Effects of caffeine intake on visual performance of the eye among normal healthy adults

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Recommended Citation
Murari, Swetha; Ho, Amiee; Hayes, John; and Cooper, Scott, "Effects of caffeine intake on visual performance of the eye among normal healthy adults" (2018). College of Optometry. 842.  
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Effects of caffeine intake on visual performance of the eye among normal healthy adults

Abstract
Purpose: The purpose of this study is to examine the effects of caffeine on visual performance of the eye among normal healthy adults.

Methods: This two-visit randomized placebo-controlled crossover study included 49 normal healthy adults aged 18 years and above who received either 200mg of caffeine or placebo capsules. Choroidal thickness, tear break-up time, accommodative power, pupil size and reading performance were assessed at baseline, 1 hour and 2 hours.

Results: Consumption of caffeine showed an increased effect on reading rate (p<0.05), average span of recognition and tear break up time (p=0.05) at 1 hour. There was no significant difference seen between the caffeine and placebo group in choroidal thickness (p=0.547), pupil size (p=0.137) and accommodative power (p=0.860). All the aforementioned metrics were not significant at 2 hours. Average span of recognition has a good correlation (r=0.855, p<0.01) with reading rate that was significant at 1 hour among the caffeine group.

Conclusion: Caffeine consumption has some effect on visual performance of the eye by increasing reading rate and tear film quality. This transient effect peaks at the 1 hour mark and can potentially help an individual have better quality of vision to improve their visual performance for near tasks.

Degree Type
Thesis

Degree Name
Master of Science in Vision Science

Committee Chair
Amiee Ho

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John Hayes

Third Advisor
Scott Cooper

Keywords
caffeine, visual performance, choroid, tear film, reading performance, accommodation

Subject Categories
Optometry

This thesis is available at CommonKnowledge: https://commons.pacificu.edu/opt/842
EFFECTS OF CAFFEINE INTAKE ON VISUAL PERFORMANCE OF THE EYE AMONG NORMAL HEALTHY ADULTS

By

SWETHA MURARI

THESIS
Submitted in partial fulfillment of the requirements for the degree of Master of Science in Vision Science

PACIFIC UNIVERSITY
FOREST GROVE, OREGON

MAY 2018

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By
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This thesis of Swetha Murari is approved for acceptance in partial fulfillment of the requirements for the degree of Master of Science in Vision Science Graduate Program at Pacific University, Forest Grove, Oregon.
EFFECTS OF CAFFEINE INTAKE ON VISUAL PERFORMANCE OF THE EYE AMONG NORMAL HEALTHY ADULTS

SWETHA MURARI
MASTER OF SCIENCE IN VISION SCIENCE PROGRAM
PACIFIC UNIVERSITY COLLEGE OF OPTOMETRY, 2018

ABSTRACT

**Purpose:** The purpose of this study is to examine the effects of caffeine on visual performance of the eye among normal healthy adults.

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**Conclusion:** Caffeine consumption has some effect on visual performance of the eye by increasing reading rate and tear film quality. This transient effect peaks at the 1 hour mark and can potentially help an individual have better quality of vision to improve their visual performance for near tasks.

**Keywords:** caffeine, visual performance, choroid, tear film, reading performance, accommodation.
ACKNOWLEDGEMENT

First and foremost, I would like to thank my subjects who took part in this study and helped me in finishing this study on time.

I would like to thank my advisor Dr. Amiee Ho, Assistant Professor at Pacific University College of Optometry; despite her busy schedule took the initiative in guiding me throughout my thesis. She has motivated me and supported me during all the challenges I faced. I thank my committee members Dr. John Hayes for his extensive support and guidance in statistical analysis, and Dr. Scott Cooper for sharing his insightful thoughts on my thesis.

I must thank my friends Dr. Deepayan Kar, Dr. Sahi Nandini Wuppukondur, Dr. Ahlam Alenazi, Dr. Arwa Arroushad and Dr. Abdullah Alejtayli who without any hesitation took part in my study many times just to help me to finish the tasks on time. I really must appreciate them for being very patient with me and guided me through with suggestions on improvising my methods.

The most humble and generous person Dr. Deepayan Kar, has been very supportive throughout my career. Very few people have the will to share their wisdom; he is one of those gems. Within this two years of graduate life, I have made many memories that I will cherish throughout my life.

I thank my lovely housemates Hoa Nguyen and Kristinoel Ludwig who helped me out in my thesis writing and made me feel like “home” by considering me as their own family. Their unconditional love and support has given me the strength to achieve my dreams; a life without them is unimaginable. I thank Nicette Quintero, my Optician Manager, for being a friend and colleague; she is valued for respecting my views and motivating me not to give up.

I thank Dr. James Kundart for sharing his extensive knowledge on visual perception and eye movement disorders that led me to explore more extensively in vision research. I truly appreciate his support regarding my career growth. His discussion on several aspects of World Optometry is something I will remember and keep in mind as a clinician, and I thank him for sharing his expertise.
I thank Dr. Pat Caroline specifically for allowing me to use the highly efficient instruments in the Contact Lens lab at Pacific University College of Optometry during his clinical hours. In addition, I thank Campus Public Safety for allowing me to access the rooms on University premises during weekends or holidays. I thank Dr. Eakland for his continuous support and encouraging words that motivated me to finish my thesis.

I must thank my College Dean Dr. Jennifer Coyle for being supportive and encouraging by helping me via scholarships and other opportunities throughout my master’s program. I also want to acknowledge in appreciation Dr. Yu Chi Tai, Vision Science Program Director, who extensively supported me with financial aid for my research work, as well as during my tough times initially at Pacific University and motivated me to carry out my work in a timely manner.

