INDOOR AND OUTDOOR EYE MOVEMENTS IN MYOPIA

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Amy Zhang

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Amy Zhang, O.D.

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10/28/16
Date

Fuensanta Vera-Diaz, O.D., Ph.D.
Graduate Faculty Advisor

Elise Harb, O.D., M.S.
Thesis Committee Member

Glen McCormack, O.D., Ph.D.
Thesis Committee Member

Thanasis Panorgias, Ph.D.
Thesis Committee Member

11-29-2016
Date

Nancy J. Coletta, O.D., Ph.D.
Director of Graduate Studies

New England College of Optometry

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Amy Zhang

New England College of Optometry, 2016

Purpose: Time spent outdoors appears to have a protective effect against the development of myopia, even when both parents have myopia. The exact mechanism for this protective effect is unknown, although most agree that the intensity and composition of outdoor light is important. Several other factors independent of lighting have been studied with inconclusive results. Previous studies indicate that the number of changes in gaze position an individual makes is task-related. Subjects with myopia may make fewer changes in fixation when reading than emmetropic subjects. It is not known whether individuals with myopia show differences in the number of changes in fixation or other eye movements when performing other everyday tasks, or whether these are different between indoor and outdoor environments. We hypothesize that individuals with myopia, who deploy more central vision attention, especially indoors, obtain more information with fewer changes in fixation (fewer saccade eye movements). The aim of our study is to evaluate whether there are differences in changes in fixation between myopes and emmetropes while performing various indoor and outdoor tasks.

Methods: Results from a pilot feasibility study were used to finalize the study design, including the tasks and pathways to be tested, as well as the instructions given to subjects during each task. This pilot study was also used to determine data analyses procedures. In the main study, we characterized changes in fixation behavior in a group of young healthy emmetropic adults (n=18, group SE: +0.43 ± 0.33 DS, ranging from -0.16 to +0.94 DS) and subjects with myopia (n=20, group SE: -3.25 ± 2.40 DS, ranging from -0.59 to -8.46 DS) during various indoor and outdoors tasks representative of common everyday activities. Eye position and changes in fixation were evaluated using a lightweight and portable *ViewPoint EyeTracker*® while subjects randomly performed 7 indoor tasks [read on laptop, type on laptop, read a book, play Tetris on laptop, watch TV, walk inside, walk inside while using an iPod Touch] and 5 outdoor tasks [observe examiner cross sidewalk, walk in park, observe statue, walk in park while using an iPod Touch, walk on busy street] for 15 seconds each. A change in fixation was defined by the eyetracker program's velocity threshold algorithm. <u>Results</u>: Significantly fewer changes in fixation were found for all subjects when performing indoor tasks compared to outdoor tasks ($Z=5.10$, $p<<0.01$). When subjects performed an identical task indoors and outdoors, i.e., walking using an iPod Touch, the results are suggestive of an association (fewer changes in fixation for the indoors compared to outdoors environment), but did not achieve statistical significance ($Z=1.73$, $p=0.08$). Subjects with myopia showed a trend towards fewer changes in fixation than emmetropes when performing indoors near tasks, reaching significance when playing Tetris ($Z=1.97$, $p=0.04$). These results indicate that myopes may deploy more attention on the task at hand than emmetropes when doing steady and demanding near tasks. On the other hand, myopes showed more changes in fixation than emmetropes when watching TV ($Z=-2.21$, $p=0.03$) and when observing a statue outdoors ($Z=-1.95$, $p=0.05$), but not for other outdoor tasks. <u>Conclusions</u>: The overall conclusion of the study is that number of changes in fixation may be associated with myopia. Our results suggest that individuals with myopia may have a less efficient visual system than emmetropes when doing steady near tasks that require high attention levels. Longitudinal investigations in children are necessary to determine if eye movements have causative effects on myopia development and/or progression.

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TABLE OF CONTENTS

1. General Introduction	1
2. Pilot Feasibility Study	7
2.1. Purpose	7
2.2. Methods	8
2.3. Results	21
2.4. Conclusions	26
3. Main Study	28
3.1. Purpose and hypothesis	28
3.2. Methods	29
3.3. Results	41
3.4. Discussion	49
4. General Conclusions	55
5. Bibliography	56
6. Appendix I: ARVO Poster	64

FIGURES AND TABLES

Figure 1, Changes in fixation from near to far viewing distance 4

Figure 2a, A subject wearing the Arrington Research *ViewPoint EyeTracker*® 9

Figure 2b, Pupils of each eye 9

Figure 3, Snapshots of the *ViewPointClient*® software 11

Figure 4, Definition of direction of gaze coordinates 12

Figure 5, Calibration stimuli used in the *ViewPointClient*® software 13

Figure 6, Custom calibration screen 14

Figure 7, View of the Commonwealth Avenue Mall 17

Figure 8, View of the Miriam & Sidney Stoneman Playground 18

Figure 9, X and Y gaze coordinates 22

Figure 10, Sample of indoor task: Reading a book 34

Figure 11, Pathway from Vera-Diaz Lab to an office down the hall 35

Figure 12, Sample of outdoor task: Watching examiner cross a four-way intersection 37

Figure 13, Sample of outdoor task: Observe a statue 38

Figure 14, *DataAnalysis* software 40

Figure 15, Mean number of changes in fixation 41

Figure 16, Changes in fixation indoors and outdoors (iPod Touch) 43

Figure 17, Changes in fixation for indoor tasks in emmetropes and myopes 44

Figure 18, Changes in fixation for outdoor tasks in emmetropes and myopes 45

1. General Introduction

Refractive error has a complex etiology that includes a combination of genetic factors, environmental triggers, and visual feedback, which are all important regulators of eye growth (Kleinstein et al, 2003; Jones et al, 2007; Rose et al, 2008a; 2008b; Dirani et al, 2009; Deng et al, 2010; French et al, 2013; Czepita et al, 2014; Ramamurthy et al, 2015). Many studies have shown that time spent outdoors is protective against the development of myopia, even when both parents are myopes (Jones et al, 2007; Jones-Jordan et al, 2012; Rose et al, 2008a; 2008b; Dirani et al, 2009; Deng et al, 2010; Guggenheim et al, 2012; French et al, 2013), although this may not be the case on slowing down the progression of myopia (French et al, 2013). The exact mechanism for this protective effect is unknown; although most agree that the higher light intensity and composition of outdoor light is important (Sherwin et al, 2012; Smith et al, 2012; Dharani et al, 2012; Schmid et al, 2013; Read et al, 2014). Other factors that have been studied with inconclusive results are vitamin D (Guggenheim et al, 2014; Yazar et al, 2014; Ramamurth et al, 2015; Tideman et al, 2016), physical activity (Read et al, 2014; Jacobsen et al, 2008; Deere et al, 2009; Guggenheim et al, 2012), and peripheral defocus (Smith et al, 2007; Flitcroft, 2012; Benavente-Pérez et al, 2014).

Retinal image quality in central and peripheral retina is important in normal emmetropization (Wallman et al, 1987; Collins et al, 2006; Smith et al, 2007; 2009; Liu et al, 2011; Sreenivasan et al, 2013; Ramamurth et al, 2015). Degraded retinal image quality can cause a failure in emmetropization and lead to excessive eye growth and myopia (Wallman et al, 1987; Smith et al, 2007; 2009; Read et al, 2010; Liu et al, 2011; Sreenivasan et al, 2013;

Ramamurthy et al, 2015). There is growing evidence on the importance of peripheral retinal input in emmetropization and refractive error development. For example, induced peripheral defocus causes axial refractive errors in animal models, which seems to indicate that a balance between central and peripheral retinal image quality is critical for normal emmetropization (Wallman et al, 1987; Smith et al, 2007; 2009; Liu et at, 2011). Note that while peripheral retinal input seems to directly affect emmetropization (Wallman et al, 1987; Collins et al, 2006; Smith et al, 2007; 2009; Liu et al, 2011; Sreenivasan et al, 2013; Ramamurth et al, 2015), peripheral refraction itself does not seem to play a role in the development of human myopia (Mutti et al, 2011; Sng et al, 2011; Atchison et al, 2015; Hartwig et al, 2016). Note that in the original study by Hoogerheide et al, peripheral refraction was measured after, not before, subjects did or did not develop myopia (Hoogerheide et al, 1971).

We hypothesize that one mechanism whereby outdoors is protective of myopia may be that eye movements are different outdoors than indoors. The proposed mechanism involves different eye movements in myopia and is explained next. First, most indoor activities involve near work that requires higher cognitive and attentional demands. The load of central vision (foveal) attention affects the dynamics of the eye movements (Wilder et al, 2009; Gerardin et al, 2015). We propose that a decrease in the number of attention shifts causes a decrease in the number of fixation changes. Most tasks performed indoors require a high level of central vision attention, which can decrease peripheral sensitivity. A recent study indicated that when attentional load is deployed on central vision stimuli, individuals with myopia experience a greater decrease in peripheral contrast sensitivity compared to emmetropes (Kerber et al, 2016). In addition, there are dioptric demand differences between indoor and outdoor environments (Flitcroft, 2012). Viewing distances are typically greater and have less dioptric variation in outdoor than indoor environments, which are dioptrically more varied. As a consequence, peripheral retinal defocus, which is associated with myopia development (Smith et al, 2007; Flitcroft, 2012; Benavente-Pérez et al, 2014, Sprague et al, 2016), may be increased indoors compared to outdoors, and a more uniform pattern of peripheral retinal defocus would be experienced outdoors. When an individual spends more time indoors and less time outdoors, as is the case of myopes-to-be, they may experience greater peripheral retinal defocus. Note that differences in eye movements are more likely to occur in indoor environments due to the variability of dioptric demands. Another consequence of the different dioptric demand, accommodation responses are greater and changes in accommodation are more frequent and larger in indoor environments while performing near tasks (Flitcroft, 2012, Gwiazda et al, 2004). This variability, and perhaps instability (Kerber et al, 2015), in accommodation responses could also cause abnormal eye movements in indoor environments. We hypothesize that individuals with myopia, who deploy more central vision attention, especially indoors, obtain more information with fewer changes in fixation (fewer saccade eye movements).

Individual differences in changes in fixation have indeed been found between indoor and outdoor images projected on a computer (Dorr et al, 2010), likely due to differences in the scene's image content. These inter-individual differences are especially evident when looking at natural scenes (Dorr et al, 2010). The characteristics of fixation and eye movements have also been found to be task-related (Mills et al, 2011). The proportion of fixations on certain objects are highly dependent on the specific task that subjects are asked to perform, with the greatest fixation being on objects that are relevant to the task (Rothkopf et al, 2007).

