THE EFFECT OF MACULAR PIGMENT OPTICAL DENSITY ON GLARE ACUITY

by

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(Under the Direction of Billy R. Hammond Jr.)

ABSTRACT

Intraocular scatter, with its associated functional manifestations, is a leading cause of automotive accidents and a significant biomarker of covert and overt ocular disease (e.g., diseases of the cornea and lens). Nearly all current methods of measuring glare suffer from a lack of ecological validity; additionally, all recent studies in the glare literature investigating the deleterious effects of glare do so by measuring stimulus detection rather than recognition. The present study utilizes a novel and ecologically valid methodology to measure recognition acuity in a sample of healthy, young subjects. Macular pigment optical density (MPOD) was measured, and its effect on glare recognition acuity was assessed.

INDEX WORDS: lutein, zeaxanthin, macular pigment optical density, MPOD, recognition, acuity, light scatter, glare, vision

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B.S., Arizona State University, 2019

A Thesis Submitted to the Graduate Faculty of The University of Georgia in Partial Fulfillment of the Requirements for the Degree

MASTER OF SCIENCE

ATHENS, GEORGIA

2021

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May 2021

ACKNOWLEDGEMENTS

I would like to sincerely thank my major professor and mentor Dr. Billy R. Hammond Jr. for giving me the motivation and inspiration for pursuing this project, as well as his continued support, insight, and guidance. Thank you to my committee members Dr. Lisa Renzi-Hammond and Dr. James Brown for their insightful contributions to the development and refinement of this project, in addition to their willingness to dedicate their time and support. I would also like to thank my lab mate Colin Gardner for his help with project development, data collection, and feedback over the course of this project. Finally I would like to thank my mother, Kristine, my grandparents, Sharon and Jerry, and my siblings, Victoria, Alexandra, and Jonathan for their unconditional support, encouragement, and positivity.

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CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

A History of Macular Pigment Research

The presence of macular pigments within the central human retina has been a point of significant interest since their earliest discovery in the late 18th century by Home (Home, 1798). At the time, the function of this retinal region was not known, nor was the composition of this 'yellow spot.' It would take another fifty-three years and the development of Hermann von Helmholtz's ophthalmoscope before macular pigment (MP) was seen in a living subject (Whitehead et al., 2006) and nearly another hundred years after that before the function of the pigment began to be understood. Wald (1945) found that the yellow pigment was able to absorb short-wavelength light maximally between 430 and 490nm. Much of the early work concerning macular pigment (MP) was conducted by biologists and their studies were focused on defining and determining its biological basis. However, after Wald's discovery of the pigment's absorption spectrum, interest in the topic expanded to other areas of the scientific community; notably interested were chemists and physicists.

Bone et al. (1985) identified the organic compounds responsible for the chemical composition of the macular pigments as the dietary carotenoids lutein (L) and zeaxanthin (Z). This landmark study further expanded the interest in MP, now to nutritionists and dieticians. Because these pigments are naturally synthesized by plants – prominently found in spinach and kale – and are fat-soluble, important dietary implications regarding MP functionality began to arise. Studies such as Erdman et al. (1993) showed that carotenoids could be delivered to tissues

within the body. Hammond et al. (1997) demonstrated specifically that the dietary carotenoids L and Z could be absorbed and transported effectively enough through dietary modification to produce an increase in MPOD.

Following the discovery of MPOD's relationship with diet and the research implications that came with it (through dietary modification), finding a reliable and efficient way to measure the density of subjects' MP became an important question of interest. As mentioned previously, MP was first able to be visualized in living subjects with the aid of an ophthalmoscope; prior to the development of the ophthalmoscope by Helmholtz, MP could only be seen postmortem and was usually studied in non-human primates. Studying and measuring MP was still widely conducted on non-human primates up until the early 1990s (see, e.g., Snodderly et al., 1984; Handelman et al., 1991) but by that time, more advanced measurement methodologies had been developed such as the three-channel Maxwellian view system as used in Hammond et al. (1997) and the earlier Hammond et al. (1996) study investigating the sex differences in MPOD. The Maxwellian view system used to measure MP utilized the procedure called heterochromatic flicker photometry first reported by Werner et al. (1987). This equipment and procedure for measuring MPOD was effective but required a 1000-W xenon arc light source and consisted of a complex optical bench system; additionally, the system utilized a grating monochromator to produce the test field. This system was effective but large and complex and not widely available.

Advancement in light source technology was necessary to further the methodological transition to a more simplistic system. This came about with the breakthrough in semiconductor technology that led to the advent of the high-brightness blue LED. Though developed in 1994, the blue LED was not applied to MP research until later in the aptly named study, "A Practical Method for Measuring Macular Pigment Optical Density" by Wooten et al. (1999). In this study,

they developed a more practical (and, hence, more widely available) way to measure MPOD in vivo. Rather than a large Maxwellian view system, this new measurement system was a small, tabletop device that rendered the use of 1000-W xenon arc lamps and monochromators unnecessary since the intensity of LEDs could be controlled electronically (as opposed to circular density filters called wedges). This use of these relatively highly-efficient LEDs was only possible through the aforementioned creation of high-brightness blue LEDs (Nakamura et al., 1994). The application of this technology into the newly-developed MPOD-measurement system provided easier access to measurement for researchers interested in the topic of MPOD. Prior to that development, only a few scientific studies per year on macular pigment were published, after that time several dozen a year were published and new academic societies were formed (like the annual macular carotenoid conference in Cambridge England).

Around the time this 'innovention' became firmly cemented in the scientific literature (late 1990s/early 2000s), the applications of MPOD began to expand into fields outside the core science fields of biology, chemistry, and physics. While the relationship existing between MPOD and the research areas of diet and nutrition were discovered shortly after unmasking MP as L and Z, the entrance of MPOD research into the social sciences did not occur until the turn of the century. Studies by Beatty et al. (1999, 2001) helped to uncover the protective nature of MP against age-related macular degeneration (AMD). Aging and the presence of unilateral AMD are the two most significant risk factors for AMD and low/absent MP was found to be associated with both (Beatty et al., 2001). In the precursory study, Beatty et. al provided circumstantial, epidemiological, experimental, and clinical evidence that suggest MP may be a protective factor against AMD and age related maculopathy (ARM) (Beatty et al., 1999). Sabour-Pickett et al. (2012) later published a review that built upon the foundation of Beatty's work and strongly

suggests that lutein-zeaxanthin (LZ) supplementation fortifies the macula's antioxidant defenses and reduces the risk of AMD and AMD progression (Sabour-Pickett et al., 2012).

Since macular pigment was such an important component of retina (a central nervous system tissue), it made sense that it might also influence brain function as well. Craft et al. (2004) originally found L and Z in brain tissue. Later studies found that LZ amounts within the retina closely tracked amounts within the brain itself (Vishwanathan et al., 2013). If L and Z serve important functions within the retina, what might there function be within the brain itself? One role might simply be to maintain the health of both tissues. There is significant comorbidity between AMD and degenerative dementia (Tsai et al., 2015). Prior to disease, L and Z might help promote normal cognitive function relationships between MPOD and cognitive function in older adults (Renzi et al., 2014; Vishwanathan et al., 2014), and MP's relationship with visual function and macular disease in populations with Alzheimer's (Nolan et al., 2014) have been confirmed.

Currently, as it relates to the topic of MP and its correlation with human biofactors, interest is expanding from the once small, niche subset of biologists and anatomists the research began with. Scientists from all expanses of the field, medical doctors, health practitioners, and policymakers all have a stake in this line of research, in addition to the average individual who has to eat to survive; what they put in their mouth has the potential to have a marked impact on not only their health, but their vision and cognitive function as well. The field of MP research has evolved greatly since its inception in the late 18th century, and there are a selection of recent hypotheses and theories that drive the current research – including the present study. These will be discussed in the following section.

Macular Pigment: The Hypotheses that Drive the Research

Much of the recent literature on MP over the last few decades has fallen into the framework outlined in Wooten & Hammond (2002) where they provide an articulation of foundational theories moving the field forward in addition to consolidating evidence and studies that lend these theories support. Following the increasing evidence that MP serves as a protective factor against AMD – in addition to the fact that LZ supplements are widely available – many studies set out to determine if vision could be improved through LZ supplementation (increasing individuals' MPOD). There are a number of major hypotheses that have driven much of the MP research for the last twenty years: for example, the protection hypothesis, acuity hypothesis, visibility hypothesis, and glare hypothesis (Wooten & Hammond, 2002). Each of these hypotheses will be discussed, in turn, in the following sections.

Briefly, the protection hypothesis was the earliest concept, incorporating both optical and biological influences to visual improvement, which are based on LZ spectral absorption/distribution (optical) and the biochemical properties of the carotenoids (biological); essentially, a more healthy eye functions better. The acuity hypothesis postulates that vision is improved through optical changes such as the reduction of chromatic aberration as light enters the eye. The visibility and glare hypotheses are based on filtering: blue haze that limits visual range or bright light that impairs vision, respectively. These hypotheses serve as the foundation the current literature builds upon, as researchers continue to explore just how MP plays a role in improving vision.