Finally, I thank God for giving me the mental strength to work efficiently and with perseverance, despite all hurdles and challenges facing me. I thank my parents, my brother and my fiancée Avinash; without them I wouldn’t have been here. I would also like to thank all the staff, faculty and my lovely OD friends here at Pacific University who have considered me as their own family.
# TABLE OF CONTENTS

**ABSTRACT** .......................................................................................................................................................... i

**ACKNOWLEDGEMENT** ......................................................................................................................................... ii

**TABLE OF CONTENTS** ....................................................................................................................................... iv

**LIST OF FIGURES** ............................................................................................................................................... vi

**LIST OF TABLES** ................................................................................................................................................ viii

**INTRODUCTION** ................................................................................................................................................ 1

**MATERIALS AND METHODS** ............................................................................................................................ 5

- Cirrus HD-OCT Choroidal thickness measurement ................................................................................................. 6
- Grand Seiko Autorefractometer (WR-5100K) .............................................................................................................. 8
- Taylor Associates Visagraph III .................................................................................................................................. 10
- Statistical Analysis .................................................................................................................................................. 12

**RESULTS** .......................................................................................................................................................... 13

- Demographics: ....................................................................................................................................................... 13

- Reading parameters: ................................................................................................................................................ 16
  - Fixations .............................................................................................................................................................. 16
  - Regressions ........................................................................................................................................................ 17
  - Average span of recognition ................................................................................................................................. 18
  - Average duration of fixation ................................................................................................................................. 19
  - Reading rate ...................................................................................................................................................... 20
  - Blink rate ........................................................................................................................................................... 21
  - Pupil size ............................................................................................................................................................ 22
  - Accommodative power ....................................................................................................................................... 23

- Ocular changes: ....................................................................................................................................................... 24
  - Non-invasive tear break-up time ............................................................................................................................ 24
  - Choroidal thickness ............................................................................................................................................. 25

- Correlations: ........................................................................................................................................................... 29
DISCUSSION .................................................................................................................. 31

Overview of caffeine half-life ...................................................................................... 31

Ocular changes: .............................................................................................................. 31

Choroidal thickness changes ......................................................................................... 31

Non-invasive tear film break-up time ............................................................................ 34

Ocular reading: .............................................................................................................. 36

Caffeine on reading performance ............................................................................... 36

Caffeine on accommodation and pupil size ............................................................... 37

LIMITATIONS ................................................................................................................. 43

CONCLUSION .................................................................................................................. 44

BIBLIOGRAPHY ............................................................................................................. 46
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>FIGURES</th>
<th>DESCRIPTION</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1</td>
<td>Measurement of sub-foveal choroidal thickness with enhanced depth imaging in Cirrus HD spectral domain OCT</td>
<td>7</td>
</tr>
<tr>
<td>Figure 2</td>
<td>Assessment of real time accommodative power with Grand Seiko autorefractometer while reading</td>
<td>9</td>
</tr>
<tr>
<td>Figure 3</td>
<td>Assessment of reading performance with Visagraph III</td>
<td>11</td>
</tr>
<tr>
<td>Figure 4</td>
<td>Graph showing mean values of fixations at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>16</td>
</tr>
<tr>
<td>Figure 5</td>
<td>Graph showing mean values of regressions at baseline, 1 hour and 2 hours among caffeine and placebo group</td>
<td>17</td>
</tr>
<tr>
<td>Figure 6</td>
<td>Graph showing mean values of average span of recognition at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>18</td>
</tr>
<tr>
<td>Figure 7</td>
<td>Graph showing mean values of average duration of fixation at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>19</td>
</tr>
<tr>
<td>Figure 8</td>
<td>Graph showing mean values of reading rate at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>20</td>
</tr>
<tr>
<td>Figure 9</td>
<td>Graph showing mean values of blink rate at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>21</td>
</tr>
<tr>
<td>Figure 10</td>
<td>Graph showing mean values of pupil size at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>22</td>
</tr>
<tr>
<td>Figure 11</td>
<td>Graph showing mean values of accommodative power at baseline, 1 hour and 2 hours among caffeine and placebo groups</td>
<td>23</td>
</tr>
</tbody>
</table>
Figure 12  *Graph showing mean values of non-invasive tear break up time at baseline, 1 hour and 2 hours among caffeine and placebo groups*  

Figure 13  *Graph showing mean values of choroidal thickness at baseline, 1 hour and 2 hours among caffeine and placebo groups*  

Figure 14  *Graph showing the reduction in choroidal thickness in non-caffeine participants alone when compared with baseline measurement*  

Figure 15  *Scatter plot showing change in choroidal thickness at 2 hours from baseline measurement among caffeine and placebo groups*  

Figure 16  *Scatter plot showing change in choroidal thickness at 1 hour from baseline measurement among caffeine and placebo groups*
# LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE</th>
<th>DESCRIPTION</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td><em>Mean and standard deviation of clinical characteristics at baseline, 1 hour</em> and 2 hours of time among caffeine group</td>
<td>14</td>
</tr>
<tr>
<td>Table 2</td>
<td><em>Mean and standard deviation of clinical characteristics at baseline, 1 hour</em> and 2 hours of time among placebo group</td>
<td>15</td>
</tr>
<tr>
<td>Table 3</td>
<td><em>Correlation analysis between choroidal thickness changes with clinical characteristics among caffeine group</em></td>
<td>29</td>
</tr>
<tr>
<td>Table 4</td>
<td><em>Correlation analysis to determine the association between reading rate with other functional changes among caffeine group</em></td>
<td>30</td>
</tr>
</tbody>
</table>
INTRODUCTION

Caffeine (1,3,7-trimethyl xanthine) (C₈H₁₀N₄O₂; CFE), the natural alkaloid, is the well-known component of coffee. This psychoactive ingredient was first isolated in 1820¹ from coffee beans and is now used in a multitude of foods and drinks.² It is widely being consumed; the amount of consumption depends on the types of beverages and populations. The biological source of coffee is the Coffea arabica (Family- Rubiaceae), cultivated in many countries.² Excessive caffeine intake has been observed in young adults (especially students) which might result in creating adverse effects. Around 85% of the US population widely consumes a caffeinated beverage everyday.³ Coincidentally, coffee typically contains more caffeine than any other beverage, ranging from 35mg to 175mg of caffeine per cup.⁴ Moreover, approximately 20-30% of the general population consumes more than 500-600mg of caffeine daily.⁵

Caffeine has its advantages as well as disadvantages. It is a central nervous system stimulant that promotes mental alertness and concentration, decreases insulin sensitivity and helps prevent Alzheimer’s⁶ and Parkinson’s disease.⁷ There are many caffeinated beverages (e.g., coffee) which consist of phenol chlorogenic acid, magnesium, caffeine and other micronutrients. Whereas phenol chlorogenic acid is responsible for reducing glucose output in liver⁸, and magnesium improves insulin secretion eventually resulting in lowering of type 2 diabetes⁹, a few studies have shown that caffeine reduces sensitivity to insulin¹⁰ which leads to risk of worsening type 2 diabetes.