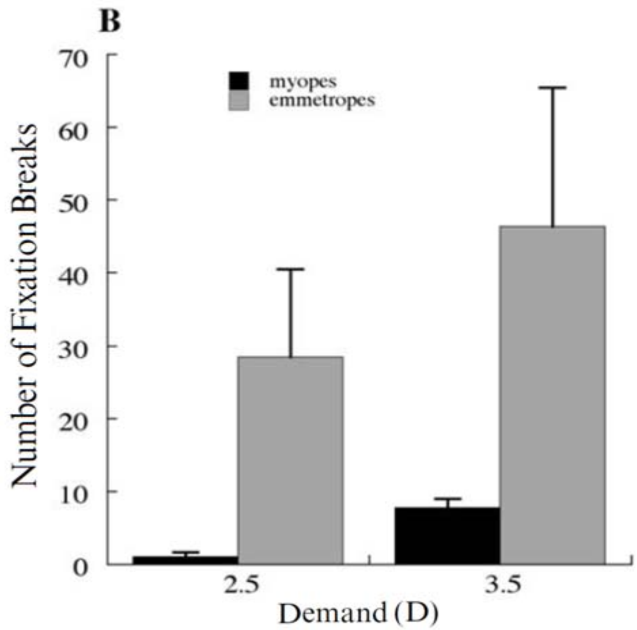

Figure 1.
From Harb et al, Vis Res, 2006, Figure 10:
Individuals with myopia (black bars) show significantly fewer changes in fixation from near to far viewing distance during a 10-minute reading task at 2.50 and 3.50D accommodative demands compared to emmetropes (grey bars). Error bars indicate ±1SD.

Furthermore, it has been shown that myopes make fewer changes in fixation (breaks from reading to looking up) when performing visually demanding tasks in indoor environments such as reading for 10 minutes (Harb et al, 2006) (Figure 1). Note that this finding, as well as those above studied in adult myopes, implies correlation, not causation. A possible explanation for this study's findings is that myopes deploy higher levels of central vision attention when doing indoor near tasks (Kerber et al, 2016).

Near tasks with high visual demands have also been investigated in studies on the development of myopia in children. For example, one study showed that near tasks such as reading, writing, and working on a computer might be associated with myopia in children of ages 6-18 years (Czepita et al, 2010). Another recent study (You et al, 2016) showed that certain near work tasks involve other behaviors that may be associated with myopia development, including: keeping an inappropriate distance when reading, writing, and watching TV, and continuing to do near work for more than 30-40 minutes without an eye break. This same study showed that these behaviors were also associated with shifts toward myopia in 6-10 years old children in Shanghai. Reading is a common and important everyday near task that has been associated with myopia development in many studies. A study found that Australian school children (12 year olds) who performed near work (i.e., completing homework, reading, using a computer) at a distance closer than 30 centimeters were more likely to have myopia than those who worked at a longer distance (Ip et al, 2008). Also, in young adults (aged 18-29 years old), near work may lead to higher prevalence of myopia (Czepita et al, 2014). With technology becoming more integrated in our everyday lives, we decided to investigate the effect of reading physical books, but also reading an article on a laptop. We are interested in exploring whether the task of reading per se is associated with myopia, or if the medium used to read influences this association.

The results of the eye movements and near work studies described above offer insight on the possible relationship between myopia and eye movements, in particular the number of changes in fixation. The findings in these studies suggest that eye movements may differ significantly between indoor and outdoor environments (Dorr et al, 2010; Mills et al, 2011). We propose that the pattern of gaze behavior typically performed while outdoors may be important in normal emmetropization.

We hypothesize that individuals with myopia obtain more information with fewer changes in fixation (fewer saccade eye movements), which in turn cause less frequent refreshing of retinal images (Martinez-Conde et al, 2006; Ghasia et al, 2015) and therefore less release of dopamine (Schmid et al, 2004; McCarthy et al, 2007; Ashby et al, 2010; Feldkaemper et al, 2013). Higher levels of dopamine in the retina have been shown to be important in normal emmetropization and prevention of myopia (Schmid et al, 2004; McCarthy et al, 2007; Ashby et al, 2010, Feldkaemper et al, 2013) in animal studies. Therefore, individuals susceptible to develop myopia may be at greater risk if they perform fewer changes in fixation. The goal of this study is to conduct an initial investigation of the importance of eye movements and variable visual input in indoor and outdoor environments in relation to myopia in order to contribute to our understanding of the development of myopia. If an association is found, longitudinal investigations in children will be necessary to determine if eye movements have causative effects on myopia development and/or progression.

2. Pilot Feasibility Study: Measurements of Eye Movements Indoors and Outdoors

2.1. Purpose

This pilot study was designed to evaluate feasibility of the methods and determine the procedures for the main study. Specifically, the purpose of the pilot study was to finalize the indoor and outdoor pathways and tasks that subjects would perform, as well as to finalize the instructions given to subjects during each trial and to find an optimal data processing and data analyses procedure.

2.2. Methods

2.2.1. Subjects

A total of three young adults with healthy vision were enrolled in the pilot study. Criteria for inclusion were: (1) no history of surgery or eye disease, (2) within 18-32 years of age, (3) best-corrected visual acuity (VA) 20/20 or better in each eye, (4) not using drugs that may affect their vision, (5) no mobility impairments (able to walk for 15 minutes while carrying a small backpack with a lightweight laptop), (6) contact lens wearer if distance vision correction was required. Refractive status was determined by open-field autorefractor that followed refractive history.

2.2.2. Procedures

For each subject, a vision screening was done to ensure that the subject met all inclusion criteria. This vision screening included an ocular history questionnaire, non-cycloplegic open-field autorefraction (Grand Seiko WR-5100K), distance VA, axial length measurements with a non-contact device (Zeiss IOL Master 900) and undilated ocular health evaluation in each eye.

Subjects were corrected with their soft contact lenses if they required distance refractive correction. In this pilot study, one subject had myopia and therefore wore contact lenses.

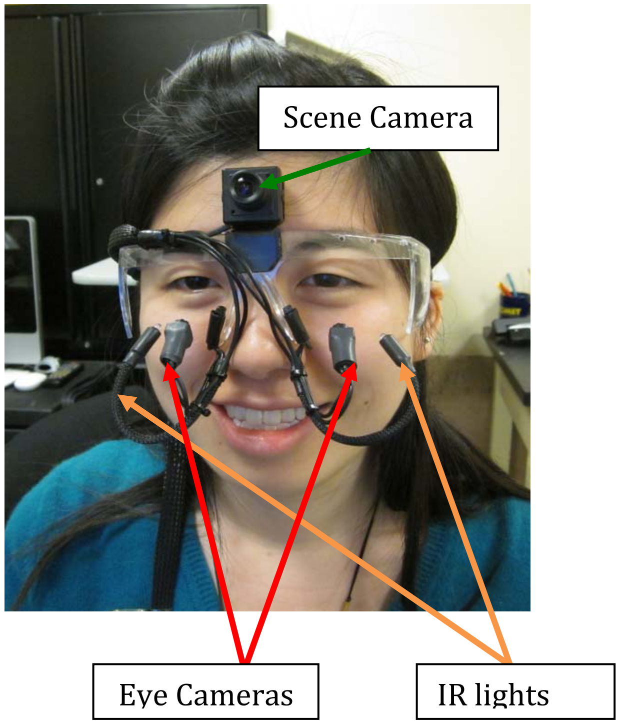

Figure 2a.

A subject wearing the lightweight Arrington Research *ViewPoint EyeTracker®* model BNE07.

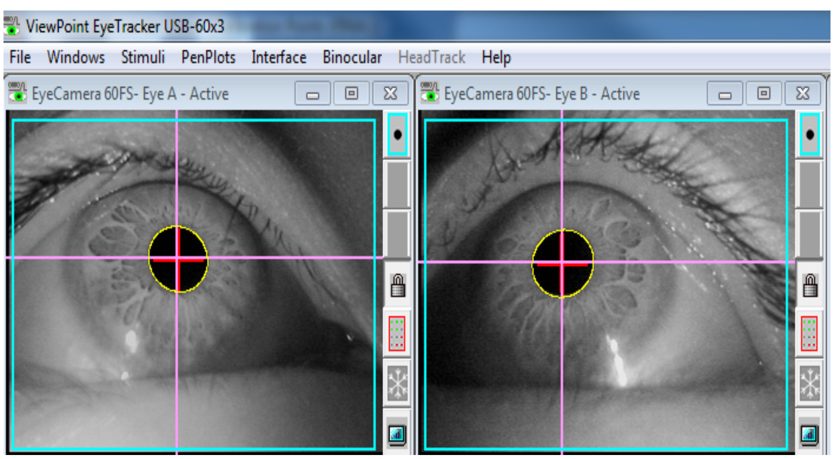

Figure 2b.

Pupils of each eye should be centered and leveled horizontally and vertically.

2.2.3. ViewPoint EyeTracker®

The FDA-approved Arrington Research *ViewPoint Eye Tracker®*, model BNE07 (http://www.arringtonresearch.com/viewpoint.html, Figure 2a) was used to record fixational eye movements while subjects freely explored a number of real world environments including a semi-controlled indoor course at the New England College of Optometry (NECO) and few outdoor courses nearby the College. Following the vision screening, the *ViewPoint EyeTracker®* was adjusted to each subject's face and eyes. Adjustment of the eye cameras and infrared lights was done by the examiner while the subject looked straight ahead at a target (letter X) projected in the center of a large screen. The examiner adjusted the IR lights to ensure they were not in the subject’s line of sight or obstructing the visual field in anyway. The examiner also adjusted the eye cameras to ensure the pupils of each eye were centered and approximately the same size (horizontal and vertical diameter) using the *ViewPoint EyeTracker® ViewPointClient* software window (Figure 2b & Figure 3). The examiner finally adjusted the IR lights temporally to the eye cameras so that each eye was illuminated by the same amount.

Some of the advantages of this eyetracker are that it is lightweight (as a pair of eyeglasses) and it minimally restricts natural head movements and the normal field of view of subjects (Figure 2a). The device is composed of a lightweight plastic frame with two tiny eye cameras modified to work in the infrared (IR) spectrum and two IR LED lights (invisible to the human eye) that connect to a processor. Binocular eye movements were recorded in real-time, depicted by two dots indicating the foveal direction of the eyes, while subjects performed the various pre-determined tasks. Note that the two dots are not visible to the subjects when they are performing the task. The dots are only visible when analyzing the data using the *ViewPoint EyeTracker® DataAnalysis* software (Figure 14). The device also has a scene/gaze camera that records real-time uncompressed videos of the scene subjects are viewing while performing the tasks (Figure 3). The videos are linked to the recorded eye movements frame by frame.