The Protection Hypothesis

The optical variant of the protection hypothesis is based on research suggesting that short-wavelength light is harmful to retinal tissue (Ham et al., 1976) and, considering the

location of MP within the retinal layers (anterior to the outer segments and cone photoreceptors), it serves a direct purpose to protect the more vulnerable layers of the retinal tissue by absorbing the harmful light. As it relates to MP's protective functionality, there are a number of studies that support this hypothesis (Ham et al., 1978; Haegerstrom-Portnoy, 1988; Masuda & Watanabe, 2000; Morgan, 2017; Stringham et al., 2019).

The biological component of the protection hypothesis refers to the actions of the pigment as an antioxidant and anti-inflammatory agent (see, e.g., Sommerburg et al., 1998; Hammond et al., 1997; Weigert et al., 2011). The two sides of this hypothesis are complementary and serve the goal of establishing a comprehensive view on just how greater MPOD benefits and protects individuals.

The Acuity Hypothesis

The foundation of the acuity hypothesis is based upon the work of Max Schültze who, in 1866, described the characteristics of MP's spectral absorption and proposed that the reduction of short-wavelength light aberration entering the eye – enabled by the absorptive qualities of MP – could potentially improve visual acuity (Wooten & Hammond, 2002; Engles et al., 2007). Walls & Judd (1933) notes four definitive optical functions of MP:

"1. To increase visual acuity by reducing chromatic aberration

2. To promote comfort by the reduction of glare and dazzle

3. The enhancement of detail by the absorption of 'blue haze'

4. The enhancement of contrast" (pp. 664–666)

As noted in Walls and Judd's first point, chromatic aberration occurs when both lateral – focal length is proportional to wavelength – and longitudinal – retinal image size is proportional to wavelength – aberration take place and light rays fail to converge at their designated point of

focus on the retina (Wooten & Hammond, 2002). The negative results associated with chromatic aberration include degradation in the quality of black and white images, blurring of contours, and overall resolution (Reading & Weale, 1974). It is suggested by the acuity hypothesis that increased absorption of light aberration caused by short-wavelength rays will lessen or work toward preventing these negative results. Research preceding the work done by Reading and Weale found that the presence of a yellow lens (such as MP) simply enhanced contrast (Luria 1972). While enhancing contrast may sound beneficial, Wooten and Hammond (2002) noted that the increased short-wavelength absorption of individuals who already possessed extremely high levels of MP would negatively impact their acuity and/or lead to a decrease in contrast sensitivity.

Empirical support for the acuity hypothesis has not supported the first of these predictions, concerning macular pigment's ability to reduce the deleterious effects of chromatic aberration. Engles et al. (2007) measured MPOD, gap acuity, and hyperacuity in two conditions – yellow (filter) and white (control). The findings of their study resulted in no significant correlation between MPOD and gap acuity or hyperacuity in both yellow and white conditions, which is inconsistent with Walls and Judd.

The Visibility Hypothesis

It is important to note, before discussing the visibility hypothesis, that Wooten and Hammond (2002) use Bennett's (1930) definition of visibility as cited in Middleton's 1952 publication, "…visibility is the clearness with which objects in the atmosphere stand out from their surroundings" (Bennett, 1930; Middleton, 1952, cited in Wooten & Hammond, 2002). As an extension of this definition, the literature most commonly operationalizes the term "visibility" to mean distance vision, or how well and how far one can discriminate objects at range (through

Earth's atmosphere). The major factor that hinders visibility is light scatter – specifically, short-wave light scatter in the atmosphere, also termed "blue haze" (Fletcher et al., 2014). Blue haze and its relation to MPOD is the primary consideration of the visibility hypothesis and the primary focus of literature investigating this hypothesis. The hypothesis itself is that higher levels of MP will correlate proportionally with higher levels of low-contrast discrimination, thus enhancing visibility and improving how far one can see in the distance. The basis for this hypothesis is similar to that of the acuity hypothesis as it relates to MP's absorptive quality – MP is responsible for reducing the amount of short-wavelength light scatter reaching the photoreceptors by absorbing the light-scattering particles (Wooten & Hammond, 2002).

Hammond et al. (2012) used a MP-spectrum matched filter to simulate changes in MP density and an 'ecologically valid broad-spectrum filter' to simulate blue haze. Visibility was assessed though measurement of participants' contrast sensitivity threshold (CST) and these values were compared to the simulated optical density (OD) values. Their results did support the visibility hypothesis, but only up to a 25% increase in OD; beyond that percentage visibility decreased, which may have resulted from participants having high baseline MPOD. Fletcher et al. (2014) found that simulated blue haze reduced participants' contrast sensitivity function (CSF) and MPOD significantly increased the energy level threshold at which participants could maintain sight of the target stimuli. This study too found support for the visibility hypothesis.

The Glare Hypothesis: Foundations for the Present Study

The protection, acuity, and visibility hypotheses have guided macular pigment research for the past twenty years and provided the field of vision science a flexible, yet focused, context with which to explore the multifunctionality of MP within the human visual system. While these three hypotheses may be some of the most popular in the field, Stringham & Hammond (2007)

built upon them to articulate the glare hypothesis, the primary goal of which was to investigate the relation between MP and visual performance under glare conditions (Stringham & Hammond, 2007). As previously mentioned, this hypothesis – and the methodology used to test it in their 2007 study – drew from foundational knowledge about glare established by the three dominating hypotheses: (1) protection hypothesis: glare produces deleterious effects, MP would reduce disability caused by glare; (2) acuity hypothesis: utilization of broadband xenon white light and six monochromatic lights ranging from 440nm-620nm; (3) visibility hypothesis: photostress recovery and grating visibility assessed, contrast grating stimulus utilized. Their findings suggest that MP does have a relationship with visual performance under glare conditions in that higher MP resulted in improvements in both glare disability and photostress recovery.

Subsequent research has provided further support for the glare hypothesis (e.g., Stringham & Hammond, 2008; Stringham et al., 2011; Hammond et al., 2013; Putnam & Bassi, 2015). Some studies have also gone on to find evidence that LZ supplementation results in increased serum levels of LZ, greater MPOD, improved chromatic contrast, and improved recovery from photostress (Hammond et al., 2014).

Glare Recognition Acuity

The present study builds on the existing body of literature investigating the glare hypothesis to examine the effect of MPOD on glare acuity. As detailed in earlier sections, the glare hypothesis has a strong foundation in the literature and tests of this hypothesis have found strong, significant relationships between MPOD and glare related variables such as glare disability and photostress recovery; however, what has not been looked at in the literature is the association between MPOD and recognition acuity under glare conditions – that is, how well one

can recognize stimuli (letters, in this study) under glare conditions. Recognition is a top-down process and L and Z are both in retina and brain. Hence, the ability of L and Z to influence both bottom-up and top-down analysis of an image was our focus.

Glare is one of the leading environmental causes of car accidents and is one of the primary reasons older adults stop driving at night. Many studies have been conducted on glare disability (Stringham & Hammond, 2007; Stringham et al., 2011; Hammond et al., 2014) which is a good assessment of detection of stimuli in the presence of glare, but no studies in the glare literature have considered recognition acuity, which is distinguishable from glare disability in that it assesses the ability to recognize stimuli rather than solely detect their presence. This distinguishing ability is important to consider, especially in the example of driving, as there is a large difference between detecting a street sign and recognizing that it says “STOP.” Similarly, there is a difference in detecting an object on the road and recognizing it as a dangerous hazard. The present study introduced a novel, ecologically valid technique for measuring glare recognition acuity. Based on the previous literature described in this introduction, it was our hypothesis that higher MPOD would result in better recognition acuity under glare conditions when compared to those with low MPOD.

CHAPTER 2

METHODS

Subjects

The target population for this research study consisted of adults (age range, 18-65) with normal or corrected to normal vision. Normal vision, for the purposes of subject inclusion criteria, was defined as 20/30 or better visual acuity in each eye – this was first determined by self-report, and then again later using a wall-mounted chart. Additionally, as inclusion criteria, the subject must have been fluent in English and able to both read and understand the consent document. Exclusion criteria broadly included subjects with ocular diseases, corneal/laser-corrective surgery, significant scotomas, hard-contact use, or astigmatism greater than 0.75 diopters. Participants were recruited primarily via the UGA SONA Systems website.

Design

This study implemented a within-person, cross-sectional design. Measurements from four different tasks were recorded. Demographic information (e.g., age, gender, ethnicity, race) was collected via a self-report, laboratory questionnaire. In addition, glasses and contact use information was also recorded via questionnaire. Iris color – both hue and lightness – was also assessed and recorded (scale is shown in Figure 1). Snellen acuity was then measured; participants were asked to stand a fixed distance (~20 ft) away from a wall-mounted Snellen acuity chart. Participants first read the chart with both eyes open, followed by the right eye and

then left. The eye with best acuity was selected as the test eye; if both eyes were of equal acuity, the test eye defaulted to the right eye.