Caffeine is also an adenosine receptor antagonist; it improves motor functions, observed in animal models with Parkinson’s disease; caffeine also enhances dopamine neurotransmission.¹¹ In addition, studies are discovering that caffeine may help with cognitive protection and be beneficial for individuals with Alzheimer’s disease, because caffeine restores brain extracellular adenosine levels leading to an increase in cerebral blood flow.⁶
However, excessive caffeine consumption can cause adverse effects such as increase in heart rate, blood pressure, restlessness, nausea, and more. For a healthy adult population, the FDA has stated that a daily caffeine intake of up to 400mg per day (about three cups) is not associated with any adverse effects.\textsuperscript{12}

In the eye, studies have found a correlation between an increase in intraocular pressure with increased caffeine consumption. This phenomenon is thought to happen because caffeine acts as an adenosine receptor antagonist which results in increasing the intracellular cyclic AMP. This stimulates the ciliary body to produce more aqueous humor and reduces smooth muscle tone of the anterior chamber angle that leads to increasing resistance in outflow of aqueous humor.\textsuperscript{13} Elevated intraocular pressure is a risk factor for developing glaucoma.\textsuperscript{14,15}

In addition, caffeine consumption inhibits the adenosine-mediated vasodilation by binding adenosine receptors. This causes vasoconstriction which results in the reduction of choroidal thickness.\textsuperscript{16} Most of the studies have seen the effect of caffeine on choroidal thickness alone but have failed to consider axial length as another clinical measure. Although a few studies on refractive power have found that choroidal thickness and axial length are negatively correlated, the effect of axial length due to caffeine intake has not been directly measured.\textsuperscript{17}

Reading speed is a strong predictor of visual ability and vision-related quality of life.\textsuperscript{18} Reading difficulty is a primary concern for people with low vision or reading disabilities. An understudied topic is the effects of caffeine on reading performance. There is one study which found that caffeine consumption will increase the pupil size and increase accommodation which might result in deterioration of vision at near.\textsuperscript{19} Increase in pupil size will cause peripheral and central rays of light to focus at different points resulting in spherical aberration, and that leads to decrease in vision. Therefore, this study suggested that caffeine may have some impact on reading performance due to changes in pupil size and accommodation, but so far there have not been any studies that directly measure the reading performance after caffeine intake.
There have also been conflicting results of caffeine’s effects on tear film. Amaechi et al\(^{20}\) had stated that caffeine intake is associated with reduced tear function whereas Arita et al\(^{21}\) claimed that caffeine has a protective effect on dry eye. While both studies were similar in that they both assessed the quantity of the tear film, the two studies approached the methodology in very different ways. The variation in methodology explains the opposing results. Tear film quality due to caffeine intake might have some impact on reading performance, but it is understudied. Due to conflicting results on tear secretion and the lack of studies on tear film quality with caffeine intake, further studies are needed and may shed light on how tears might change visual performance.

Therefore, the purpose of this study is to observe the direct effect of caffeine ingestion on tear break up time (TBUT), choroidal thickness (ChT), pupil size, accommodation and reading performance on normal healthy adults.
MATERIALS AND METHODS

A placebo-controlled randomized crossover study included 49 normal healthy subjects recruited from Pacific University, Forest Grove, Oregon, USA. Inclusion criteria included subjects above 18 years old with best corrected visual acuity 20/30 or better and well versed with the English language. Spherical equivalent (SE) was used to classify the refractive status of the eye. Myopes were defined as SE greater than -1D and non-myopes between -1D to +0.75D. Subjects with any ocular diseases or abnormalities, systemic illness, refractive surgeries, binocular vision problems, smoking and pregnancy were excluded from the study. Initial vision screening on all subjects was performed based on the eligibility criteria. Informed consent form was reviewed and taken from each subject in accordance with principles of the Declaration of Helsinki. The study was conducted upon approval from the Institutional Review Board (IRB) of Pacific University, Forest Grove, Oregon, USA.

The subjects were randomized into 2 groups: the treatment group (caffeine intake) and control group (placebo). The quantity of caffeine ingestion was controlled by administering discrete caffeine capsules to the treatment subjects (200mg). Similar amount of placebo capsules containing magnesium calcium powder was administered to the controls. Magnesium calcium capsules were chosen over the traditional sugar placebo capsules due to the concern that sugar might have some effect on some of the ocular metrics being measured for this study, potentially leading to variable results. A baseline measurement of ocular parameters was taken prior to any capsule intake. The baseline measurements include: choroidal thickness with Cirrus HD Optical Coherence Tomography 500 Enhanced Depth Imaging (Carl Zeiss Meditec), axial length with IOL master 500 (Carl Zeiss Meditec), tear film break up time with Medmont E300 corneal topography (Medmont), pupil size along with real-time accommodative power was inspected with Grand Seiko autorefractor (WR-5100K) and reading performance was assessed with Taylor Associates Visagraph III. After capsule intake, all ocular parameters were assessed at the same time in both visits to avoid the diurnal fluctuations at two different intervals of time:
1 hour and 2 hours. Each subject served as their own control and had two separate visits. One visit was the control visit (ingesting placebo capsule) and another visit was the treatment visit (ingesting caffeine capsules).