Several previous studies have used eyetrackers to evaluate eye movements while subjects walk and also while they perform more complicated tasks. For example, subjects have been asked to walk and pick up objects (Rothkopf et al, 2007); or walked up and down stairs while wearing an eyetracker (Den Otter et al, 2011). Previous studies have used the *ViewPoint EyeTracker®* and reported accurate tracking of the eyes as well as accurate recording of fixations and saccades while performing tasks such as reading labels (Dorris et al, 2007; Leske et al, 2007).

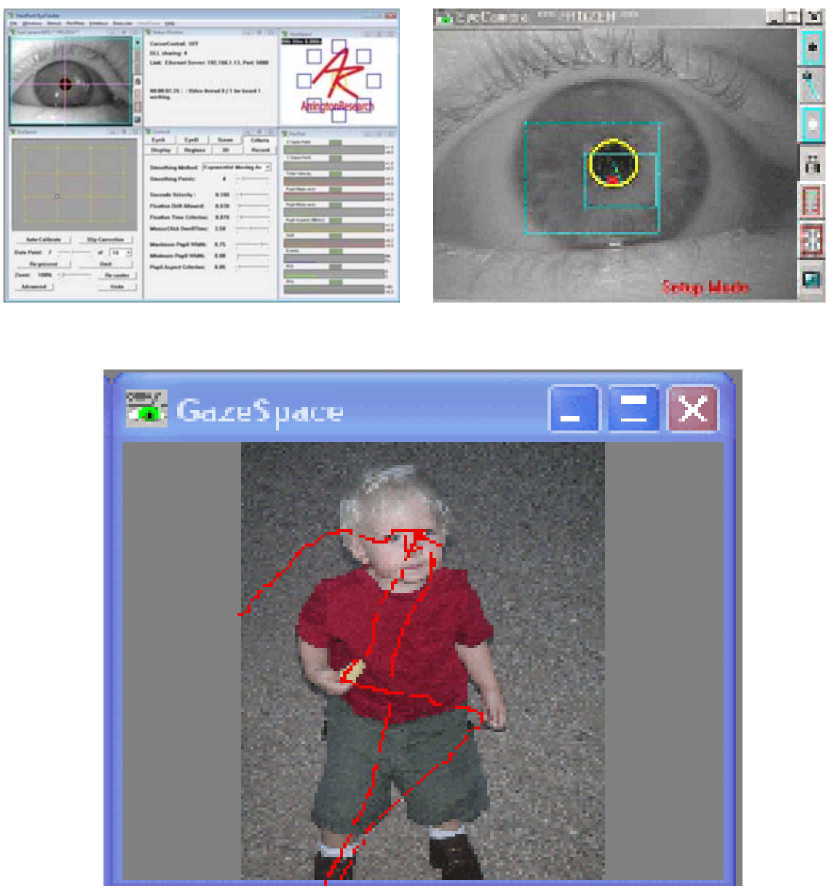

Figure 3. Snapshots of the *ViewPointClient®* software, available to record and process eye movements.

Top images: snapshot of the software screen and eye tracking.

Bottom image: snapshot of the scene camera recording with eye movements trajectory superimposed.

The *Viewpoint EyeTracker®* DataAnalysis software records a number of data values, two of which we were particularly interested in. One data value of interest was gaze coordinates, which depicts the point in space where each eye looks at during each task. Figure 4 shows the direction of the gaze coordinates defined by the eye tracker software system. The gaze coordinates do not intuitively correspond to the normal orientation of up and down; instead, the software's definition of up and down is flipped. The other data value of interest was the software's automated measurements of fixation changes.

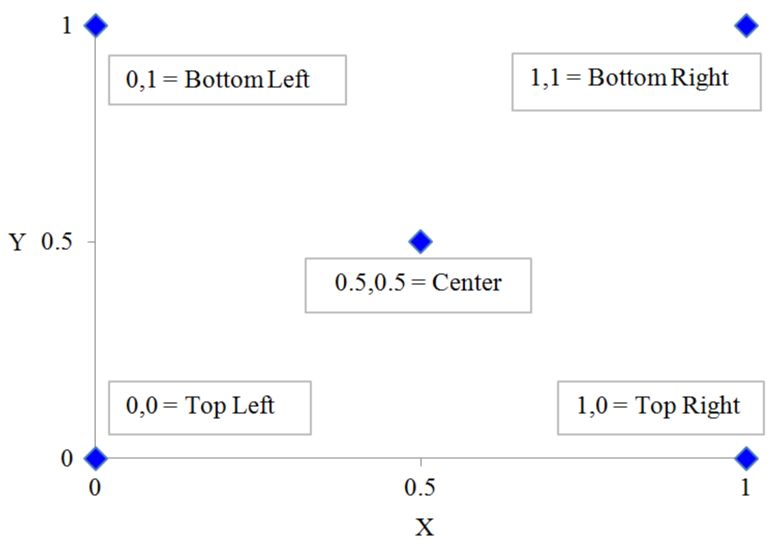

Figure 4. Definition of direction of gaze coordinates as defined by *ViewPoint EyeTracker® DataAnalysis* software. For example, the X,Y coordinates 0,1 show that subject's eyes were looking at the bottom left hand corner of the laptop screen.

2.2.4. Calibration

Calibration of the eyetracker was performed as described in the *Viewpoint EyeTracker®* user guide manual and in consultation with Arrington Research company. We chose to use the "pupil only" calibration method because the "glint-pupil vector" method is more sensitive to z-axis movement of the head as described in the *Viewpoint EyeTracker®* user guide manual.

Two calibration methods were tested, both using a display to present stimuli that subjects were asked to follow. The standard method used stimuli projected on a 14 inch laptop, and the custom method used stimuli projected on a 55 inch LCD display. The three subjects were tested using both screens to determine if the larger display provided greater accuracy when recording larger ranges of eye movements, such as those typically performed outdoors. The scene camera was added to the device later in the main study and was therefore not used during calibration.

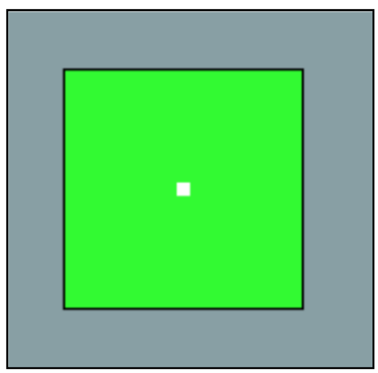

Figure 5. Calibration stimuli used by the *ViewPointClient®* software.

The standard calibration method, included with the *Viewpoint EyeTracker®* software, is called "Tunnel Motion." This calibration mode uses shrinking motion of a rectangular frame (Figure 5) that captures the subject's visual attention. Smooth pursuits bring the subject's gaze point to each of nine calibration points randomly projected on a 14 inch laptop. Subjects were instructed to not move their heads and to follow the stimulus as it randomly appeared in the screen. Due to the small size of the laptop screen, this calibration method was limited to a small range of eye movements, as demonstrated by the small visual angles (34 x 21 degrees, horizontally and vertically respectively). This range was insufficient for the tasks we intended to evaluate in the main study, which included walking outdoors.

Therefore, a custom method modeled after that used by the *Viewpoint EyeTracker®* software was created. The calibration stimulus was a letter X that followed the "Tunnel Motion" shrinking motion used by the *Viewpoint Eyetracker®* software. Nine calibration points were also tested. The stimulus was projected on to a 55 inch LCD screen (Figure 6). During calibration, subjects were instructed to not move their heads, but to look and follow the stimulus as it randomly appeared in the screen. With this display, we were able to calibrate the eyetracker for a wider range of visual angles (37 x 23 degrees, horizontally and vertically respectively) (Figure 6), and therefore this method was used in the main study.

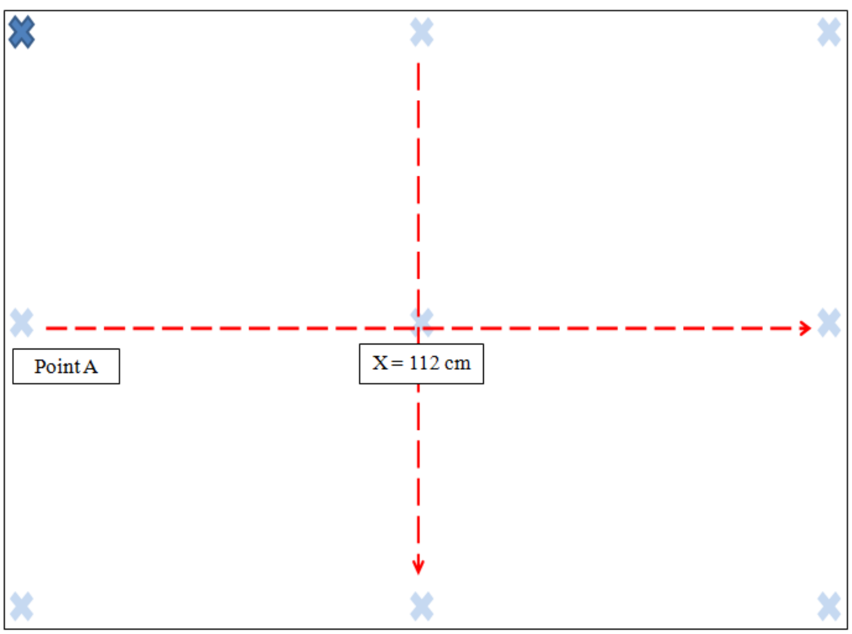

Figure 6. Custom calibration screen with the nine positions used to calibrate the eyetracker. During calibration, subjects were asked to accurately follow a letter "X" as it randomly moved to these nine positions on the screen without moving their heads.

2.2.5. Pathways and Visual Tasks

After completion of calibration, each subject was instructed to perform a number of tasks that included walking on designated pathways while carrying a small backpack that contained a laptop and the *ViewPoint EyeTracker®*. The eyetracker tracked and recorded the subject's eye movements as well as recorded where the subject was looking.

A trial run was performed to ensure that the subject understood the instructions and was familiar with the pathways. The examiner gave general instructions at the beginning and directed the subject during each trial. Subjects were instructed to walk normally on a designated pathway or normally performed the designated visual tasks while wearing the eye tracker glasses.

The indoor pathways and visual tasks were conducted in and around the Vera-Diaz Research Lab at NECO. The eyetracker recording was turned on before each trial and off before moving to the next. A complete non-randomized trial run consisted of:

1. Subject reads a document, the same for all subjects, on a laptop placed at 40 cm.
2. Subject stands up and walks from the desk to the sink.
3. Subject walks towards the instrument table, picks up book and flips through it.
4. Subject walks over to the desk with the phone, sits down, picks the phone up and pretends to make a phone call and talk to someone for 30 seconds.
5. Subject stands up, walks to another chair, and watches TV at 150 cm for 30 seconds.
6. Subject stands up, walks back to the first desk and sits down.
7. Subject reads text in a book, same for all subjects, at 40 cm.