Measurement of MPOD

MPOD was measured through the use of heterochromatic flicker photometry (HFP) using the system described in Wooten et al., 1999. Participants were instructed to look through an eyepiece that presents a flickering target disk. The disk varies in size, and the different sizes correspond with different retinal eccentricities (30', 1°, 2°, and 7° eccentricities were used). The target disk is composed of two monochromatic lights – a 460nm blue LED light, strongly absorbed by macular pigment and a 570nm green LED light, not absorbed by macular pigment – presented in counter-phase. The participant was given a dial that controls the intensity of the short-wave (460 nm) light relative to the mid-wave (570 nm) light. Macular pigment (LZ) absorbs short-wave light; as a result, participants with higher MPOD required more intense short-wave light to make a luminance match with the mid-wave light, which makes the perception of flicker stop. Five trials were conducted for each target eccentricity in which the subject was instructed to stop the flicker of the target disk. The blue-light absorption for each trial was recorded in addition to the overall blue-light intensity averages, green-light intensity averages, standard deviations (SD), and optical densities (OD) for each target eccentricity – all target eccentricities were recorded during data collection, however, only 30' was relevant to, and used, in the analysis.

Measurement of Glare Acuity

After MPOD, the final measurement to be recorded was glare acuity (detailed in Nightingale & Hammond, 2021). This was done through a letter recognition task via an optical bench testing methodology. A conceptual drawing of the system is shown in Figure 2 (a-j). It

begins with a bright white light source (a) that simulates sunlight (xenon bulbs are typically a good choice, 1000 watts provides sufficient intensity). Light from the source passes through a collimating lens (b) and is then cooled with a water bath (transparent to visible light) (c); from there, it is then manipulated by a focusing lens (d) that carries the light through a circular neutral density filter (e) which attenuates the light that can then be either blocked by an occluding lens (f) or passed through a lens purposed to expand the focused light (g). The light then reaches a wheel, equipped with letter-shaped apertures (h). The subject sits at a fixed distance from the isolated stimulus (about 7 meters) and views the stimulus through a lens (i) that is either glass (no correction needed) or refractive (correction needed) with one eye at a time (eye position fixed by an eye cup). What the subject sees is a series of letters that are themselves the glare source. When the light is too intense for a given subject, consistent correct identification is not possible. Glare acuity thresholds were defined utilizing two psychophysical tests and recorded via a digital potentiometer (j) connected to the circular neutral density filter.

For the first test, participants were given a letter to view at a low intensity, dim setting. The participant would attempt to name the letter and the researcher gradually increased the intensity of the light until the participant could no longer make out the unique features of that letter. This procedure was conducted for each of the 8 letters on the wheel. The second test utilized a forced-choice method. Participants were given a randomly selected letter to view and the light was passed through the letter cut-out at the brightest intensity. Participants were given a set of choices and instructed to pick the choice that they thought they could see through the glare of the arc lamp. For example, a participant may have been given the letter "E" and was then asked if the letter they could see was an "E" or an "F." If answered correctly, the participant was then asked how sure they were of their response. The intensity of the light was then decreased

until they were 100% sure of the letter they are viewing. This task was repeated for each of the 8 letters on the wheel. Below is a detailed protocol on the design of the optical system illustrated in Figure 2.

Design Protocol

1.1 Begin with an optical table, the best choice is a breadboard with a grid of mounting holes (commonly, the imperial ¼” -20 UNC on a 1” grid is standard – in metric this would convert to an M6 screw thread on a 25 mm grid). The minimum size necessary is about 36" x 48" or 91 cm x 122 cm.

1.2 Install a 1000 W xenon arc lamp with the associated power supply at the posterior end of the bench (see a of Figure 2). One limitation with these systems is that, if the light output is not constant (within and across sessions), small variations would be interpreted as variation in behavioral thresholds. Hence the power supply should be highly regulated with optical feedback sensors in order to ensure constant light output across experimental sessions and over time.

1.3 Next in sequence, install the first lens at a position that collimates the light from the source (see b of Figure 2). All lenses within the system are plano-convex achromats with anti-reflection coating. The effective focal length is about 100 mm and the diameter is about 5 cm (slightly larger than the exit aperture of the light source).

1.4 Following the first collimating lens, introduce an optical element to remove heat within the optics generated by the intense light source (see c of Figure 2). Infrared filters are one

possibility but they often intrude into the visible. A water bath is a nice alternative. In the current system, two optical flats enclosed a tube filled with water.

1.5 Introduce the next lens (see d of Figure 2) within the optical system so as to focus light to a small point on the 100 mm circular neutral density filter (see e of Figure 2). This circular filter attenuates light over a linear range of about 2 log units optical density. Since the filtering is done over a gradient, light needs to be focused to a fairly small area (4-9 mm2) when passing through the circular filter (this position is also good for baffling using a small aperture that only passes the focused light). The nominal position of the filter is indicated by a digital readout, coupled to a potentiometer (see j of Figure 2). The actual amount of light transmitted that corresponds to the circular filter's position is determined using a calibrated radiometer. Utilize this same radiometer to periodically confirm that the overall energy within the system remains constant over the course of the experiment.

   a. Use a mechanical shutter or simply a blocking filter and holder to occlude the stimulus between trials (see f of Figure 2).

1.6 Add the next lens to the system, a collimating lens (see g of Figure 2), placed such that light expands to match the diameter of each letter aperture (10.16 cm), fully illuminating the optotype (7.62 cm).

1.7 Construct the letter apertures (they can also be purchased as metal stencils); in total, 8 letter optotypes were used: P, L, D, U, Z, E, T and F (see h of Figure 2) – these letter apertures were approximately 15 X 6 X 25 mm (about 0.17°) and were chosen because they are classic Sloan optotypes and approximately the same size. Place the letter apertures in a circular rotator (to allow for easy alternation between letters) with spring-

loaded tabs and divots to lock each letter in place so there is no movement of the wheel during the experiment. In our system, luminance measured at the letter aperture was 4000 lux; 40 lux when measured at the plane of the eye.

1.8 Next, baffle the system such that subjects can only see the back-illuminated letter apertures (e.g., the intense light coming out of an "E") – one easy method for doing this is to have the optics of the system in one room with the subject in an adjoining room. A hole can be positioned within the doorway adjoining the rooms and aligned so that subjects cannot see the experimenter, stray light, etc. Should the participant be unable to hear the experimenter's instructions, add an intercom system.

1.9 One limitation is that the position of the eye relative to the visual system must be fairly precise; hence, create some form of head and chin rest assembly – a rubber eye cup mounted on a black tube (both mounted on a movable cart) was used. As done in this protocol, add a mount behind the tube to allow for the use of trial lenses to correct for refractive error using standardized lenses (i.e., no tinting, etc.); this will also allow for the use of a glass "blank" in order to ensure that the optical effects of those who did not require refractive correction match those who required refractive corrective optics (see i of Figure 2).

a. Additionally, ensure the viewing station is secured so that it does not move between subjects.

b. Use a laser level to ensure alignment of the eye piece with the optics (7 meters from the plane of the eye).

Instruments

The laboratory demographics questionnaire used in this study consists of basic screening questions – age, gender, ethnicity, race – and collects basic, self-report optical information – glasses use, contacts use, history of eye injury/disease, history of eye surgeries. This information was collected because certain demographic characteristics (iris color, visual correction, etc.) could influence the effect of MPOD on glare acuity; the data obtained from these demographics are addressed in the analysis. This specific questionnaire format was chosen to ensure a broad representation of subjects and to address some of the exclusion criteria as mentioned previously. A standardized iris color scale was used to measure the subject's iris color, Figure 1. A standardized Snellen acuity test was utilized to measure visual acuity. Visual acuity was recorded to address exclusion criteria, test for necessity of visual correction, and test for dominant (better acuity) eye. The HFP device used in this study is the same as the highly-efficient, tabletop device described in Wooten et al. (1999). This device has proved to be highly accurate and valid in assessing MP (for further information regarding device and device's validity, refer to Wooten et al., 1999). The optical bench setup and letter detection task used to measure glare acuity are a novel design based on prior methods used to measure glare disability (see, e.g., Stringham et al., 2011; Hammond et al., 2013; Hammond et al. 2014) but altered in a novel way (a letter detection task) to measure recognition as opposed to detection. The letter recognition task utilizes the same letters as the Snellen acuity chart and applies the same principles of visual acuity to this novel measure of glare acuity.

Procedure Description

The procedures outlined in this method adhere to all institutional guidelines relating to human subject's research. This study was approved by the University of Georgia institutional

review board, and the experimental procedures were conducted in accordance with Good Clinical Practice Guidelines and the ethical principles of the Declaration of Helsinki.

At the beginning of the experimental session it was confirmed that all optical elements within the system have been correctly aligned, light intensity (with no attenuation) is correct, and the subject's eye is in the proper position. The task was then explained to the subject (letter identification) and the stimuli were presented in random order at differing levels of intensity. The goal was to find the highest intensity at which a subject can still correctly identify individual letters (with the actual threshold defined probabilistically at 75% correct detection, 6 correct out of 8). Individuals with "optimal glare acuity" are those able to recognize letters at much higher intensities than those with poor glare acuity. The procedures followed and psychophysical methods used are outlined below.