**Cirrus HD-OCT Choroidal thickness measurement**

Choroidal thickness was analyzed by using the high definition (HD) 5 Line Raster scan protocol of spectral domain OCT (Cirrus HD, Carl Zeiss Meditec Ophthalmic Systems Inc, Dublin, California, USA). The HD 5 Line Raster scan protocol consists of 6mm parallel lines with 1,024 A-scans/B-scans. Sub-foveal choroidal thickness is measured manually as the distance between the retinal pigment epithelium (RPE) and the choroid-scleral interface (Figure 1). The subjects focused at internal fixation target without moving their eyes while the scans were acquired. Scans with signal strengths of at least 6, well-centered and devoid of motion or blinking artifacts were taken into the study. Two examiners (AB, CD) were masked to the OCT images and they measured the choroidal thickness manually. The average of the two measurements was taken; the differences between the readings were within 10µm. There was no inconsistency in the readings observed between the examiners. The inter-examiner reproducibility of the choroidal thickness was assessed with intra-class correlation coefficient (ICC).
Figure 1: Measurement of subfoveal choroidal thickness with enhanced depth imaging (EDI) in Cirrus HD Spectral domain OCT
**Grand Seiko Autorefractometer (WR-5100K)**

Grand Seiko autorefractometer WR-5100K (Grand Seiko Co. Ltd., Hiroshima, Japan) is a commercially available open field device that is used to measure refractive power, pupil size and accommodative power. It is extensively used in the field of accommodative research. This instrument is developed based on the principle of a ring target of infrared light that is imaged after reflection off the retina. The instrument was connected to a computer running the WCS-1 software with the Grand Seiko WR-5100K set to Hi-Speed (continuous recording) mode, which allows refractive data collection at a temporal resolution of 5 Hz. The software records dynamic results, including time (in seconds) of each reading; pupil size; and mean spherical equivalent refractive power in the form of an Excel Comma Separated Values (CSV) file. The subjects were seated in their comfortable position with head and chin placed firmly on the rest (Figure 2). They were asked to read an *American Scientific* article placed at 40 centimeters with their habitual near correction. The near target was held with near reading rod placed on the instrument. The accommodative power was measured at baseline, 1 hour and 2 hours.
Figure 2: Assessment of real time accommodative power with Grand Seiko autorefractometer while reading.
**Taylor Associates Visagraph III**

Visagraph III is an eye movement monitoring device that is used for assessing the reading performance; it is made by Taylor Associates Communications, Inc., Vermont, USA. It consists of safety goggle-type device where infrared emitters and detectors are mounted to detect the position of eye movements. It calculates reading speed and average number of fixations every 100 words. The subjects were seated comfortably and asked to hold the book at a distance of 40 centimeters inclined at an angle of approximately 30 degrees down from the vertical. The goggle-like device was placed over their correction and adjusted for interpupillary distance. The reading material consisted of Level 10 paragraphs (Figure 3B) designed for college students or adults. The paragraph was 10 lines long, double spaced with 12 point Times bold font (approximately 20/70 near Snellen equivalent). The words were equally spaced throughout the paragraph. All subjects were made to read Level 10 paragraphs since it was designed for college students or adults only to avoid any discrepancies. Subjects were not randomized to any paragraphs; they chose the paragraph as per their preference. They were instructed to read the paragraph silently with no time restriction. At the end of the reading task, reading comprehension was assessed via a questionnaire. The subjects were required to score a 70% or greater on the questionnaire (Figure 3C). There was no prior learning trial before the actual measurements were taken.
Figure 3A. Assessment of reading performance with Visagraph III.

Figure 3B. Level 10 reading paragraph. Figure 3C. Level 10 reading comprehension.
Statistical Analysis

Statistical analysis was done with SPSS V.20.0 software (SPSS Inc., IBM Corp, Chicago, IL). The data were tested for normality with Q-Q and P-P plot and the data follows normal distribution. Descriptive statistics, scatter plot, mixed model analysis, Pearson correlation and analysis of covariance was used in this study. Mixed model analysis was used to evaluate the effect of caffeine over time on treatment group and control group. Scatter plot was used to observe the relationship between baseline, 1 hour and 2 hours of interval. Pearson correlation was used to see the associations between structural and functional variations. Analysis of covariance was used to see the change in effect compared to baseline measures. Intraclass correlation coefficient (ICC) was analyzed to quantify the inter-examiner reproducibility of choroidal thickness measurement. Statistical significance was set at a probability of 5% (p<0.05). A sample size of 49 subjects had 90% power to detect an effect size of 0.5 at an alpha = 0.05 with correlation between baseline covariate and follow-up assumed to be $r = 0.7$. 
RESULTS

Demographics:

Forty-nine normal healthy adults (32 females and 17 males) took part in this placebo-controlled crossover study. All subjects were between 22 and 51 years old. Mean age was 26.86 ± 4.97 years. Subjects included were myopic and non-myopic; their spherical equivalent mean was -2.66D ± 2.61D. Axial length was measured for all the subjects and its mean value was 24.64 ± 1.22mm. Table 1 and 2 show the mean values of clinical characteristics of the subjects at baseline, 1 hour and 2 hours of time, among caffeine and placebo groups respectively. There were 38 habitual caffeine users who consumed less than 400mg of caffeine per day and 11 non-caffeine users. None of the participants reported any adverse effects to the caffeine or placebo capsules.
Table 1: Mean and standard deviation of clinical characteristics at baseline, 1 hour and 2 hours of time among caffeine group.

<table>
<thead>
<tr>
<th>CAFFEINE</th>
<th>Baseline</th>
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<td>Ocular reading parameters</td>
<td></td>
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<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Fixations (ms)</td>
<td>111.72</td>
<td>41.272</td>
<td></td>
<td>113.61</td>
<td>46.969</td>
<td>111.91</td>
<td>45.582</td>
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<td>Regressions (ms)</td>
<td>18.74</td>
<td>13.795</td>
<td></td>
<td>19.4</td>
<td>17.112</td>
<td>18.53</td>
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<td>Average span of recognition</td>
<td>1.005</td>
<td>0.383</td>
<td></td>
<td>1.004</td>
<td>0.397</td>
<td>1.02</td>
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<tr>
<td>Average duration of fixation (ms)</td>
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<td>0.267</td>
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<td>0.269</td>
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<tr>
<td>Reading rate (wpm)</td>
<td>225.73</td>
<td>83.616</td>
<td></td>
<td>230.18</td>
<td>85.468</td>
<td>233.41</td>
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<td>Blink rate (blinks/sec)</td>
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<td>0.150</td>
<td>0.137</td>
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<td>4.08</td>
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<td>4.06</td>
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<td>Tear break up time (s)</td>
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<td>5.720</td>
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<td>Choroidal thickness (µm)</td>
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<td>294.73</td>
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Table 2: Mean and standard deviation of clinical characteristics at baseline, 1 hour and 2 hours of time among placebo group.