The tasks tested were chosen because they are everyday tasks people perform. Near tasks in particular have been observed in many studies concerned about development of myopia in children. For example, studies have indicated near tasks such as reading, writing, and working on a computer might be associated with the occurrence of myopia in children and young adults (Ip et al, 2008; Czepita et al, 2010). Thus, we included near tasks such as reading and typing in our study. And with technology becoming more integrated in our everyday lives, we decided to not only ask subjects to read a book but also to read on a laptop. This would allow us to also observe if simply the task of reading plays a role in myopia, or if the medium used to read influences this association.

For the outdoor tasks, a busy pathway (Newbury street) and a quiet pathway (Commonwealth Mall park) were chosen to simulate common environments that people normally encounter when walking outside. Subjects were first asked to do a practice trial by walking on the sidewalk of Beacon Street for one block. Once the subject and the examiner felt comfortable with walking outside while wearing the eyetracker, three outdoor pathways were tested:

1. Newbury Street:
    a. Subject walks 1 block on the sidewalk of Newbury Street starting from Hereford Street to Gloucester Street, and back.

Figure 7.
View of the Commonwealth Avenue Mall.

Step 1: Subjects were instructed to walk towards the statue.

Step 2: Subjects were instructed to describe the statue to the examiner.

Step 3: Subjects were instructed to walk past the statue and walk towards Gloucester Street.

2. Commonwealth Mall park (Figure 7):

   b. Subject walks 1 block in the pedestrian path in the Commonwealth Avenue Mall from Hereford Street to Gloucester Street, and back, performing the following tasks:

      i. Starts at the entrance of the park on Hereford Street and walk towards the statue.

      ii. Describes the statue to the examiner.

      iii. Walks past the statue towards Gloucester Street.

      iv. Turns around and walks back towards Hereford Street.

Figure 8. View of the Miriam & Sidney Stoneman Playground.
- For the proposed Pathway #1, subjects were asked to walk around the play structure (pictured on the left).
  Step 1: Subjects were instructed to enter the playground.
  Step 2: Subjects were instructed to walk towards the play structure.
- For proposed Pathway #2, subjects were asked to walk to the benches and trees in the periphery of the play structure (pictured on the right).
  Step 1: Subjects were instructed to walk to first tree and then the second tree.
  Step 2: While at the second tree, subjects were instructed to walk about the second tree.
  Step 3: Subjects were instructed to walk to the bench.

3. Miriam & Sidney Stoneman Playground:

   a. Pathway #1 (walks around the play structure) (Figure 8):

      i. Starts at the entrance to the playground.

      ii. Walks towards the play structure.

      iii. Walks around the entire play structure.

      iv. Walks under the slide.

      v. Walks towards the bench.

      vi. Walks around the swings.

      vii. Walks back to the entrance of the playground.

   b. Pathway #2 (walk to the benches and trees in the playground) (Figure 8):

i. Starts at the entrance to the playground.

ii. Walks past the tire swing and walk towards the bench.

iii. Walks to tree #1.

iv. Walks to tree #2 and walk around it.

v. Walks to bench #1.

vi. Walks to bench #2.

vii. Walks back to the entrance of the playground.

Subjects were always asked to walk leisurely and normally during each pathway and specific instructions as to where to go next were given by the examiner.

2.2.6. Data Analyses

The *ViewPoint EyeTracker® DataAnalysis* software was used to analyze eye movements data. For this pilot study, the gaze position and number of fixations of each subject's eyes were obtained and analyzed. The software provided the gaze position (X and Y coordinates of both eyes) as well as the data on number of fixations for each task. In order to determine the accuracy of the data, we manually inspected each video as well as used the Quality code that the software provided for each data point measured. The Quality code ranges from 0 to 5 and is used by the software to grade the quality of each data point allowing us to determine if the data is valid or not for our study. Quality codes 2 to 5 indicated different criteria that were not met in other methods and thus did not apply to our study. Quality code 0 only applied to the "glint-pupil vector" method, which was not used in this study. Therefore, we were only interested in a quality code of 1, which was defined by the software as "the pupil was successfully located" when using the "pupil only" method for recording the eye movements.

2.3. Results

The purpose of this pilot feasibility study was to determine the indoor and outdoor pathways and tasks that subjects would perform in the main study, as well as to finalize the instructions given to subjects and to find an optimal data processing and data analyses procedure. We did not evaluate outcome data in this portion of the study for any other purposes.

A total of three subjects participated in the feasibility study. Figure 4 provides the definition of the direction of the gaze coordinates defined by the eye tracker software system, which do not intuitively correspond to the normal orientation of up and down. Gaze location coordinates obtained from the *ViewPoint EyeTracker® DataAnalysis* software were initially plotted as scatter plots (Figure 9). In figure 9 we show an example data point indicated by a red circle on the scatter plot. This data point has the X, Y coordinate of approximately (0, 0.8), which indicates that the subject's eye was looking close to the bottom left hand corner of his/her field of vision. The axes in this figure do not show units because they are raw coordinates that were not transformed to visual space measures as we concluded not to use this method as a way to analyze the data.

Nevertheless, from figure 9 it appeared that for indoor environments subjects moved their eyes less (more clustered data points). This anecdotal analysis method had several bias problems due to its subjectivity and separate analyses for each eye and was not used in the main study. In addition, this method was not effective in comparing the effect of visual task in eye movements because many data points were clustered in one area making it difficult to quantify how often subjects moved their eyes during each task.

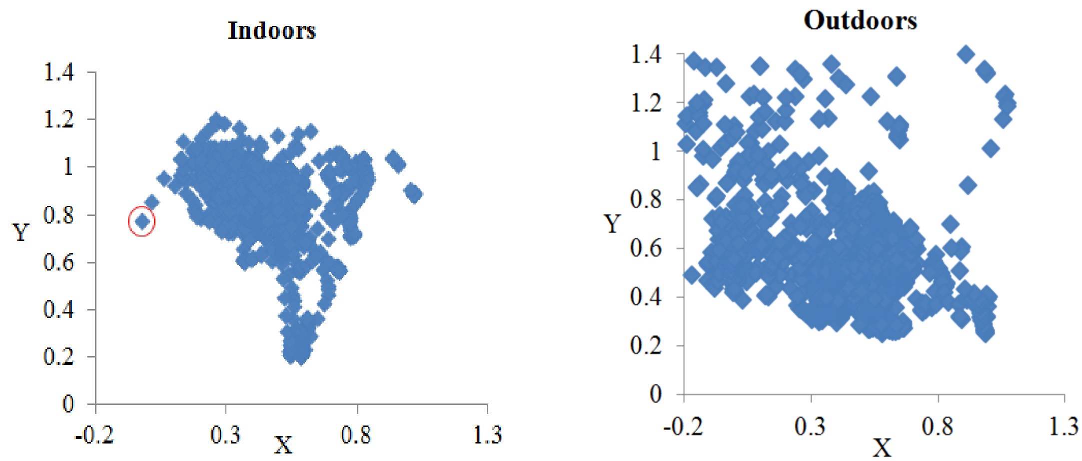

Figure 9. X and Y gaze coordinates without units were extracted and used to plot the gaze locations of each eye.
Two sample scatter plots are shown above for one eye performing two different tasks: to the left indoor tasks and to the right outdoor tasks.
The circled point (in red) in an example of X, Y coordinates of approximately (0, 0.8), which indicate that the subject's eyes were looking close to the bottom left hand corner of his/her field of vision. Note the cluster of data points in the center would make it difficult to quantify how often subjects moved their eyes for each task. This analysis method was therefore discarded.

The *DataAnalysis* software also provides information on when there is a change in fixation by both eyes together. For the purposes of the main study, we used the *ViewPoint Eye Tracker*® program's velocity threshold algorithm to define fixation. The velocity threshold algorithm finds fixations and saccades by classifying a saccade as the velocity of a data point greater that the velocity threshold. Any data points that are not saccades are fixations. Fixation was calculated by the *ViewPoint Eye Tracker*® program as the "length of time that the velocity was below the saccade velocity criterion which was 0.10 m/s." The program's fixation time criterion was 0.070 seconds. We therefore decided to use this objective method to investigate the number of fixation changes made by each subject during each task and this way we will be able to compare the large amount of data to be collected in the main study.

Since the purpose of our main study was to evaluate the relationship of eye movements with myopia, we chose common everyday tasks that are thought to play a role in the development of myopia, e.g., reading (Ip et al, 2008; Czepita et al, 2010; Czepita et al, 2014). It was more difficult to choose the outdoor tasks, since many studies do not specify a specific task performed outdoors. These studies focused solely on possibility that the time spent outdoors has a protective effect on myopia (Jones et al, 2007; Jones-Jordan et al 2012; Rose et al, 2008a; 2008b; Dirani et al, 2009; Deng et al, 2010, Guggenheim et al, 2012; French et al, 2013). Thus, we decided on common outdoor tasks that are performed every day (i.e. walking outside). We added common technology such as laptops and smart phones since they are widely used mediums.

This feasibility study allowed us to determine the most suitable outdoor and indoor pathways to be used in the main study. After careful analyses of the indoor tasks we had originally chosen in the pilot study, we discovered that some modifications were necessary for the main study. One such change was to tailor the tasks and instructions given in a way that made the tasks more realistic and similar to everyday tasks. During the pilot study, we found that eye movements differ based on the task given and how the task was presented to the subject. For example, the instructions given for the task of reading a document on the laptop were: "Please read the document on the laptop" in the pilot study. With vague instructions, the eye movements measured could potentially not depict the same eye movements an individual makes while scanning for a particular piece of information or keyword compared to leisurely reading. Thus, the measured eye movements may show more fixation changes because the subject was browsing the document casually. In order to imitate the real world as much as possible, we modified the instructions to: "Read this text as if you are reading it for class" for the main study. This encouraged the subject to focus on reading the document, which would show fewer fixation changes since they are more focused on reading and understanding the material instead of just casually browsing it. We decided to not use the task of flipping through a book since instructions could be misinterpreted which would not provide valid data for our study. Eye movements while reading are more focused, but potentially not when an individual casually browses through a book without purpose. If a task is performed without purpose, the subject could potentially be not as focused on performing the task. Therefore, the following tasks were selected for testing indoors: (1) read on laptop, (2) type on laptop, (3) read a book, (4) play Tetris on laptop, (5) watch TV, (6) walk to an office, and (7) walk back to lab using an iPod Touch. Recording of the eye movements required the eye tracker to be connected via USB cable to the laptop at all times, which hindered our flexibility in deciding the order of the tasks. The order of the indoor tasks was decided based on a sequence that would allow us to record the least amount of excess data. This pilot study allowed us to test different arrangements in task order to determine the optimal arrangement to record large amount of data in a timely fashion without having to switch back and forth to different devices or configurations.

