that approached significance ($p = 0.064$). Axial length for all subjects decreased after reading in room light, and in bright light there was an initial increase in axial length followed by return to baseline. For choroid thickness, there was no significant interaction between time and lighting. For the most part choroid changes were inversely related to changes in axial length. Even though some studies in both humans and animals show a protective effect of light on eye growth, we cannot yet recommend increased indoor lighting as a viable therapy to protect against the development and progression of myopia in human eyes.

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APPENDICES

5.1. Appendix 1: Clinical Data Questionnaire

Clinical Data Questionnaire

INSTRUCTIONS FOR COMPLETION
Please answer the following questions regarding demographic information, general health history and ophthalmic history.

Today's Date (mm/dd/yyyy)	_____ (mm / dd / yyyy)
Full Name (First, middle initial, last)	_____ First MI Last
Date of Birth (mm/dd/yyyy)	_____ (mm / dd / yyyy)
Gender (male/female)	_____
Ethnicity **a.** Please select from the following the category that you believe best describes your ancestral ethnic heritage: 1. American Indian/Alaska Native 2. Asian 3. Black/African American 4. White/Caucasian 5. Indian 6. Native Hawaiian/Pacific Islander 7. Other **b.** Are you of Hispanic or Latino descent? (Yes/No) **c**. If you selected 'Other' above, please describe your ethnic background.	**a.** _____ **b.** _____ **c.** _____
General Health **a.** Please list any medications you are currently taking, including over-the-counter (OTC) medications. **b.** Have you ever suffered a serious injury or illness? If so, please specify the approximate date(s) and nature of the incident(s).	**a.** _____ **b.** _____ _____ _____

Ophthalmic History	
a. Do you use corrective eyewear such as glasses or contact lenses? (Yes/No) i. If so, when did you first start wearing your corrective eyewear? (Year/Age) ii. If so, are you nearsighted (have trouble seeing far away) or farsighted (have trouble seeing up close)? (Please circle one)	**a.** _____ **i.** _____ Year Age **ii.** Nearsighted Farsighted
b. Do you wear contact lenses? (Yes/No) i. If so, are your contacts considered 'extended wear'? (Yes/No)	**b.** _____ **i.** _____
c. Have you ever been told you have a lazy eye, eye turn or squint? (Yes/No)	**c.** _____
d. As best you can, please specify your refractive error for both the right and left eyes (prescriptions can usually be found on your box of contacts, and may look similar to one of the examples below) Ex. Right Eye **(OD)** -6.75 +0.25 X 96 Left Eye **(OS)** +2.25 -0.75 X 180	**d.** **OD** _____ **OS** _____
e. Have you ever had Corneal Refractive Therapy (CRT) or Orthokeratology (Ortho-K)? (Yes/No)	**e.** _____
f. Have you ever had Laser Assisted In Situ Keratomileusis (LASIK) or Photorefractive Keratectomy (PRK)? (Yes/No)	**f.** _____
g. Do you regularly use eye drops? (Yes/No)	**g.** _____
h. Have you ever sustained an injury to either eye? (Yes/No) i. If so, for each injury please specify <u>which eye</u> and the nature and date of the injury.	**h.** _____ **i.** _____ _____ _____

Light Therapy History **a.** Have you ever used light therapy for Seasonal Affective Disorder? (Yes/No) i. If yes, when did you start and end light therapy? (start year, end year, and Age) ii. If so, how long was the duration of your light therapy? (Hours/Week)	**a. _____** **i. _____** **ii. _____**
Additional Notes Are there additional considerations of which you think we should be aware? If so, please describe as succinctly as possible.	_____ _____ _____ _____

5.2. Appendix 2: 24 Hour Activity Log

INSTRUCTIONS TO PARTICIPANTS:

1. This Activity Log is a reflection of the past 24 hours prior to your appointment: Please begin the Activity Log at the hour that is 24-hours prior to your appointment. You will need to continue the log onto a second day to complete the full 24 hours.

2. The Activity Log should be completed as the day progresses.

3. Write an "X" for all activities that you did during each hour period. You can indicate more than one activity during each hour (e.g., watching TV and reading).

Dates of Activity Log: ___ ___ /___ ___ /___ ___ ___ ___ and ___ ___ /___ ___ /___ ___ ___ ___
mo day year mo day year

- These days are:

o School Day o Work Day o Summer Vacation/Day Off and o School Day o Work Day o Summer Vacation/Day Off

- Days of week of Activity Log (check only 2):
  o Monday o Tuesday o Wednesday o Thursday o Friday o Saturday o Sunday

TIME at start of hr time period	WORK/ SCHOOL	READING/ WRITING	COMPUTER USE	TV OR MOVIE	OTHER INDOOR ACTIVITY	DRIVING	OUTDOOR ACTIVITY	SLEEP
12:00 AM								
1:00 AM								
2:00 AM								
3:00 AM								
4:00 AM								
5:00 AM								
6:00 AM								
7:00 AM								
8:00 AM								
9:00 AM								
10:00 AM								
11:00 AM								
12:00 PM								
1:00 PM								
2:00 PM								
3:00 PM								
4:00 PM								

5:00 PM								
6:00 PM								
7:00 PM								
8:00 PM								
9:00 PM								
10: 10:00 PM								
11:00 PM								

TIME at start of hr time period	**WORK/ SCHOOL**	**READING/ WRITING**	**COMPUTER USE**	**TV OR MOVIE**	**OTHER INDOOR ACTIVITY**	**DRIVING**	**OUTDOOR ACTIVITY**	**SLEEP**
12:00 AM								
1:00 AM								
2:00 AM								
3:00 AM								
4:00 AM								
5:00 AM								
6:00 AM								
7:00 AM								
8:00 AM								
9:00 AM								
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