<table>
<thead>
<tr>
<th>PLACEBO</th>
<th>Baseline</th>
<th>1 hour</th>
<th>2 hours</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<tr>
<td>Fixations (ms)</td>
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<td>121.53</td>
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<td>Regressions (ms)</td>
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</tr>
<tr>
<td>Average span of recognition</td>
<td>0.947</td>
<td>0.369</td>
<td>0.946</td>
</tr>
<tr>
<td>Average duration of fixation (ms)</td>
<td>0.273</td>
<td>0.061</td>
<td>0.266</td>
</tr>
<tr>
<td>Reading rate (wpm)</td>
<td>211.53</td>
<td>73.374</td>
<td>218.45</td>
</tr>
<tr>
<td>Blink rate (blinks/sec)</td>
<td>0.158</td>
<td>0.117</td>
<td>0.150</td>
</tr>
<tr>
<td>Accommodative power (D)</td>
<td>-2.14</td>
<td>0.686</td>
<td>-2.15</td>
</tr>
<tr>
<td>Pupil size (mm)</td>
<td>4.05</td>
<td>0.682</td>
<td>4.00</td>
</tr>
<tr>
<td>Tear break up time (s)</td>
<td>4.81</td>
<td>3.181</td>
<td>5.53</td>
</tr>
<tr>
<td>Choroidal thickness (µm)</td>
<td>302.51</td>
<td>83.401</td>
<td>298.81</td>
</tr>
</tbody>
</table>
**Reading parameters:**

**Fixations**

There was no significant effect seen between the placebo and the caffeine group at one hour (F=1.926, p=0.168, d=0.19) and at two hours (F=0.137, p=0.712, d=0.05).

*Figure 4: Graph showing fixations (mean±SEM) at baseline, one hour and two hours among placebo and caffeine group.*
Regressions

Regressions showed insignificant difference between caffeine and placebo group at one hour (F= 0.367, p=0.546, d=0.08) and two hours (F=0.085, p=0.772, d=0.04).

Figure 5: Graph showing regressions (mean±SEM) at baseline, one hour and two hours among caffeine and placebo groups.
**Average span of recognition**

This calculates the number of fixations needed to read a given number of words. There was significant difference seen between the groups at one hour ($F = 3.617$, $p<0.05$, $d=0.27$) but insignificant at two hours ($F=1.024$, $p=0.313$, $d=0.14$).

![Graph showing average span of recognition (mean±SEM) at baseline, one hour and two hours among placebo and caffeine groups.](image)
**Average duration of fixation**

It is the amount of time taken to fixate; this depends on vision and recognizing words. There was no significant difference seen between two groups at one hour (F=0.534, p=0.466, d=0.09) and two hours (F=0.362, p=0.549, d=0.07).

![Graph showing average duration of fixation (mean±SEM) at baseline, one hour and two hours among caffeine and placebo groups.](image_url)
**Reading rate**

There was an increase in reading rate among caffeine group compared to placebo group at one hour ($F=7.292$, $p<0.05$, $d=0.38$) but no difference observed at two hours ($F=0.266$, $p=0.607$, $d=0.07$).

*Figure 8: Graph showing reading rate (mean±SEM) at baseline, one hour and two hours among caffeine and placebo groups.*
**Blink rate**

It is defined by number of blinks per second. There was no difference seen between caffeine and placebo groups at one hour \((F=1.161, p=0.283, d=0.15)\) and two hours \((F=0.133, p=0.716, d=0.06)\).

![Graph showing blink rate (mean±SEM) at baseline, one hour and two hours among caffeine and placebo groups.](image-url)
**Pupil size**

Pupil size assessment did not show any difference between caffeine and placebo groups at one hour (F=2.237, p=0.137, d=0.21) and two hours (p=0.075, d=0.25).

*Figure 10: Graph showing pupil size (mean±SEM) at baseline, one hour and two hours among placebo and caffeine groups.*
**Accommodative power**

Accommodative power is the amount of accommodation in demand at 40 centimeters (equivalent to 2.50D); it showed no difference between caffeine and placebo group at one hour ($F=0.031$, $p=0.860$, $d=0.02$) and two hours ($F=1.520$, $p=0.220$, $d=0.17$).

![Figure 11: Graph showing accommodative power (mean±SEM) at baseline, one hour and two hours among caffeine and placebo groups.](image-url)
**Ocular changes:**

**Non-invasive tear break-up time**

Non-invasive tear break-up time was measured to see the tear film quality. There was no significant difference between caffeine and placebo groups at one hour ($F=3.73$, $p=0.055$, $d=0.27$) and two hours ($F=0.255$, $p=0.615$, $d=0.07$).

*Figure 12: Graph showing tear break-up time (mean±SEM) at baseline, one hour and two hours among caffeine and placebo groups.*
**Choroidal thickness**

Choroidal thickness showed no difference between the caffeine group and the placebo group at one hour (F=0.365, p=0.547, d=0.08) and two hours (F=0.008, p=0.931, d=0.01). A sub data was taken to see the true effect of caffeine on choroidal thickness and it showed a reduction in choroidal thickness at one hour (t=3.249, p<0.05, d=0.16) and two hours (t=3.799, p<0.05, d=0.15) compared to baseline measurement among caffeine and placebo groups. There was a higher intraclass correlation coefficient (ICC) on choroidal thickness (ICC=0.986, p<0.01).

![Graph showing choroidal thickness (mean±SEM) at baseline, one and two hours among caffeine and placebo groups.](image-url)

*Figure 13: Graph showing choroidal thickness (mean±SEM) at baseline, one and two hours among caffeine and placebo groups.*
Figure 14: Graph showing the reduction in choroidal thickness (mean±SEM) in non-caffeine participants alone when compared with baseline measurement.
Figure 15: Scatter plot showing change in choroidal thickness at one hour from baseline measurement among caffeine and placebo groups.
Figure 16: Scatter plot showing change in choroidal thickness at two hours from baseline measurement among caffeine and placebo groups.
Correlations:

**Choroidal thickness correlation**

There was a significant correlation seen between choroidal thickness, axial length and spherical equivalent as seen in Table 2. Axial length and choroidal thickness are negatively correlated showing that, with increase in axial length, there will be a decrease in choroidal thickness. Spherical Equivalent is positively correlated to choroidal thickness; the higher the minus power, the thinner the choroid. Therefore, myopes had thinner choroid and non-myopes had thicker choroid.