For the outdoor paths, we decided to use two of the three paths initially tested: Newbury Street and Commonwealth Mall. The rationale was that these two pathways complement each other and are two commonly traveled paths in the outdoor environment that people use every day.

The Commonwealth Mall is a quiet and spacious area and Newbury Street is a busy and crowded shopping area, which will allow us to evaluate if eye movements might be affected by the external characteristics of these environments. Additional tasks were included based on everyday tasks that people perform while in the outdoor environment. The final tasks to be included in the main study were: (1) observe examiner cross sidewalk (activity commonly performed), (2) walk in a quiet park and observe a statue (leisurely environment), (3) walk in park while using an iPod Touch (use of portable electronic devices while walking is increasingly prevalent), and (4) walk on a busy street. Note that the task to walk while using an iPod Touch was tested in both the indoor and outdoor environments allowing direct comparison between the two.

Additionally, the pilot study served to create, modify based on feedback from subjects and observation, and finalize the instructions to be given to subjects for each specific task. We also made sure the instructions were easy to understand and perform. For all tasks, we ensured that distances used for calibration and testing were uniform by measuring the distances for each subject. The pilot study was also conducted to investigate different methods to analyze the data such as looking into the use of ellipse area method or simply fixation duration times. We decided to use the number of fixation changes during a small time frame for each task in the main study.

2.4. Conclusions

We showed with this initial pilot study that the *ViewPoint EyeTracker®* was an adequate tool to measure eye movements in indoor and outdoor environments while subjects performed a number of everyday tasks.

This pilot study allowed us to create an optimal procedure for the main study, determining the most useful indoor and outdoor walking pathways and tasks that subjects would perform. Our custom calibration stimulus and display allowed measurement of a wider range of eye movements extensive enough for the purpose of our study, including walking outside.

The feasibility pilot study also revealed potential limitations and biases. For example, we noticed that subjects could potentially perform a task differently the first time, during a practice run, than when the task was performed again. This is because familiarity with a task affects eye movements (Mills et al, 2011). In order to limit this source of bias in our main study, we explained the instructions clearly to the subject before each task and allowed time for questions, but did not allow the subject to perform the task twice.

As discussed in the results section, the instructions given to subjects are likely to affect their eye movements, therefore a strict script was developed and used consistently for each subject tested. In addition, it was not possible to randomize the order of the tasks performed during indoor and outdoor pathways due to the requirement that the eye tracker had to be connected via USB cable to the laptop at all times and to record the least amount of excess data in a logical order. However, in the main study, we did randomize the order of which environment (indoors or outdoors) each subject was going to begin with.

Lastly, this initial pilot study was used to explore various options to analyze the eye movements' data and determine an optimal data processing and data analyses procedure for the main study.

3. Main Study: Indoor and Outdoor Eye Movements in Myopia

3.1. Purpose and Hypothesis

This study was an investigation of the importance of variable visual input in indoor and outdoor environments in refractive error development. We hypothesize that individuals who make fewer changes in fixation position, particularly in outdoor environments, may have a higher risk of developing myopia. Therefore individuals with myopia may make fewer eye movements compared to emmetropes (Dorr et al, 2010; Mills et al, 2011; Flitcroft, 2012). This study evaluated the changes in fixation, in a group of emmetropes and myopes while performing various indoor and outdoor tasks. We hypothesized that myopes will make fewer changes in fixation than emmetropes, more so for visually demanding tasks. This study may contribute to our understanding of the development of myopia.

3.2. Methods

3.2.1. Subjects

Criteria for inclusion and exclusion were: (1) no history of surgery or eye disease, (2) within 18-38 years of age, (3) best corrected VA=20/20 or better in each eye, (4) not using drugs that may affect their vision, (5) no mobility impairments (able to walk for 20 minutes while carrying a small backpack with a lightweight laptop), (6) refractive error between -8.00DS and +6.00DS (spherical equivalent), (7) no more than 1.50DS of astigmatism in either eye, (8) no more than 1.50DS of anisometropia, and (9) soft contact lens wearer if distance vision correction is required, (10) habitual distance corrected VA (uncorrected or with contact lenses) 20/20 or better in each eye.

Non-cycloplegic refractive status was determined by open-field auto refractor (Grand Seiko WR-5100K). Subjects were classified into three refractive groups: emmetropes, defined as spherical equivalent (SE) in each eye between +0.75 to -0.25 DS; myopes, defined as SE in each eye between -0.50 to -8.00 DS; and hyperopes, defined as SE in each eye between +1.00 to +8.00 DS.

3.2.2. ViewPoint EyeTracker®

Fixational eye movements were recorded with a light and portable eyetracker, FDA-approved, Arrington Research *ViewPoint Eye Tracker*®, model BNE07 (Figure 2a), while the subject performed several tasks in two real world environments: (1) a semi-controlled indoor course at NECO, and (2) outdoor courses nearby the College.

3.2.3. Procedures

1. Subject's eligibility and refractive error group inclusion was determined with a vision screening that consisted of:
    - A screening questionnaire was used to obtain subject's eye and health history and refraction history.
    - Objective refraction (Grand Seiko WR-5100K autorefractor), best-corrected VA, and habitual VA, with contact lenses if necessary.
    - Axial length using a non-contact device (Haag-Streit Lenstar LS 900, http://www.haag-streit.com/haag-streit-diagnostics/products/biometry/lenstar-ls-900/).
2. Following the vision screening, the *ViewPoint EyeTracker*® was adjusted and calibrated for each subject.
    - Adjustment of the eye cameras and infrared lights was done by the examiner while the subject looked straight ahead at a target (letter X) projected in the center of a large screen. The examiner adjusted the IR lights to ensure they were not in the subject's line of sight or obstructing the visual field in any way. The examiner also adjusted the eye cameras to ensure the pupils of each eye were centered and approximately the same size (horizontal and vertical diameter) using the *ViewPoint EyeTracker*® *Viewpoint* window (Figure 2b). The examiner finally adjusted the IR lights temporally to the eye cameras so that each eye was illuminated by the same amount.

- After the adjustment of the eyetracker frame, the height of the subject’s eyes to the floor and the distance from the subject’s eyes to the center of the TV screen were measured with a measuring tape. These measurements were later used to calculate the gaze visual angle during analyses of eye movements.
- The *ViewPoint EyeTracker®* was calibrated using a custom method, as described in section 2.2.4 (Figure 6).
- Once the eyetracker was successfully calibrated, the subject was asked to practice walking in the lab while wearing the eye tracker glasses and carrying a small backpack with a lightweight laptop that was used to record the eye movements.
- The experimental testing consisted of two pathways that included semi-freely exploring real world environments for a total of up to 20 minutes (broken up into brief periods of approximately 30 seconds each), as described in section 3.2.4.
- During each task, subjects were instructed to move their heads and eyes normally throughout the task and try to ignore that they were wearing the eye tracker glasses. In addition, subjects were instructed to walk normally and to not keep their head stiff or change the way they would normally move their head or body due to wearing the eye tracker.
- Recordings of fixational eye movements were done in both indoor and outdoor environments in a random order and as described below.

3.2.4. Indoor and Outdoor pathways

a. **Semi-controlled indoor pathway** at NECO and in Vera-Diaz Research Lab:

- Each task of this pathway was recorded separately. Instructions for each task were explained to the subject prior to the task while their eyes were closed, to avoid recording excess useless data. Subjects were instructed to only open their eyes when they started the experimental task. Additionally, and prior to each task, subjects were reminded to walk and move their head and body normally as if they were not wearing the eye tracker.
- The following tasks were tested:
  1. Read a research article: “Binocular Saccades in Myopes and Emmetropes” on a laptop:
     a. Laptop at high illumination
     b. At 40 cm
     c. 30 seconds
     d. Instructions: “Read this text as if you are reading it for class.”
  2. Type a few dictated sentences on a laptop:
     a. Examiner dictates from the book “Myopia and Nearwork, page 173”, while subject types on a Word document (Font: Times New Roman, size: 12)
     b. Laptop at high illumination
     c. At 40 cm

d. 30 seconds

e. Instructions: "I will now start reading a few sentences from a book. Please type what I read on the Word document open on the laptop."

3. Play the video game *Tetris* (www.freetetris.org) on a laptop:

   a. Game is set to Level 1 to ensure that subject will not lose in the game before the 30 seconds of recording.

   b. Examiner explains how the game works and what keys are used to play the game.

   c. Laptop at high illumination

   d. At 40 cm

   e. 30 seconds

   f. Instructions: "Now you will be asked to play the game Tetris for 30 seconds. The goal of the game is to take pieces of various orientations and sizes that move from the top of the screen to the bottom and to create lines while getting the highest score while the pieces slowly begin to drop at a faster rate. The arrow keys and space bar will allow you to change the orientation of the blocks."

4. Watch a video recording of the examiner crossing a street (same as performed in outdoor task #1) on a large screen:

   a. At 150 cm

   b. 30 seconds

c. Instructions: “Please watch this short video on the TV normally. You may move your head if you want to.”

5. Read from a book (Figure 10):

   a. “Myopia and Nearwork,” Page 173

   b. At 40 cm

   c. 30 seconds

   d. Instructions: “Please read this book as if you are reading it for class and you were going to be tested on its content.”

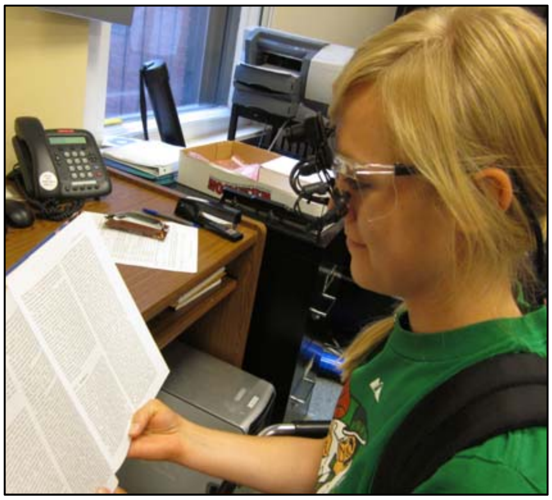

Figure 10. Sample of indoor task: Reading a book.

Note that the eyetracker does not affect the head or eye movements (Dorris et al, 2007).