Procedure

2.1 The method of limits (to get close to the threshold) was used by increasing the intensity of the glare source until the participant could no longer recognize the letter features, and then constant stimuli by then presenting a random sequence of the additional 7 letters to obtain a precise value of the subject's glare recognition acuity threshold – there are more accurate psychophysical methods available (signal detection, forced choice, etc.) but this method was implemented given the number of measures and time constraints.

2.2 The letters used in the present method were P, L, D, U, Z, E, T and F.

2.3 A random letter generator was used to organize the letters on the wheel into a unique, random order for each subject.

2.4 Before beginning the protocol, the nature of the experimental task was explained by showing the subject suprathreshold stimuli.

2.5 It was ensured that the subject was aware that the task is fairly simply (“can the letter be seen or not?"). Derivation of an accurate probalistic threshold was achieved by running multiple trials – enough to generate a psychometric function.

CHAPTER 3

RESULTS

Descriptive Statistics

Descriptive statistics are provided for all variables in Table 1. Despite the relatively homogenous sample of healthy young adults, there was wide variance for all visual measures: MPOD at 30' ranged from 0.16 – 1.01 (mean = 0.45, SD = 0.18), average log-relative energy (LRE) ranged from 1.18 – 2.04 (mean = 1.47, SD = 0.21), average letters seen ranged from 2 – 8 (mean = 5, SD = 1.72), and average letters not seen ranged from 0 – 6 (mean = 3, SD = 1.72). Visual representations of subject variation for LRE scores and Letters Recognized can be seen in Figure 3 and Figure 4, respectively.

Between-groups Analyses

Paired Sample *T*-tests were conducted to find between-group differences for Iris Color (Light & Dark), MPOD (High & Low), and Visual Correction (Correction & No Correction). Paired samples statistics for LRE scores can be seen in Table 2. Paired samples correlations for LRE scores are shown in Table 3. Table 4 shows the *T*-test results for LRE scores. There was no significant difference found between light irises (M = 1.45, SD = 0.20) compared to dark irises (M = 1.35, SD = 0.27), $t(3) = 0.52$, $p = 0.637$. Similarly, there were no significant differences found between High MPOD (M = 1.49, SD = 0.18) and Low MPOD (M = 1.47, SD = 0.23), $t(10) = 0.19$, $p = 0.854$ or Visual Correction (M = 1.48, SD = 0.16) compared to No Visual Correction (M = 1.50, SD = 0.31), $t(6) = -0.17$, $p = 0.87$.). Pared samples statistics for Letters Recognized can be seen in Table 5. Paired samples correlations for LRE scores are shown in Table 6. Table 7

shows the *T*-test results for Letters Recognized. There was no significant difference found between light irises (M = 6.00, SD = 2.71) compared to dark irises (M = 3.75, SD = 2.36), $t(3) = 1.57$, $p = 0.215$. Similarly, there were no significant differences found between High MPOD (M = 4.64, SD = 1.63) and Low MPOD (M = 5.27, SD = 1.79), $t(10) = -0.81$, $p = 0.439$ or Visual Correction (M = 5.14, SD = 2.41) compared to No Visual Correction (M = 5.29, SD = 1.80), $t(6) = -0.97$, $p = 0.926$. Visual representations of subjects' LRE scores by Iris Color and Visual Correction can be seen in Figure 5 and Figure 6, respectively. For visual representations of subjects' Letter Recognition scores by Iris Color and Visual Correction, refer to Figure 7 and Figure 8.

Correlations

Bivariate Pearson Correlations were conducted for both MPOD & LRE and MPOD & Letters Recognized. Among participants in this sample, there was no significant correlation found between MPOD and LRE, $r(21) = 0.028$, $p = 0.450$. These results are shown in Table 8. There was also no significant correlation established between MPOD and Letters Recognized, $r(21) = 0.021$, $p = 0.463$. These results are shown in Table 9. For a visual representation of subjects' LRE and Letter Recognition scores by MPOD, refer to Figure 9 and Figure 10, respectively.

Partial correlations controlling for Age, Iris Color, and Visual Correction were also conducted for both MPOD & LRE and MPOD & Letters Recognized. When controlling for Age, no significant relationship was found between MPOD and LRE, $r(21) = -0.010$, $p = 0.482$. Similarly, no significant relationship was found when controlling for Iris Color, $r(21) = 0.087$, $p = 0.350$ or Visual Correction, $r(21) = 0.040$, $p = 0.430$. These results can be seen in Table 10. The partial correlations for MPOD and Letters recognized controlling for Age, $r(20) = -0.032$, p

= 0.444, Iris Color, $r(20) = 0.018$, $p = 0.469$, and Visual Correction, $r(20) = 0.008$, $p = 0.468$ did not reveal any significant relationships. These results can be seen in Table 11.

Additional Findings

Table 12 shows the Letter-Specific Recognition Ratios indicating which letters could be seen more frequently by participants and which ones could not. These data can also be interpreted visually in Figure 11.

CHAPTER 4

TABLES AND FIGURES

Table 1

Descriptive statistics (n = 23)

Variable	**Average**	**SD**	**Range**	**n Analyzable**
Age	19.17	1.34	4, 18 to 22	23
MPOD (30')	0.45	0.18	0.85, 0.16 to 1.01	23
Average LRE	1.47	0.21	0.86, 1.18 to 2.04	23
Average Letters Seen	5.04	1.72	6, 2 to 8	23
Average Letters Not Seen	2.96	1.72	6, 0 to 6	23
Vision Correction	30% vision correction 70% no vision correction	N/A	N/A	23
Iris Color (Hue)	22% Blue 4% Green 17% Hazel 57% Brown	N/A	N/A	23
Iris Color (Lightness)	17% Light 17% Medium 66% Dark	N/A	N/A	23

Table 2

Between-groups Analyses (LRE): Paired Samples Statistics

	Variable	Mean	N	SD	Std. Error Mean
Pair 1	Light	1.445	4	0.201	0.101
	Dark	1.353	4	0.266	0.133
Pair 2	High MPOD	1.489	11	0.183	0.055
	Low MPOD	1.471	11	0.232	0.070
Pair 3	Correction	1.476	7	0.159	0.060
	No Correction	1.499	7	0.314	0.119

Table 3

Between-groups Analyses (LRE): Paired Samples Correlations

Variable	N	Correlation	Significance
Light & Dark	4	-0.135	0.865
High MPOD & Low MPOD	11	-0.172	0.613
Correction & No Correction	7	-0.024	0.959

Table 4

Between-groups Analyses (LRE): Paired Samples T-tests

Variable	Mean	SD	Standard Error Mean	Lower 95% CI	Upper 95% CI	t	df	Significance (2-tailed)
Light & Dark	0.093	0.354	0.177	-0.471	0.656	0.523	3	0.637
High MPOD & Low MPOD	0.018	0.319	0.096	-0.196	0.233	0.189	10	0.854
Correction & No Correction	-0.023	0.355	0.134	-0.351	0.305	-0.170	6	0.870

Table 5

Between-groups Analyses (Letters Recognized): Paired Samples Statistics

	Variable	Mean	N	SD	Std. Error Mean
Pair 1	Light	6.00	4	2.708	1.354
	Dark	3.75	4	2.363	1.181
Pair 2	High MPOD	4.64	11	1.629	0.491
	Low MPOD	5.27	11	1.794	0.541
Pair 3	Correction	5.14	7	2.410	0.911
	No Correction	5.29	7	1.799	0.680

Table 6

Between-groups Analyses (Letters Recognized): Paired Samples Correlations

Variable	N	Correlation	Significance
Light & Dark	4	0.365	0.635
High MPOD & Low MPOD	11	-0.168	0.622
Correction & No Correction	7	-0.703	0.078

Table 7

Between-groups Analyses (Letters Recognized): Paired Samples T-tests

Variable	Mean	SD	Standard Error Mean	Lower 95% CI	Upper 95% CI	t	df	Significance (2-tailed)
Light & Dark	2.250	2.872	1.436	-2.320	6.820	1.567	3	0.215
High MPOD & Low MPOD	-0.636	2.618	0.789	-2.395	1.123	-0.806	10	0.439
Correction & No Correction	-0.143	3.891	1.471	-3.742	3.456	-0.097	6	0.926

Table 8

Pearson Correlation (MPOD and LRE)

	Variable	MPOD	LRE
MPOD	Pearson Correlation	1	0.028
	Significance (1-tailed)	N/A	0.450
	n	23	23
LRE	Pearson Correlation	0.028	1
	Significance (1-tailed)	0.450	N/A
	n	23	23

Table 9

Pearson Correlation (MPOD and Letters Recognized)

	Variable	**MPOD**	**Letters Recognized**
MPOD	Pearson Correlation	1	0.021
	Significance (1-tailed)	N/A	0.463
	n	23	23
Letters Recognized	Pearson Correlation	0.021	1
	Significance (1-tailed)	0.463	N/A
	n	23	23

Table 10

Partial Correlations (MPOD and LRE)