*Table 3: Correlation analysis between choroidal thickness changes with clinical characteristics among caffeine group.*

*Correlation is significant at the 0.01 level (two-tailed)*

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 hour</th>
<th>2 hours</th>
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</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pear Corr</td>
<td>0.013</td>
<td>0.001</td>
<td>-0.006</td>
</tr>
<tr>
<td>p value</td>
<td>0.901</td>
<td>0.988</td>
<td>0.954</td>
</tr>
<tr>
<td><strong>SE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pear Corr</td>
<td>0.455*</td>
<td>0.444*</td>
<td>0.447*</td>
</tr>
<tr>
<td>p value</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>Axial Length</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pear Corr</td>
<td>-0.376*</td>
<td>-0.332*</td>
<td>-0.338*</td>
</tr>
<tr>
<td>p value</td>
<td>0.0001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Accommodative power</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pear Corr</td>
<td>-0.015</td>
<td>-0.028</td>
<td>0.065</td>
</tr>
<tr>
<td>p value</td>
<td>0.882</td>
<td>0.786</td>
<td>0.524</td>
</tr>
</tbody>
</table>

Pear Corr = Pearson correlation

SE = Spherical Equivalent
**Correlation of reading rate**

There was a significant correlation seen between reading rate, average span of recognition, average duration of fixation, and blink rate. The following table 3 shows that reading rate is positively correlated to average span of recognition and blink rate; while negatively correlated to average duration of fixation.

*Table 4: Correlation analysis to determine the association between reading rate with other functional changes among caffeine group at 1 hour.*

<table>
<thead>
<tr>
<th></th>
<th>Pearson correlation (r)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average span of recognition</td>
<td>0.855</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Average duration of fixation</td>
<td>-0.257</td>
<td>0.011*</td>
</tr>
<tr>
<td>Fixations</td>
<td>-0.703</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Regressions</td>
<td>-0.543</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Blink rate (blinks/sec)</td>
<td>0.286</td>
<td>0.004*</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.05 level (two-tailed)*
DISCUSSION

There have been few studies investigating the effect of caffeine on structural and functional changes in the eye, but the exact mechanism for such change is still unclear. In this crossover study, we investigated by observing the effect of caffeine on visual performance among normal healthy adults. The results will be categorized into 2 sections, namely ocular changes and ocular reading performance.

Overview of caffeine half-life:

Caffeine reaches its maximum peak plasma concentration between 20-120 minutes and its plasma half-life is between 3-6 hours. Therefore, caffeine is eliminated from our bodies after 4 hours of ingestion. Thus, for this study we focused on seeing the caffeine effect only at the peak levels of plasma concentration, at the 1 and 2 hour mark.

Ocular changes:

**Choroidal thickness changes**

The choroidal structure has many functions, such as giving oxygen and nutrients to the outer retinal layers. A change in choroidal vasculature can significantly alter the choroid. Thus, it is important to have normal choroidal vasculature to keep normal choroidal structure and function to avoid any retinal damage which can lead to retinal pathologies.

In this study, we found no significant difference between caffeine and placebo group as seen in figure 13. Though it is not significant, we still saw a minimal amount of reduction in choroidal thickness among caffeine and placebo groups. However, when analyzing a subset of the data involving subjects that normally do not ingest caffeine-containing foods, we found that there was a significant (p<0.05) reduction in choroidal thickness compared to baseline measurement (Figure 14). The clear effect of caffeine on this non-caffeine group suggests
that the reduction of choroidal thickness is observed at peak plasma concentration level which is about 20-120 minutes.

There have been studies discussing the effect of caffeine on ocular microcirculation. Lotfi and Grunwald investigated the acute effects of 200 mg of caffeine on the retinal circulation with findings that support caffeine causes a 13% reduction in retinal blood flow. Another study observed a decrease of 6% in chorioretinal blood flow at 60 minutes after oral administration of 100 mg caffeine. Retrobulbar hemodynamic studies detected a significant increase in the resistive index of the ophthalmic, central, and short posterior ciliary artery after an oral application of caffeine. Terai et al found a significant vasoconstrictory response of the retinal vessels 1 hour after caffeine intake. Vural et al investigated the effect of a cup of Turkish coffee on sub-foveal choroidal thickness and found a significant decrease in choroidal thickness for at least 4 hours after drinking coffee. Like our study, Mehmet et al and Zengin et al performed a study with 200mg of caffeine, instead of a cup of coffee, to minimize the effect of other nutrients on choroidal thickness. The study showed a reduction in choroidal thickness at caffeine's peak level of concentration compared to baseline measurements. Therefore, past literature and data from this study suggests caffeine results in choroidal thinning; this occurs due to an increased vascular resistance of retinal vessels resulting in a decrease in choroidal blood flow.

It has been hypothesized that mild choroidal thinning in inherited retina disease may be due to loss of choriocapillaries, with more advanced thinning related to greater and more widespread loss of choroidal tissue. The sudden reduction of choroidal thickness with ingestion of caffeine was observed at one hour and reverted back to habitual thickness at the two hour time interval. This finding suggests that the effects of caffeine is transient, and our body adjusts to this change relatively quickly. With chronic use of caffeine and repeated insults, this reduction in choroidal thickness can have a severe impact on people with retinal or choroidal pathologies, since it causes more vasoconstriction of blood vessels. Therefore,
caffeine ingestion should be considered as one of the factors while examining choroidal structure in patients with retinal or choroidal pathologies. However, longer term research is needed to study the effects of chronic use of caffeine in patients with retinal or choroidal pathologies to consider if this finding has a serious or detrimental long-term effect on choroidal structures.