6. Walk from the Vera-Diaz Research Lab to an office down the hall:

   a. Before the start of the task, the examiner ensured that the path was clear of people or other objects.

   b. Pathway: Subject starts at the first white line marked in the lab, walks around the left of the trash located on the second white line, exits the Lab and walks towards the office down the hall (Figure 11).

c. 30 seconds

d. Instructions: “Walk towards the office down the hall as you would normally walk, be sure to move your head or not as you would normally do.”

Figure 11. Pathway (indicated by red arrows) from Vera-Diaz Research Lab to an office down the hall.

7. Use an iPod Touch while walking back from the office to Vera-Diaz Research Lab:

    a. All subjects used the same device.

    b. Test for 30 seconds

    c. Instructions: “While you walk back, please look for the weather app and tell me what the weather in Boston is.” If there was time remaining before the 30 seconds, subjects were asked to check the weather in other cities.

b. **Semi-controlled outdoor pathway**:

This pathway comprised of five tasks. Each task was recorded separately. Before each task, the instructions were explained to the subject while they kept their eyes closed. Subjects were instructed to only open their eyes when they started the task.

The following five tasks were tested while subject was outdoors:

1. Before reaching the Commonwealth Avenue Mall Park, the subject was instructed to stand stationary at the corner of a four-way intersection (at the corner of Marlborough and Hereford Street) and watch the examiner as she crossed the three corners of the intersection (Figure 12). Note this task was pre-recorded and also shown in a video as part of the indoor course (see indoor task #4 above).
    a. Instructions: “Please stand at this corner. While you are standing at the corner, the task is to watch me cross this intersection.”

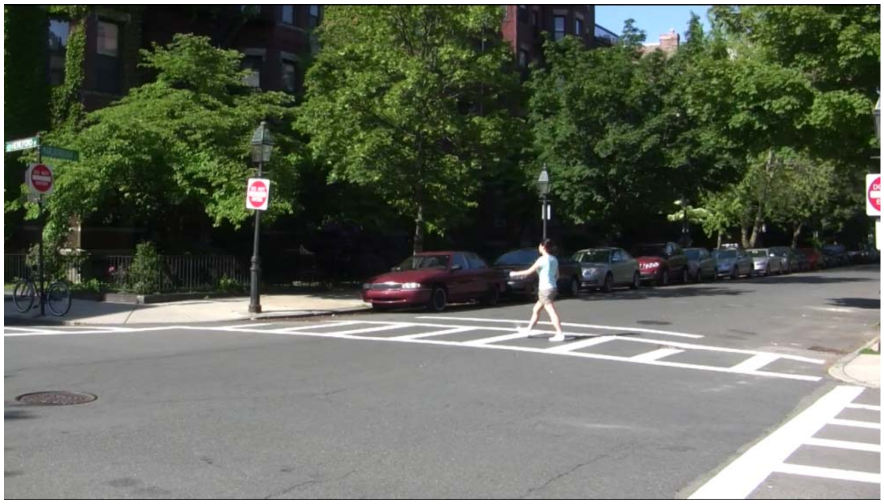

Figure 12. Sample of outdoor task: Watching examiner cross the corners of a four-way intersection.

2. Walk in the pedestrian Commonwealth Avenue Mall Park, from Hereford Street towards the statue:
    a. Instructions: “Please walk straight ahead leisurely towards the statue, as you would if you were going for a leisurely walk in an unknown city. Please ignore that I am walking next to you and do not talk to me.”
3. Once the subject arrives at the statue, subject is asked to describe the statue to the examiner (Figure 13):
    a. Instructions: "Now please give a short description of the statue to me."
4. Walk from the statue to the end of Gloucester Street while using an iPod Touch (same device for all subjects):
    a. Instructions: “While you walk back, please look for the weather app and tell me what the weather in Boston is.” If there was time remaining before the 30 seconds, subjects were asked to check the weather in other cities.

5. Walk on the sidewalk (right side) of Newbury Street from Gloucester Street to Hereford Street:
    a. Instructions: "Please walk towards the end of this street and move your head as you would normally do, as if you were going on a leisurely walk in an unknown city. Please ignore that I am walking next to you and do not talk to me."

Figure 13. Sample of outdoor task: Observe a statue.

In order to reduce variability in light levels, all testing and recording took place during the late Spring/Summer months, and only on overcast days or at dusk as high light levels on sunny days would have made recording difficult.

3.2.5. Data Analyses

Changes in fixation were measured in 15 second intervals during each 30 second task (started 5 seconds after the beginning of the task) using the *ViewPoint EyeTracker® DataAnalysis* software. This was done in order to ensure that the subject was performing the task and to confirm when the task was started and stopped. We also believe that starting our measurements after 5 seconds did not cause the loss of important fixation points because we start the video recording while the subjects have their eyes closed. Therefore, in the 5 seconds we have chosen to exclude from our analyses, they would have not started the task and no fixation points would be lost. The specific procedure for data processing and analysis for each task was as follows:

1. Each data and video file was opened with the software.

2. Each video was manually inspected frame-by-frame and compared to the times provided to ensure it was the correct task and to track fixation losses (Figure 14).

3. The start and stop times for each task were determined using the video footage.

4. The text file containing the number of fixations made during the task was retrieved and exported to Microsoft Excel.

5. In Excel, the start and stop times determined in step 3 above were highlighted, and the 15 seconds to be analyzed determined from 5 seconds after the task’s start time.

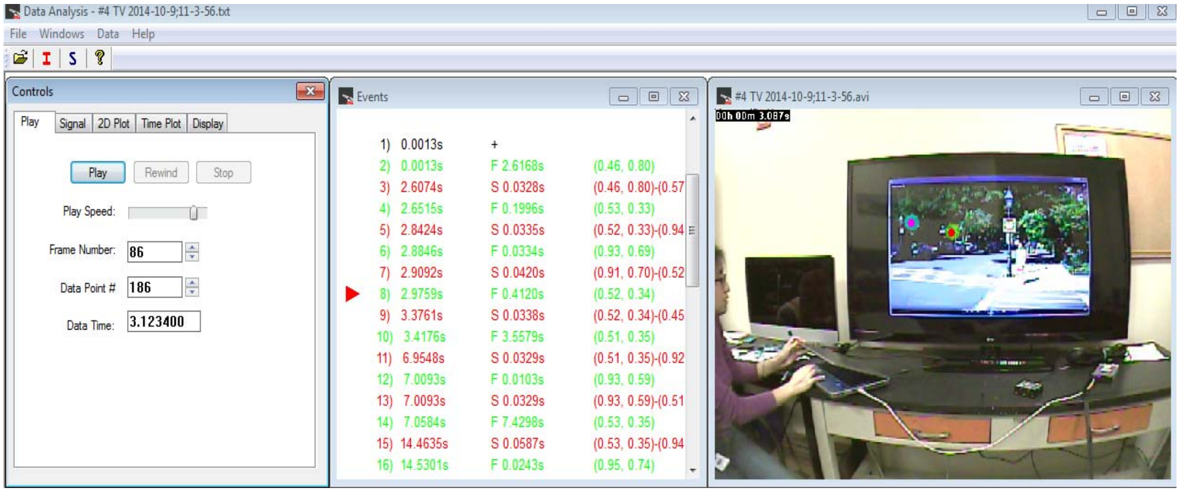

Figure 14. *DataAnalysis* software, data and manual inspection of the videos. The “controls” window of the software (left) allows easy maneuvering through the recorded videos. The "events" window (middle) provides the times when saccades and fixations were made. The "scene" window (right) provides a visual of where the eyes were looking (indicated by green and blue dots) during a task.

This procedure was used to determine the number of changes in fixation made by each subject during the 15 second interval for each task. For the purposes of our study, we used the *ViewPoint Eye Tracker®* program's velocity threshold algorithm to define fixation. Fixation was calculated by the *ViewPoint Eye Tracker®* program as the "length of time that the velocity was below the saccade velocity criterion which was 0.10 m/s." The program's fixation time criterion was 0.070 seconds.

Non-parametric multivariate repeated-measures analyses of variance (Kruskal Wallis Tests and Kolmogorov Smirnov Tests) were used to compare frequency and duration of fixations between the refractive error groups. Mann-Whitney U test with post hoc test correction was used to compare changes in fixation for each task. Statistical analyses were performed using JMP® 10 (www.jmp.com).

3.3. Results

A total of 41 young adult (21-32 years old) subjects were recruited from the New England College of Optometry population for this study. Data for 38 subjects were included in the analyses. Three subjects with hyperopia were excluded from the refractive group analyses due to the low number of participants with hyperopia. For the subjects included in the analyses, the refractive error ranged from SE +0.94 DS to -8.46 DS. Of these, 20 subjects were myopes (Mean: -3.25±2.40 DS, ranging from -0.59 to -8.46) and 18 emmetropes (Mean: +0.43±0.33 DS, ranging from -0.157 to +0.935).

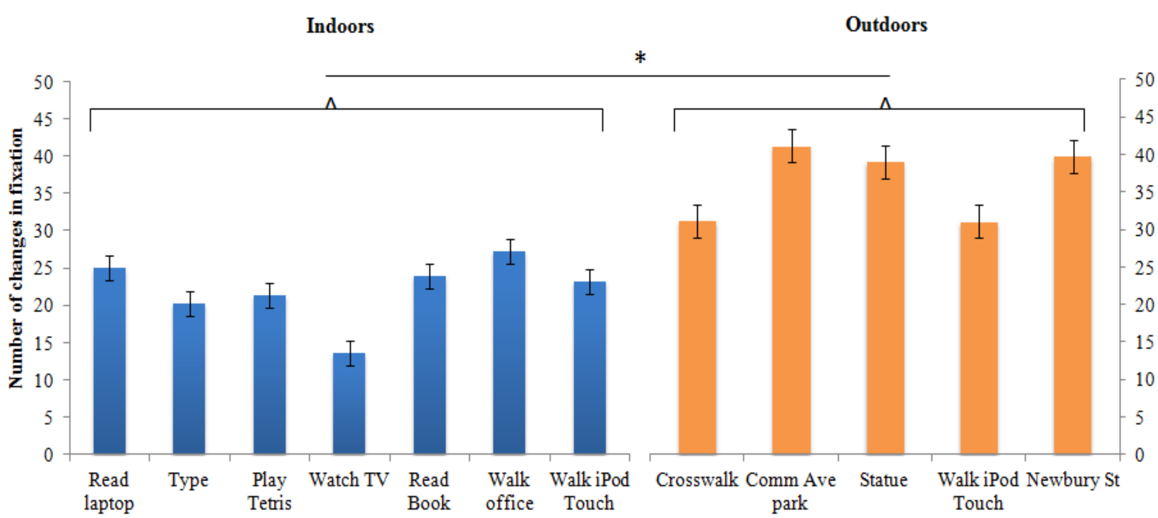

Figure 15. Mean number of changes in fixation in 15 seconds for all subjects and each indoor and outdoor task. Error bars represent ±1 standard error. *Denotes statistically significant findings.