AGE	Variable	MPOD	LRE
MPOD	Correlation	1.000	-0.010
	Significance (1-tailed)	N/A	0.482
	df	0	20
LRE	Correlation	-0.010	1.000
	Significance (1-tailed)	0.482	N/A
	df	20	0

IRIS COLOR	Variable	MPOD	LRE
MPOD	Correlation	1.000	0.087
	Significance (1-tailed)	N/A	0.350
	df	0	20
LRE	Correlation	0.087	1.000
	Significance (1-tailed)	0.350	N/A
	df	20	0

VISUAL CORRECTION	Variable	MPOD	LRE
MPOD	Correlation	1.000	0.040
	Significance (1-tailed)	N/A	0.430
	df	0	20
LRE	Correlation	0.040	1.000
	Significance (1-tailed)	0.430	N/A
	df	20	0

Table 11

Partial Correlations (MPOD and Letters Recognized)

AGE	Variable	MPOD	Letters Recognized
MPOD	Correlation	1.000	-0.032
	Significance (1-tailed)	N/A	0.444
	df	0	20
Letters Recognized	Correlation	-0.032	1.000
	Significance (1-tailed)	0.444	N/A
	df	20	0

IRIS COLOR	Variable	MPOD	Letters Recognized
MPOD	Correlation	1.000	0.018
	Significance (1-tailed)	N/A	0.469
	df	0	20
Letters Recognized	Correlation	0.018	1.000
	Significance (1-tailed)	0.469	N/A
	df	20	0

VISUAL CORRECTION	Variable	MPOD	Letters Recognized
MPOD	Correlation	1.000	0.008
	Significance (1-tailed)	N/A	0.468
	df	0	20
Letters Recognized	Correlation	0.008	1.000
	Significance (1-tailed)	0.468	N/A
	df	20	0

Table 12

Letter-Specific Recognition Ratios

Letter	Seen	Not Seen
D	18	5
L	20	3
F	19	4
T	8	15
U	4	19
E	20	3
P	9	14
Z	18	5

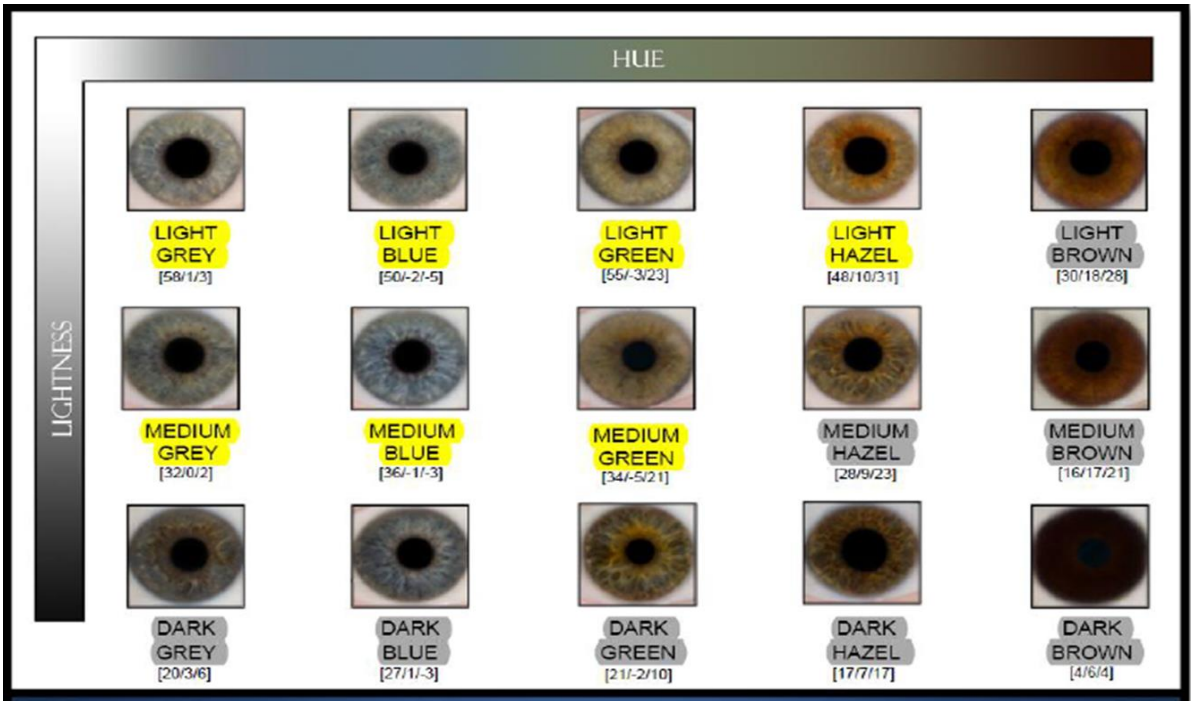

*Figure 1***.** Iris Color Scale.

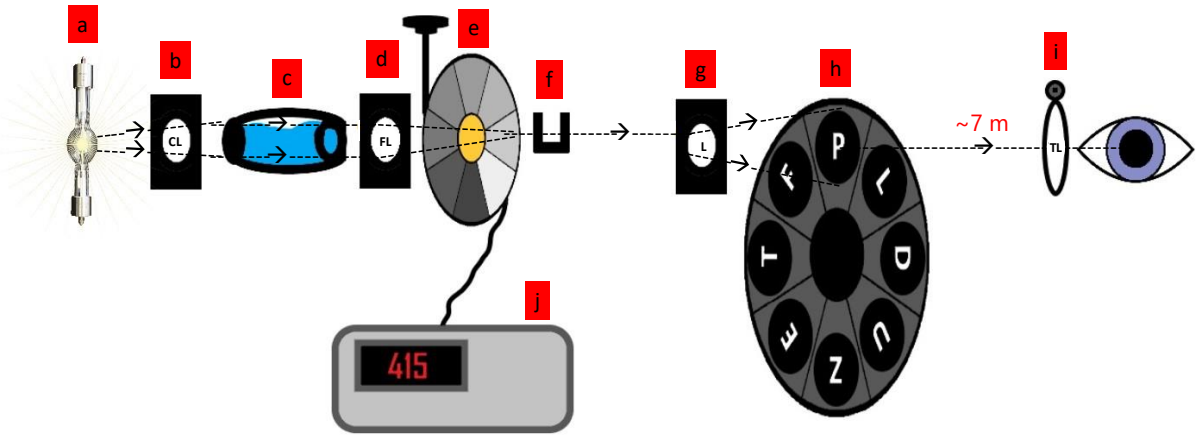

Figure 2. Glare Acuity Schematic including (a) xenon light source (b) collimating lens (c) water bath (d) focusing lens (e) circular filter (100 mm neutral density filter) (f) filter holder (g) lens (h) letter apertures in circular rotating wheel (i) refraction correction (trial lenses) (j) digital readout of circular filter potentiometer.

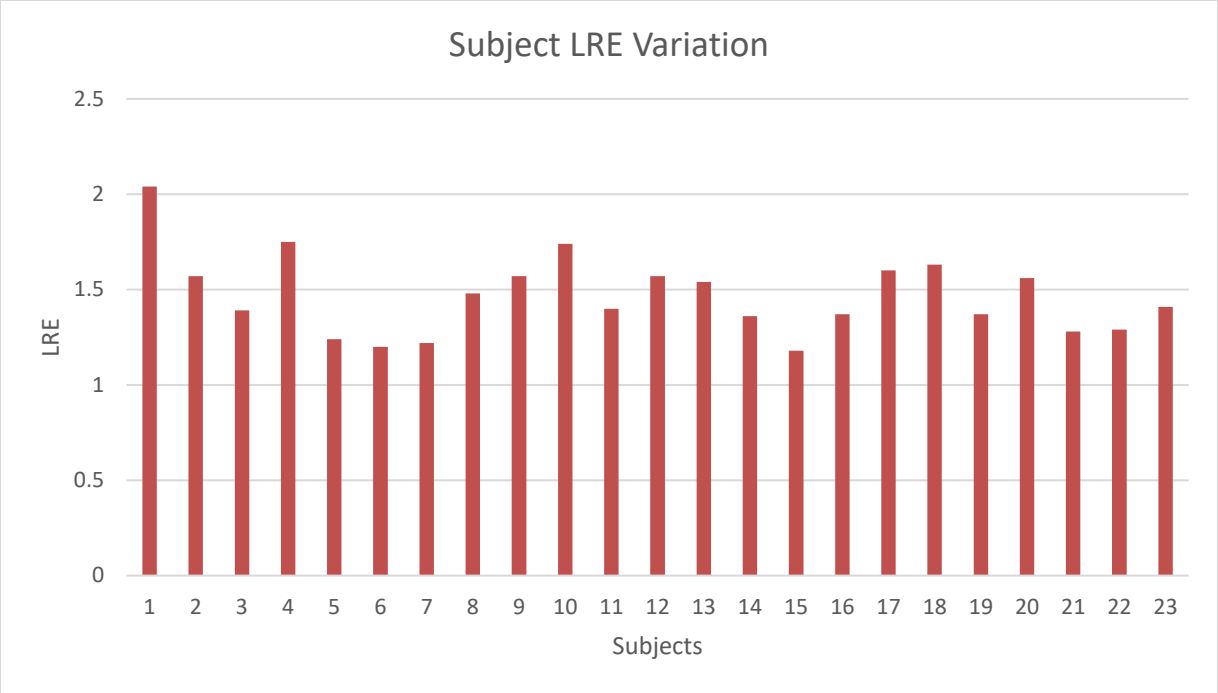

Figure 3. Variation in LRE of All Subjects.