Moreover, we found a significant \( p<0.05 \) negative correlation between axial length and choroidal thickness in the caffeine group (table 3), showing that choroidal thickness was reduced with increased amounts of axial length. Woodman et al\(^\text{34} \) had performed a study observing the axial length and choroidal thickness changes for prolonged accommodation among myopes and emmetropes. Their study found a negative correlation between axial length and choroidal thickness. But no study so far has examined if caffeine has any effect on axial length alone; this makes it difficult to verify if there is an association between axial length and choroidal thickness with caffeine intake.

Likewise, in this study, we also observed a negative correlation between axial length and choroidal thickness with caffeine consumption. This supports the findings that an increase in axial length will decrease the choroidal thickness. This finding shows that subjects with high myopia should be very cautious in consuming high dosages of caffeine as there is a chance that they might be more prone to choroidal damage due to a thinner choroid. Although this change is only transient, there is concern that with chronic caffeine consumption this daily insult could amount to something significant. Because this study only examined the short-term effects of caffeine, more long-term studies should be conducted to verify these concerns.

Meanwhile, during any clinical investigation of the choroid, it is advisable to assess the choroidal structure after one hour of caffeine consumption since this study, as well as other earlier studies, have observed the effect of caffeine mostly between thirty minutes to one hour of time interval.
**Non-invasive tear film break-up time**

Studies on how caffeine intake affects tear film have focused on tear film quantity alone and have shown contradictory findings thus far. Unlike other preceding studies, this study has assessed the quality of tear film on the potential impact on visual performance. Caffeine has shown stimulatory effects on the quantity of tear film. It increases acetylcholine which is one of the neurotransmitters for the parasympathetic pathway. Acetylcholine acts on main lacrimal gland by stimulating the muscarine receptors leading to activation of ionic channels that results in secretion of water, protein, electrolytes and stimulation of tear secretion.35

To my knowledge, this is the first study so far that has investigated the effect of caffeine on tear film quality. The tear break-up time increased with caffeine and placebo intake at 1 hour (p=0.05) which was significant but not at 2 hours (p=0.615), as seen in figure 12. From these results, the placebo and caffeine groups did show an increase in tear break up time at one hour; this increase among the placebo group could be attributed to the use of magnesium calcium capsules instead of using a placebo capsule for the control group. Using magnesium calcium placebo capsules may have had an impact on tear film break-up time of the control group. There was one study conducted by Tsubota et al35, where he investigated the efficacy of calcium ointment on dry eye patients and saw an improvement in the dry eye. The study found that calcium ion is involved in the control of various cell functions; therefore, a decrease in calcium levels in precorneal tear film may be involved in pathogenesis of dry eye. Thus, comparing it with this study results, the increase in tear film break up time among the placebo group might be due to calcium nutrients present in the capsules. This increase in tear film quality might act as a protective effect on dry eye along with caffeine. This suggests a flaw in the experimental design in establishing a true placebo group which potentially could have confounding results. To prevent this mistake, the placebo
group should only be dosed with placebo capsules instead of with nutrient contents (or magnesium calcium in our case) present.

Arita et al\textsuperscript{21} had investigated the effect of caffeine on tear meniscus height using a crossover design where subjects received caffeine and placebo capsules as in with our study. Their findings suggested an increased tear volume (tear meniscus height) after caffeine consumption. Similarly, Osei et al\textsuperscript{36} investigated the effect of caffeine on tear secretion with a Schirmer test. Their study was a placebo-controlled crossover study where subjects were exposed to caffeine and drinking water in two different sessions. Their findings indicated an increase in tear secretion after caffeine intake but did not observe any effect with drinking water. Studies on the efficacy of drinking water to improve dry eye are small-scale and not widely known, warranting further studies including accounting for multiple variables such as caffeine intake and others in their design. Further studies in this area might help to clarify the mechanism behind dry eye management.

However, from this study results, it showed an improvement in tear film quality at one hour, which coincides with caffeine’s peak plasma concentration level. After two hours, this improvement was not observed, suggesting that the effect is short lived. Therefore, we can at least conclude that caffeine has some temporary effect on tear film and our results are comparable to previous studies conducted by Osei and Arita. Tear film stability over corneal surface is crucial to maintain excellent quality of vision. Reduced tear volume or irregularity of tear film will enhance optical aberrations that contribute to reduced retinal image quality which is associated with reduced visual functions or performance.\textsuperscript{37} Although previous studies were more focused on tear film quantity, both tear film quality and quantity together are important in supporting a healthy ocular surface. Hence, the data is suggestive that caffeine has a transient protective effect on dry eye by improving tear quality and quantity and improving an individual’s visual performance.
Ocular reading:

Caffeine on reading performance

Prior to this study, there is no evidence investigating the effect of caffeine ingestion on ocular reading performance. From the results, we found no significant differences between caffeine and placebo groups except for reading rate (Figure 8) and average span of recognition (Figure 6). Reading rate and average span of recognition increased with caffeine at one hour but there was no difference at two hours. Since there was an increase, an analysis was performed to examine a correlation between reading rate and average span of recognition (Table 4). The analysis yielded significant data supportive of a positive correlation between them (p<0.05). To increase the ability to recognize words more rapidly and develop strong visual memory, fewer fixations with fewer regressions in reading are needed.\textsuperscript{38,39} Table 4 shows there was a negative correlation between reading rate with fixations and regressions; this suggests an improvement in reading rate as indicated by less regressions and fixations. Similarly, a decrease in average duration of fixation will increase reading rate, as it is suggestive that subjects are faster at recognizing words when reading. This shows that with caffeine intake, reading rate can be improved by recognizing words faster than without any caffeine intake. These effects help to improve visual performance during reading tasks.

Span of recognition is one of the criteria involved in assessing reading performance. McConkie & Raynor\textsuperscript{40} stated that the usual span of recognition is 10 letter spaces. The span is defined as the region around the point of fixation where the characters of a given size can be resolved. The boundary of span indicates the horizontal retinal eccentricity at which letters formatted as text are no longer recognizable in reading. If there is a lesser span of recognition, the person will not be able to recognize words and their reading rate will reduce, which might lead them to be a poor reader. To improve reading performance, increase in span would help a person be a stronger reader.
Furthermore, visual span\textsuperscript{41} has the most vital role in text reading among people with low vision. To improve one’s visual performance, reading has been a challenge especially for people with low vision and reading disabilities. From this study, we saw that there is an association between reading rate and span of recognition. When there is an increase in span of recognition, reading rate will improve with caffeine. So, low vision individuals may benefit from consuming caffeine as it might improve their reading performance. Most low vision individuals have reduced contrast sensitivity due to ocular media opacities or retinal pathologies. This reduction in retinal image contrast (contrast sensitivity) will narrow the visual span making it difficult to recognize letters. Therefore, they saccade through text in smaller steps leading to reduced reading speed affecting their visual performance overall.\textsuperscript{41} Improving visual performance through measuring reading rate in low vision subjects needs further investigation. This study included a younger population with no ocular pathology or low vision subjects, so further studies need to be conducted to investigate the effects of caffeine on reading rate among the geriatric population with retinal pathologies.