3.3.1. Group Data

For this group of 38 subjects, significantly fewer changes in fixation (Mann-Whitney U test, $Z=5.10$, $p<<0.01$) were found for indoor tasks (Mean 21±8 fixation changes) compared to outdoor tasks (Mean 37±13 fixation changes) (Figure 15). Fewer changes in fixation were also apparent when all subjects performed the same task, using an iPod Touch indoors (Mean 23±24 changes in fixation) vs. outdoors (Mean 31±24 changes in fixation), although the difference did not reach statistical significance (Mann-Whitney U test, $Z=1.73$, $p=0.08$) (Figure 16). Note that while we did not analyze each gaze position when performing these tasks, we expect that subjects would not have looked up during the very brief period they performed the near tasks. Due to the specific instructions we gave to the subjects and the short duration of each task (30 seconds each), we expect that subjects were focused on performing the task and would not look up from the task. This is a different scenario from Harb et al study (2006), where subjects read for a longer time (10 minutes) and were allowed to look up from the text. The instructions given to the subjects were also not as specific as the instructions we gave in our study.

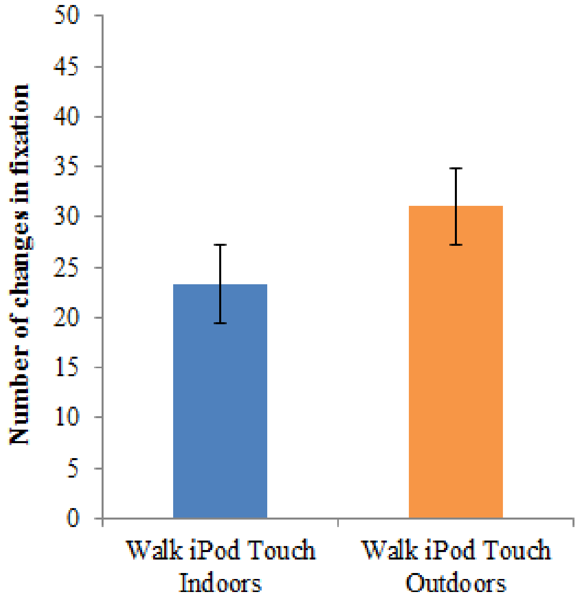

Figure 16. Group data, comparison of the number of changes in fixation when walking using an iPod Touch indoors (blue) and outdoors (orange). Error bars represent ±1 standard error.

3.3.2. Myopes versus Emmetropes

Subjects with myopia showed a trend towards fewer changes in fixation than emmetropes while performing all indoor near tasks. This difference only reached significance for the near tasks of reading on a laptop (Myopes 22±12, Emms 28±15 changes in fixation) (Kruskal Wallis, Z=2.23, p=0.03) and playing Tetris (Myopes 19±8, Emms 24±10 changes in fixation) (Kruskal Wallis, Z=1.97, p=0.04) (Figure 17). Myopes also showed fewer changes in fixation when walking indoors while looking at the weather app on an iPod Touch (Myopes 20±13, Emms 27±31 changes in fixation) (Kruskal Wallis, Z=5.86, p=0.02) (Figure 17).

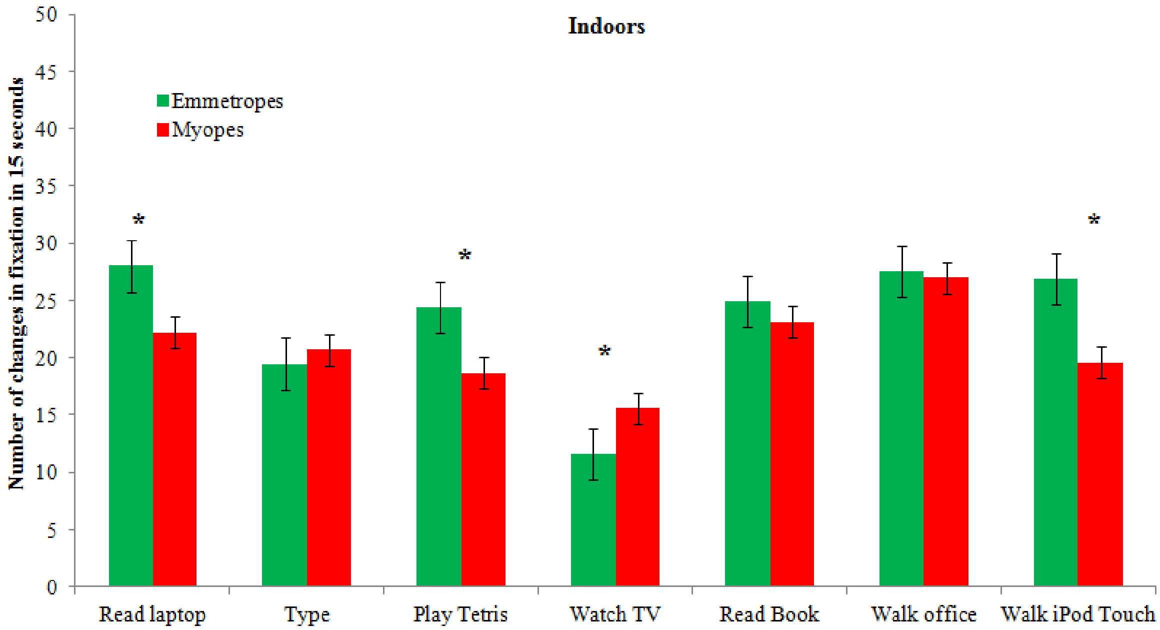

Figure 17. Comparison of number of changes in fixation for indoor tasks between emmetropes and myopes. Error bars represent ±1 standard error. * Denotes statistically significant findings.

On the other hand, when watching TV, myopes showed significantly more fixation changes than emmetropes (Myopes 16±7, Emms 12±9 changes in fixation) (Kruskal Wallis test, Z=-2.21, p=0.03) (Figure 17). All subjects performed the lowest number of changes in fixation during this task compared to the other indoor tasks.

When walking outdoors, myopes showed a trend towards a higher number of changes in fixation than emmetropes in almost all paths. This difference reached significance when observing a statue (Myopes 44±22, Emms 34±24 changes in fixation) (Kruskal Wallis test, Z=-1.95, p=0.05), but not for other outdoors tasks (Walking in Commonwealth Mall park: Myopes 43±21 changes in fixation, Emms 39±11; Walking on Newbury street: Myopes 42±19, Emms 37±13) (Figure 18). The finding of greater number of fixations being made outdoors is expected because the outdoors environment is an unfamiliar and riskier environment for the subjects, whereas the indoors path at NECO is very familiar for the subjects as they were all recruited from NECO.

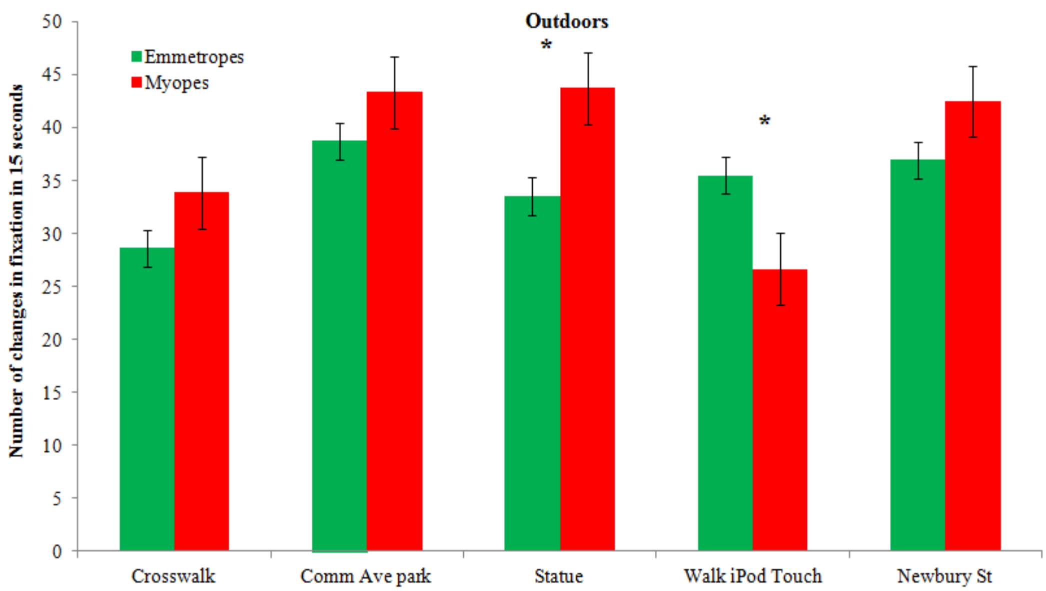

Figure 18. Comparison of number of changes in fixation for outdoor tasks between emmetropes and myopes. Error bars represent ±1 standard error. * Denotes statistically significant finding.

Interestingly, this trend towards more fixation changes in myopes when walking outdoors was reversed when subjects walked while looking at weather reports on an iPod Touch, with myopes making significantly fewer fixation changes than emmetropes (Myopes 35±22, Emms 27±16 changes in fixation) (Kruskal Wallis test, Z=2.85, p=0.03) (Figure 18).

3.3.3. Emmetropes

When comparative analyses were performed within the emmetropic refractive group, significant effects were found in a number of tasks. Significantly more fixation changes were observed in emmetropes when walking in Commonwealth Mall park normally (Emms 39±11 changes in fixation) compared to walking indoors (Emms 28±7 changes in fixation) (Mann-Whitney U test, Z=11.00, p=0.04). Fewer changes in fixation were made by emmetropes when walking outside while using an iPod Touch (Emms 35±29 changes in fixation) (Mann-Whitney U test, Z=-9.50, p=0.03) and when walking inside while using an iPod Touch (Emms 27±31 changes in fixation) (Mann-Whitney U test, Z=14.0, p=0.02) compared to walking in Commonwealth Mall park normally (Emms 39±11 changes in fixation) (Figures 17 & 18). There was also a trend towards more fixation changes when walking in the quiet Commonwealth Mall park (Emms 39±11 changes in fixation) compared to walking on busy Newbury Street (Emms 37±13 changes in fixation), but this difference did not reach significance (Mann-Whitney U test, Z=2.00, p=0.43) (Figure 18). While more fixation changes were observed when subjects were outdoors and watching the examiner cross the intersection (Emms 29±20 changes in fixation) compared to watching a video of the same task on a large TV indoors (Emms 12±9 changes in fixation), this difference only approached significance (Mann-Whitney U test, Z=10.0, p=0.10) (Figures 17 & 18).