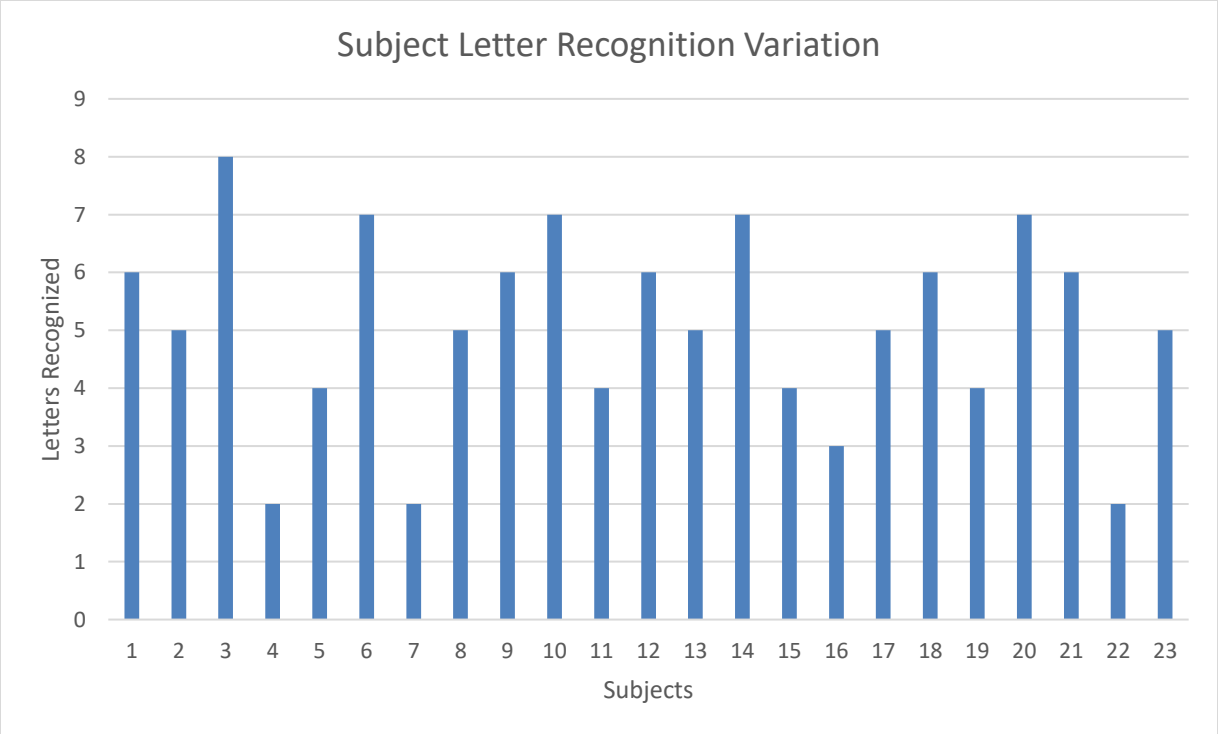

Figure 4. Variation in Letters Recognized by All Subjects.

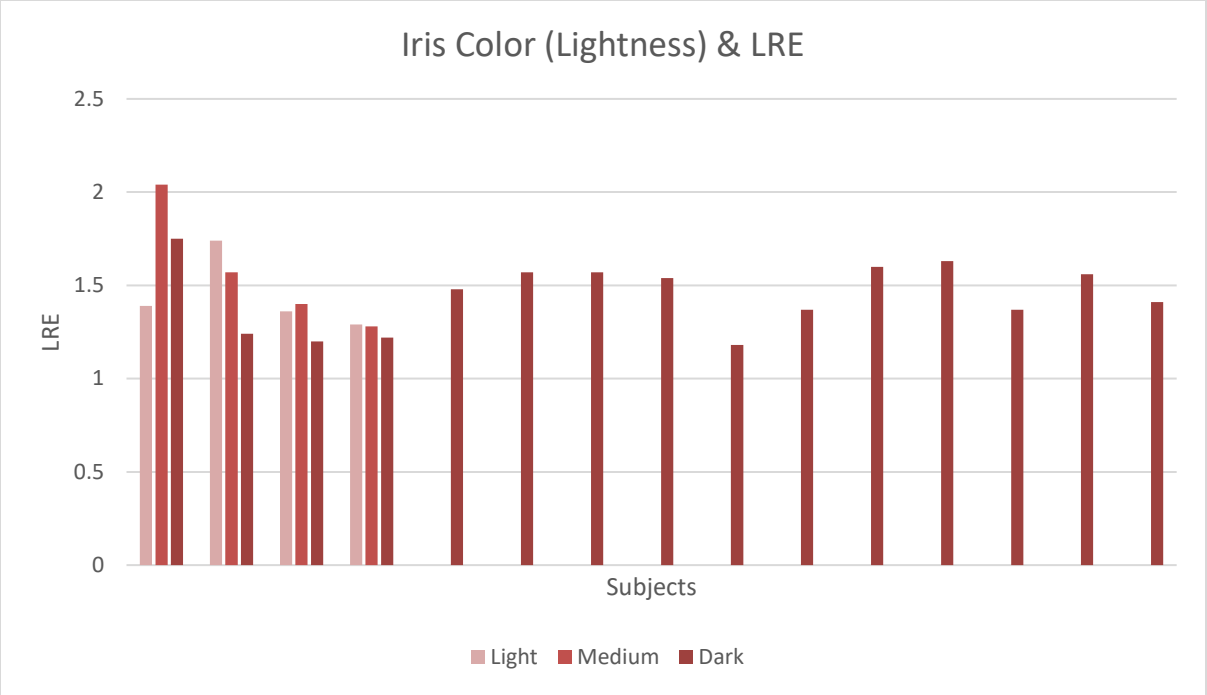

Figure 5. LRE of Subjects with Light, Medium, and Dark Irises.

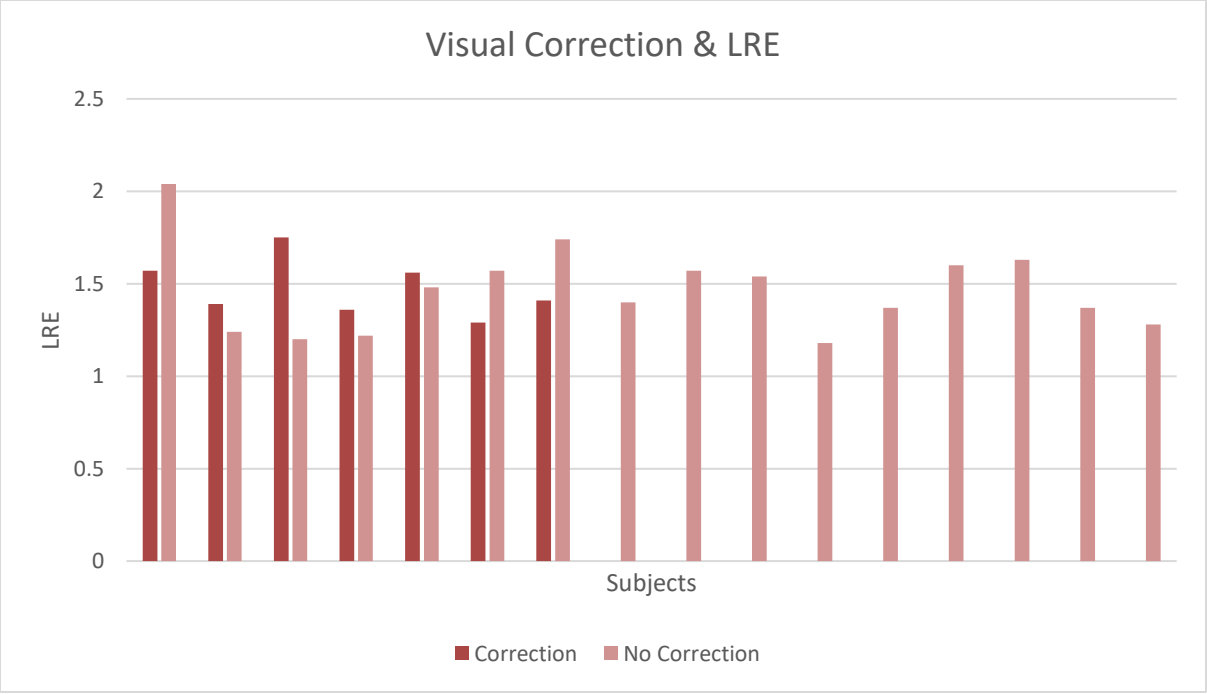

Figure 6. LRE of Subjects with Correction and No Correction.