\textit{Caffeine on accommodation and pupil size}

There have been a few studies that evaluated the effect of caffeine on accommodation and pupil size. Ajayi et al\textsuperscript{42} had investigated the effect of caffeine on the amplitude of accommodation and near point of convergence among caffeinated and decaffeinated groups. In their study, they performed near point of convergence with pencil push up test and amplitude of accommodation was evaluated with minus lens method. They found that there was an increase in accommodation in first 30 minutes and did not show any variability after 30 minutes. Near point of convergence did not show any difference with caffeine ingested.

The observed increase in accommodation is postulated to have occurred due to the stimulatory effects of caffeine on parasympathetic nerves responsible for ciliary muscle constriction allowing the crystalline lens to thicken and hence increase ocular refractive power. This increase will allow the eye to focus objects closer than needed leading to an
increase in the amplitude of accommodation. This study did not investigate the association between an increase in refractive power and amplitude of accommodation.

Similarly, Abokyi et al\textsuperscript{19} examined the effect of caffeine on pupil size using millimeter ruler and amplitude of accommodation with a push up technique. In their study, they examined only one randomized eye on all subjects throughout the study. They found an increase in the amplitude of accommodation as well as in pupil size. Bardak et al\textsuperscript{43} conducted a study on single administration of coffee on pupil size and ocular wave front aberration measurement on healthy subjects. The subjects ingested 57mg of Turkish coffee. They did not find any prominent change in pupil size after coffee intake but found an increase in higher order aberrations. This is a contradictory finding because with no change in pupil size, aberrations should remain the same. This increase in aberration might have occurred due to corneal ultrastructural changes, however, this parameter was not assessed in this study. One of the limitations in their study was not assessing accommodation along with pupil size measurement.

Previous studies\textsuperscript{19,42} have already mentioned that caffeine has stimulatory effects on sympathetic nerve that causes pupil dilation but in the Bardak study that was not observed possibly due to the lower dosage of caffeine. Like the Bardak’s study, we did not find any change in pupil size on healthy subjects. The subjects were reading the text at 40 centimeters while pupil size was assessed with Grand Seiko autorefractometer; the pupil would be more constricting rather than dilating due to the near triad effect. This objective measurement was a real time measurement, while the subject was actively reading text, the methods differ with the aforementioned studies. Room illumination is one of the factors that can alter the pupil size. A study with Berman et al\textsuperscript{44} examined the luminance-controlled pupil size affecting word reading accuracy. They found that better reading accuracy correlated with smaller pupils in comparison to larger pupils, potentially due to reduced aberrations. In our study, we did not control for room illumination, simply using the same settings for each trial. This may or may not have prevented finding a change due to caffeine ingestion.
Because most of the subjects in this study were habitual caffeine users, any significant effects of caffeine on the subjects might have been dampened. We did not include any vergence functions in this study associated with accommodation due to near triad, which might have added more evidence to this study. Further studies are suggested to be conducted to know the association between accommodation, vergence and pupil size with caffeine ingestion for better understanding.
LIMITATIONS

In this study, most of the subjects were habitual caffeine users. Subjects that regularly ingest caffeine might have yielded insignificant results because of the tendency for them to develop a tolerance level towards the effect of caffeine.\textsuperscript{45} There was non-equal gender distribution and an underrepresentation of the geriatric population. Few subjects included had some degree of presbyopia might have caused a bias in the data.

The Cirrus HD OCT is a spectral domain instrument using single wavelength of light to see retinal and choroidal structures. This instrument has less depth penetration (sensitivity roll off) providing very poor reflectance of choroidal structure resulting in variation in choroidal thickness measurement. The number of images averaged was less compared to other types of OCT such as swept source that produces higher resolution of choroidal structure. The choroidal thickness was assessed manually instead of using any algorithm for calculation of the thickness objectively.

Reading performance was assessed with clinical screening instrument, the Visagraph III, which may limit the ability to assess eye movements in the reading task as precisely as desired. The reading duration was short with the Visagraph III since all subjects read the paragraph of choice once during each time of measure, which might have led to insignificant results. Head posture varied among all subjects while assessing reading performance. Prolonged reading time with eye tracker might have added a better data for this study.
CONCLUSION

Caffeine has an impact on ocular structures and on visual performance. There was an increase in tear film quality, reading rate and average span of recognition but the effect was small. These parameters are considered as important criteria for better quality of vision.

Increase in tear film quality at first hour of caffeine consumption might have a minimal effect on dryness since it was a transient effect and the test was performed on normal healthy adults. Although there are contradictory studies on tear film, further investigations on the effect of caffeine among dry eye population would shed more light on the potential cause and mechanism behind the observed improvement on tear film quality.

Reading rate and span of recognition increase with caffeine consumption which might have a small effect on visual performance. Further investigations on the effect of caffeine on cognitive performance with reading comprehension might help us further understand extensive effects on the eye and the mechanism to support these findings.

In this study, the impacts of caffeine in tear film quality, reading rate, and span of recognition are short lived since the effects were mostly seen at 1 hour during the maximum plasma level concentration. In addition, habitual caffeine users may have developed a tolerance to caffeine that is not comprehended in our results and analysis.

Based on this limited study as well as the current literature (to the best of the author’s knowledge), it is not known what possible long-term effects of these transient changes from caffeine can have on the eye. Therefore, longitudinal studies observing the effect of caffeine on subjects with retinal and/or choroidal pathologies and on the geriatric population might help to better understand the long-lasting effects of caffeine.
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