When following the indoor paths, we observed a trend towards fewer fixation changes made when emmetropes used an iPod Touch (Emms 27±31 changes in fixation) compared to walking to an office (Emms 28±7 changes in fixation), but this difference was not statistically significant (Mann-Whitney U test, Z=-8.00, p=0.09) (Figure 17). For indoors near tasks, emmetropes made significantly more fixation changes when reading an article on a laptop (Emms 28±15 changes in fixation) compared to reading an article in a book, even with the same instructions given (Emms 25±14 changes in fixation) (Mann-Whitney U test, Z=-9.00, p=0.05) (Figure 17).

3.3.4. Myopes

Subjects with myopia made significantly more fixation changes while walking in the quiet Commonwealth Mall park (Myopes 43±21 changes in fixation) compared to walking indoors (Myopes 27±11 changes in fixation) (Mann-Whitney U test, Z=13.5, p=0.03); also compared to walking with an iPod Touch outdoors (Myopes 27±16 changes in fixation) (Mann-Whitney U test, Z=-17.5, p=0.04); or indoors (Myopes 20±13 changes in fixation) (Mann-Whitney U test, Z=17.0, p=0.01) (Figures 17 & 18). No statistically significant differences (Mann-Whitney U text, Z=-1.00, p=0.54) were found when comparing fixation changes between the tasks of walking in the quiet Commonwealth park (Myopes 43±21 changes in fixation) and walking on the busy Newbury street (Myopes 42±19 changes in fixation). However, significantly more changes in fixation were made when subjects watched the examiner cross the intersection outdoors (Myopes 34±18 changes in fixation) compared to watching the same task on a large TV indoors (Myopes 16±7 changes in fixation) (Mann-Whitney U test, Z=16.5, p=0.03) (Figure 17 & 18).

While indoors, subjects with myopia showed a trend towards more fixation changes when walking normally to another office (Myopes 27±11 changes in fixation) compared to walking while using an iPod Touch (Myopes 20±13 changes in fixation), but this difference did not reach statistical significance (Mann-Whitney U test, $Z=-5.50$, $p=0.50$) (Figure 17). When comparing changes in fixation between the tasks of reading on a laptop (Myopes 22±12 changes in fixation) and reading a book (Myopes 23±15 changes in fixation), myopes showed no significant differences (Mann-Whitney U test, $Z=3.00$, $p=0.37$) (Figure 17).

3.4. Discussion

Our results show that for both refractive groups, myopes and emmetropes, the number of changes in fixation were significantly lower during indoor tasks compared to outdoor tasks (Zhang et al, 2016 - Appendix I). In a previous study, Dorr et al (2010) had also showed that observers made fewer changes in fixation when watching indoor scenes compared to natural outdoor scenes. Although it is important to note that both scenarios in Dorr's study were simulated on a computer. Our study is therefore the first to report differences in fixation changes between indoor and outdoor scenarios using real environments. The most plausible explanation for this difference is that indoor environments are more familiar than outdoor environments and therefore individuals do not require moving their eyes to obtain information from peripheral objects. Another possible explanation is that the tasks performed by our subjects in the indoors and outdoors environments are simply different, with different information content that drives a different number of changes in fixation. Indoor near tasks (i.e., reading a book) require viewing highly detailed objects thus subjects need to make more changes in fixation to scan the object during such tasks.

Importantly, we showed that individuals with myopia made fewer changes in fixation than emmetropes while performing visually demanding near tasks indoors, in particular when reading on a laptop, playing Tetris on a laptop as well as when walking indoors while using an iPod Touch. As a group, myopes showed no significant differences between reading an article on a laptop compared to reading an article in a book. On the other hand, emmetropes as a group made more fixation changes when reading an article on a laptop compared to reading an article in a book. Certain near tasks such as playing video games might require higher central visual demand than reading a book, even when we instructed subjects to read carefully, as if they were preparing for class. This is because when playing video games such as Tetris, the eyes need to track moving objects and determine where to place said moving object. In addition, the visual angle is different when using a laptop to read compared to reading in a book, and more changes in fixation may be necessary. Another possible explanation is that there are different luminance levels between the two tasks as a laptop has higher luminance, particularly for the blue wavelengths.

Note that all the near tasks described so far require high levels of central vision attention. Walking indoors while looking up information on a weather app on an iPod Touch is also a task that requires high levels of central visual attention. These results suggest that myopes may have a less efficient visual system when performing steady and demanding near tasks. On the other hand, it is possible that myopes, who have been shown to deploy higher levels of central attention (Kerber et al, 2016), are better at judging spatial position and peripheral movement without moving their eyes as much. In line with these results, Harb et al (2006) found that when reading, a visually demanding task, indoors for 10 minutes myopes made fewer changes in fixation than emmetropes (Harb et al, 2006). One difference to note between Harb et al (2006) study and our study is that our analyses do not include data points of eye movements when subjects moved their eyes away from the task, while Harb et al (2006) study specifically reported those data points.

The most plausible explanation for Harb et al (2006) as well as our results is that myopes have a greater decrease in peripheral vision when deploying high levels of central attention compared to emmetropes (Kerber et al, 2016). Myopes seem to be more efficient at deploying central vision attention and as a consequence they do not use their peripheral vision as much as emmetropes. This would be an advantage in a world where humans spend the majority of their time indoors and where most visual tasks occur within a near range. It may also be the result of an evolutionary adaptation for myopes, who are individuals adapted for the vastly near visual world. However, this adaptation mechanism may also be a risk for myopia development as it affects the central and peripheral retinal visual input balance.

Interestingly, this trend towards myopes making fewer fixation changes indoors was not observed while subjects watched TV, when myopes made more fixation changes than emmetropes. This result is expected as watching TV is an indoor task that does not require high central visual attention compared to near tasks such as reading a book. Alternatively, this result may be an effect of viewing distance, as subjects watched TV at a further distance than the other indoors near tasks.

An opposite trend was observed across refractive groups when subjects performed outdoors tasks. Myopes showed more changes in fixation than emmetropes for most outdoors tasks performed in this study, reaching statistical significance when they observed a statue in the Commonwealth Mall Park, but not for the other outdoor tasks. However, when walking while using an iPod Touch, again a task that requires high central vision attention, myopes made fewer fixation changes than emmetropes. In general, myopes seem to naturally make more changes in fixation. However, when they are required to perform visually demanding near tasks even in an outdoor environment, it appears that they drastically make fewer fixation changes. This finding additionally supports the hypothesis that when myopes are to perform a task that requires high levels of central visual attention, they are more efficient at deploying attention at the task at hand and are therefore more efficient at performing these near tasks (Thorn et al, 1998; Saw et al, 2007; Sreenivasan et al, 2013), but as a consequence their peripheral vision is diminished (Kerber et al, 2016).

When comparing the task of watching the examiner cross the intersection outdoors versus watching the same action on TV indoors, myopes as a group, made significantly more fixation changes while watching the task outdoors than indoors. Emmetropes also showed a trend towards more fixation changes in this outdoors task compared to watching the indoor video of the same task, but this was not significant.

In addition, myopes as a group made more fixation changes while walking outdoors in Commonwealth Mall Park compared to walking indoors. The same was observed for emmetropes as a group. The most plausible explanation for this difference is that indoor environments are more familiar than outdoor environments. Therefore when asked to explore an unfamiliar outdoor environment, individuals seem to require more eye movements in order to obtain information from peripheral objects. This finding suggests that the outdoors environment may provide stimuli that trigger more changes in fixation than indoor environments.

There are a number limitations and biases in this study. One important limitation is that we are unable to directly compare eye movements between tasks because the tasks performed indoors and outdoors are different. Even for the most similar tasks of using the iPod Touch indoors or outdoors, there are some differences since subjects walked in two different pathways and the indoors pathway (NECO) is more familiar to our subjects because they spend the majority of their time at NECO. The goal of this study was to evaluate differences between emmetropes and myopes, not among the various tasks. Future studies should evaluate the same task indoors and outdoors, for example evaluate eye movements while subjects use a handheld electronic device while sitting indoors and sitting outdoors. However, it will also be interesting to evaluate eye movements during dynamic tasks while subjects are mobile.

Another limitation of our study is that gaze location and vergence data were not analyzed. Therefore, we do not know exactly where subjects looked at during each task at all times. In our study, we can only affirm that subjects were performing the required task by manual inspection of the videos. Analyzing gaze location data would provide information on exactly where subjects looked at during each task at all times. With this information, we would be able to analyze how vergence was changing during each task and how eye movements would be affected. Future studies should also analyze the gaze location and vergence data in order to better compare the tasks.

Finally, eye movements data may have been affected by the level of interest, i.e., attention, for each individual subject. However, special care was taken to give identical and specific instructions to all subjects for each task. For example, for the reading on a laptop task, we ask subjects to read the article, which was the same for all subjects, as if they were going to be questioned about it in class. If subjects had been allowed to choose a reading material they were interested in, their eye movements may have been different, but we would have also not been able to compare among subjects. When reading a favorite book, it is possible that we would measure fewer changes in fixation while more changes in fixation would be seen when reading a boring article.

The results from this study support the hypothesis that myopes make fewer changes in fixation than emmetropes while performing highly demanding near visual tasks. This difference in eye movements between refractive groups may be related to myopia development. Further studies are needed to determine possible causative effects of eye movements in myopia. Investigations including children prior to the development of myopia are needed to determine if eye movements have causative effects on myopia development and progression. If it is determined that eye movements have causative effects on myopia, vision therapies to train eye movements may be developed, similarly to training eye movements of individuals with tunnel vision, e.g., due to retinitis pigmentosa or glaucoma (Luo et al, 2006). From our data, we hypothesize that vision therapy to train children make more fixation changes in highly demanding near tasks could protect children from the development of myopia.

4. General Conclusions

The overall conclusion of these studies is that fixational eye movements may be associated with myopia. Young adults with myopia make fewer changes in fixation compared to emmetropes when performing visually demanding near tasks indoors. All subjects made fewer changes in fixation while performing indoor tasks compared to outdoor tasks. This difference may be explained by indoor environments being more familiar than outdoor environments. Interestingly, myopes made more fixation changes than emmetropes for all outdoors tasks except when required to perform a visually demanding near task.

If these results can be extended to children at risk for myopia, or with progressing myopia, they would suggest that outdoor environments provide a larger number of changes in fixation that may provide necessary signals to normal emmetropization.

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6. Appendix I: ARVO Poster