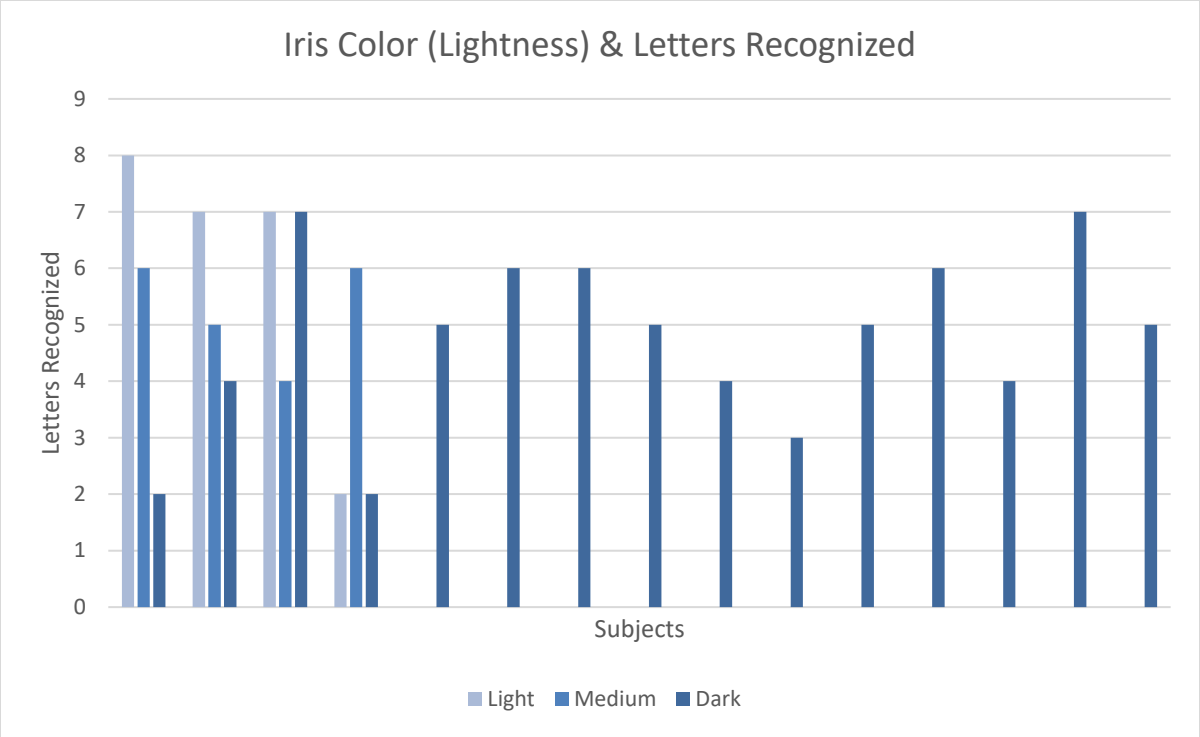

Figure 7. Number of Letters Recognized by Subjects with Light, Medium, and Dark Irises.

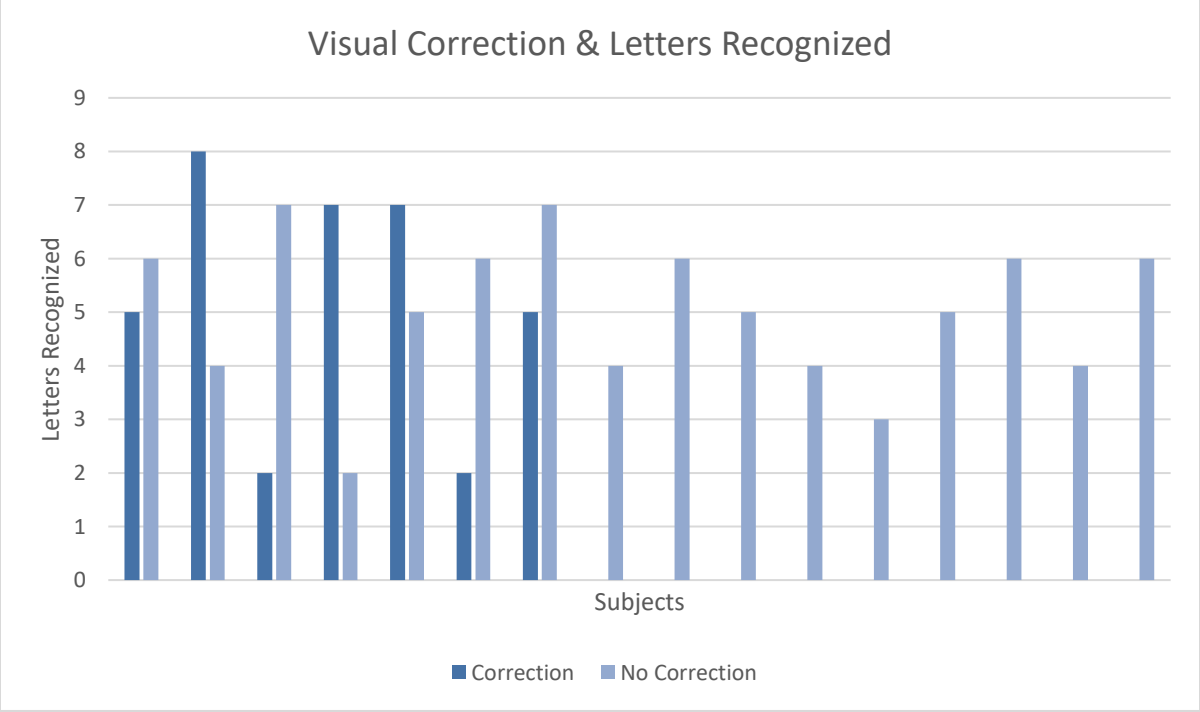

Figure 8. Number of Letters Recognized by Subjects with Correction and No Correction.

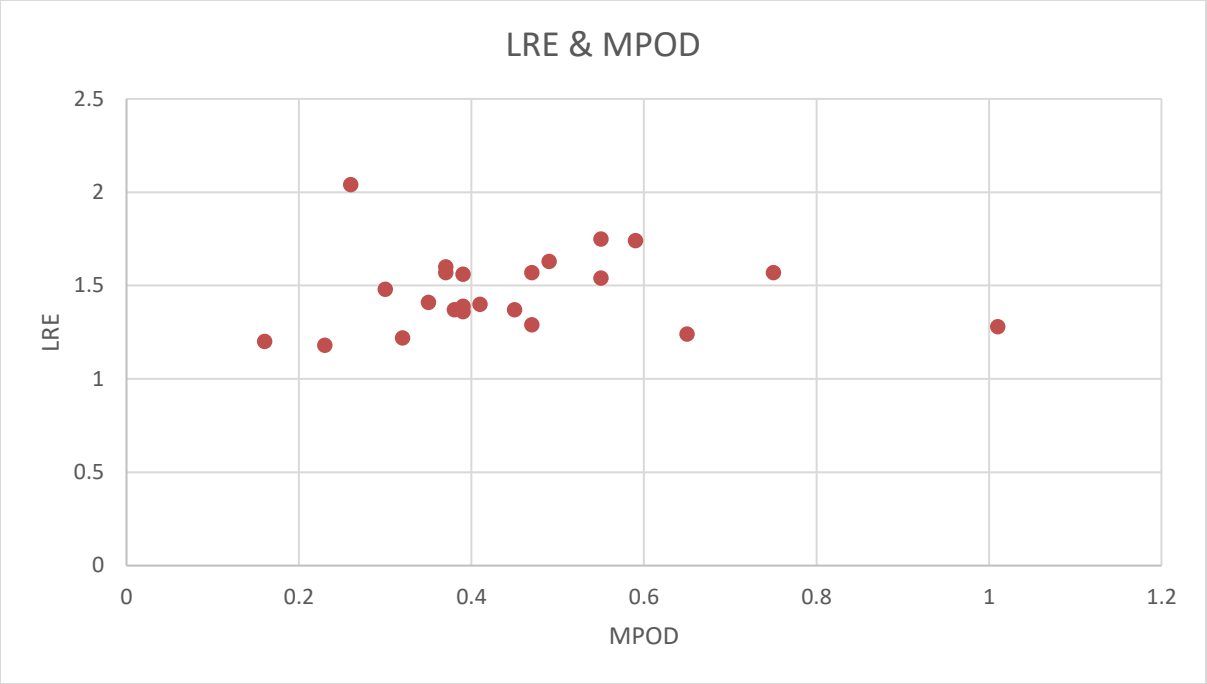

Figure 9. Distribution of LRE Scores, Organized by Subjects' MPOD.

Figure 10. Distribution of Letter Recognition, Organized by Subjects' MPOD.

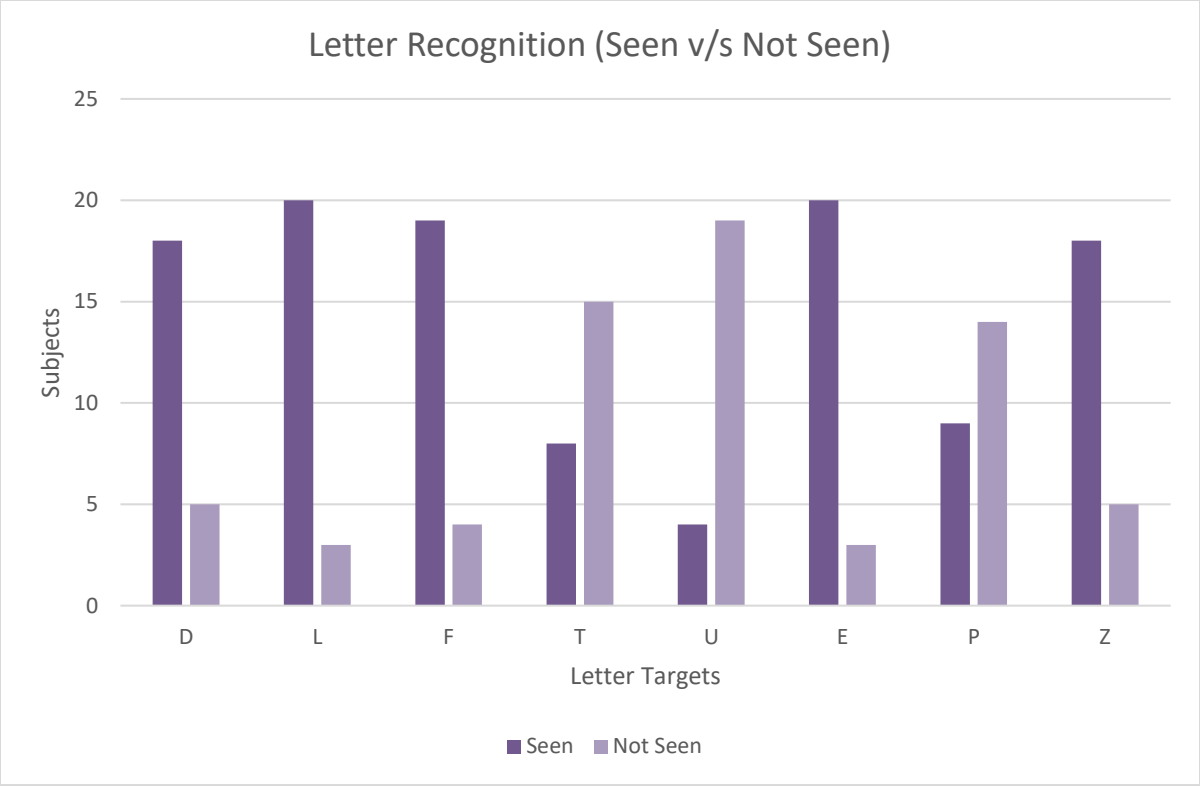

Figure 11. Letter-Specific Recognition Ratios.

CHAPTER 4

DISCUSSION

Anatomical research on the macular pigments lutein and zeaxanthin, has shown that the pigments are located throughout the central nervous system. This distribution is not incidental. The pigments appear to serve important functions within the eye and within the brain. No studies, however, have been done that looked at behaviors that are strongly and simultaneously mediated by both optical factors and higher level central nervous system processing. To this end, we designed a task that would be strongly impacted by ocular optics (light scatter within the anterior media of the eye) and yet still require a higher-level judgement (recognition of letter features) by the subject. 23 subjects were assessed. We did not find significant correlations between MPOD and glare acuity.

The present study tested if MPOD, a concentration of lutein and zeaxanthin within the retina, was related to performance in a recognition (acuity) task under glare conditions. Our hypothesis was directional in nature and it was expected that higher MPOD would result in better recognition acuity when under the effects of glare – higher LRE threshold scores and greater number of letters recognized. MPOD did not correlate with LRE, producing a correlation coefficient of 0.028, or Letters Recognized, producing a correlation coefficient of 0.021. Both correlations being nearly 0 indicate that MPOD had no effect on recognition acuity under the influence of glare. The graphs produced in Figures 9 and 10 illustrate this lack of effect. Average MPOD (0.45) and the range (0.85) were relatively consistent with other studies measuring MP density, as was the sample of young, healthy student-age subjects. Finding such wide variation in

a relatively homogenous sample raises a number of questions. Firstly, why did MPOD not moderate the effect of glare on stimulus recognition in a similar way to stimulus detection? And secondly, what processes may have contributed to this variation in our relatively healthy, homogenous sample?

Referring back to the Acuity Hypothesis may help in addressing the first question of why MPOD did not have an effect on recognition acuity. The acuity hypothesis, as mentioned previously, is one of the foundational hypotheses leading up to the Glare Hypothesis of MP functionality, and it is the only one directly associated with visual acuity. Engles et al., 2007 assessed MPOD's effect on resolution acuity (RA) using a gap detection task and hyperacuity (HA) using a vernier acuity task; this was the first empirical evaluation of the hypothesis. In their evaluation, they received null results, finding no effect of MPOD on resolution acuity or hyperacuity. They concluded that the "predictions of the acuity hypothesis do not hold" (2007), stating that, despite their small sample-size, "if MP is related to improvements in RA that are smaller, such effects are too weak to be of interest" (2007). Based on the results of this study, and the present one, it seems that the protective effects of MP do not extend to mitigating the deleterious effects of chromatic aberration caused by sunlight – effects that have the potential to blur features of objects, specifically edges.

The second question is more difficult to answer and, while no definitive conclusion can be made based on the results of this study, the wide variation in both threshold for recognition and number of letters recognized may suggest that higher-level, cognitive differences play a larger role in performance on the letter recognition task than biological differences such as MPOD. In a 2002 study on the Neural Specialization for Letter Recognition, Polk et al., using functional neuroimaging, found a region of the brain in the left ventral occipitotemporal area that

responded more significantly to letters, compared to digits, in both passive and active (string-matching) viewing tasks. Because letters are a category of stimuli that are culturally defined and acquired over the course of many postnatal years (2002), it is possible that the development and resulting architecture of this "letter region" looks different from person to person. Letter recognition, especially recognition under glare conditions may be more difficult for subjects whose letter region architecture is underdeveloped for the English alphabet due to cultural, developmental, or other cognitive constraints. Additionally, some subjects may have a "better" or more comprehensive alphabetic framework, from which they are able to recall and process letter features more effectively compared to others. For subjects who may have had a more developed letter region/alphabetic framework, it is possible that when paired with the foreknowledge that a letter would be shown, their cognitive advantages overturned any effect of higher MPOD on superior recognition acuity.

One limitation present with these results is the sample size; it is likely that we did not have a sufficiently large sized sample. Hammond et al. (2013) examined the relation between MPOD and glare disability and tested 150 subjects. In that study, MPOD explained about 5% of the variance in glare disability (similarly conducted on a sample of young UGA students). Studies have also been done looking at the relation between cognitive function and MPOD on younger subjects (e.g., Saint et al. 2018). These studies tend to also see correlations on the order of about 0.2-0.3). An a priori power analysis for correlational effects (one-tailed alpha = 0.05, power (1-beta) = 0.80, and an r = 0.50) predicted a total sample size of 23 which is what was used given the ongoing pandemic and limited subject pool. In keeping with convention, however, an effect size of r = 0.30 would have been more representative of earlier studies such as the ones previously mentioned. Using power analyses for correlational effects (one-tailed alpha = 0.05, 1-

beta = 0.80 and an r = 0.30) predicts a sample size of 67 using G*Power. A sample this size would have given a similarly powered sample, more closely matching the sample size of those of experiments looking at MPOD's effect on glare disability and cognitive function. Ultimately, subject availability was limited due to the pandemic and, hence, we focused on refining the methodology (see Nightingale & Hammond, 2021). Because there are no current methods of measuring glare recognition acuity, developing a novel, ecologically valid method of doing so was one of the primary objectives of this study. However, once we can expand our subject selection (post-pandemic), we would like to continue the sampling for this study.

Some future directions for this line of research are to address some of the possible contributing factors to the null effect of MPOD and to expand upon the scope of the present study. As previously mentioned, the limitation of the current study's sample size can be addressed by continuing sampling for the study once a post-pandemic research environment resumes; a smaller effect size and more participants will produce results more directly comparable with the literature. To address the detrimental role chromatic aberration plays in acuity, lenses could be introduced to the system to correct for longitudinal chromatic aberration (wavelength-dependent blurring) responsible for potentially blurring the contours of the letter stimuli – this would decrease the overall ecological validity of the methodology, as chromatic aberration effects would not normally be filtered out of natural sunlight, but it would provide a more direct look at MPOD's role in the context of acuity. Differences in recognition acuity could be recorded for native English speakers v/s non-native English speakers to address potential differences in the development and efficiency of the letter region of the brain and the role of having a more preferential "alphabetic framework" for English letters. Expanding on the scope of the present study, further methodological changes could be made to assess geometric shapes

rather than letters, 2D v/s 3D objects (square v/s cube), and the full alphabet (uppercase and lowercase English letters).

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