MACULAR PIGMENT: TESTING THE ACUITY AND VISIBILITY HYPOTHESES

by

MICHAEL ENGLES

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

ABSTRACT

The macular pigment (MP) is composed of diet-derived carotenoids that screen blue light and are concentrated in and around the fovea. Several functions for the MP have been proposed. The earliest hypothesis, termed the Acuity Hypothesis, predicts that increased MP optical density should improve spatial vision by reducing the deleterious effects of chromatic aberration, an optical phenomenon whereby short-wave light is blurred to a much greater extent than long-wave light. In light of the fact that the atmosphere preferentially scatters short-wave light, termed blue haze, Wooten & Hammond (2002) proposed the Visibility Hypothesis. They assert that increased MP optical density should improve distance vision by selectively reducing the veiling effects of short-wave veiling light such as “blue haze.” These two hypotheses have been tested using a specially designed optical device and a rigorous psychophysical procedure. The results do not support the Acuity Hypothesis, however our results do support the Visibility Hypothesis. Future testing should work toward establishing a causal relation between MP optical density and CS by supplementing subjects with lutein and zeaxanthin.

INDEX WORDS: Macular pigment, contrast sensitivity, Acuity Hypothesis, Visibility Hypothesis

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Graduate School. Wow. This document certifies that I have endured five years of self-induced torture to produce a work that I will never allow to be read by any of my closest friends. But it's not about the work. It's about the relationships we forge now that will last for the rest of our lives, even when we don't want them to. To be honest, I have never met a group of people that I have liked more, which is saying something considering that I tend to be very pessimistic.

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DEDICATION

I dedicate this dissertation to my dad. He pushed me harder than anyone could, even myself, and I never thanked him for it. He taught me the value of a strong work ethic that will stay with me for the rest of my life. He was a great man and I love him very much.

I would also like to dedicate this dissertation to my mother and my brother. They have supported and encouraged throughout my entire graduate career, and for whatever reason, continue to do so.

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CHAPTER 1: INTRODUCTION

"Erst wenn die Wolken schlafengehn,

kann man uns am Himmel sehn."

Excerpt from Engel, by Till Lindemann

Overview

Achieving optimal seeing has been one of the many goals of vision science and it extends from the realm of the very small to the very distant. In recent years, fantastic advances have been made to ocular aids, such as contact lenses, intraocular lens implants and corneal replacements (e.g., Liang, Williams & Miller, 1997). Fewer studies have addressed improving vision so that one can see across greater distances (e.g., visibility), however there is some work to suggest that even this can be improved in some cases (e.g., Clark, 1969; Wolffsohn et al, 2000). To date, the vast majority of studies address the age and pathological related changes within the eye's optical components. Consequently, very little attention has been devoted to studying the eye's natural mechanisms for optimizing seeing. Nevertheless, it would be of great interest to researchers and clinicians to identify those features of the eye itself which facilitate optimal vision.

It has been suggested that the macular pigment (MP), a yellow chromophore located at the fovea, is one of these features. For example, the earliest proposed function of the MP was as an optical filter that improves visual resolution by reducing the blurring effects of chromatic aberration (Schültze, 1866). This has been termed the Acuity Hypothesis (e.g., Wooten & Hammond, 2002). Despite the age of the Acuity Hypothesis, it has only recently been empirically tested (Engles et al, 2007). Since Schültze, several new functions of the MP have been proposed. For instance, using the same mechanism described by Schültze, Eckmiller (2004) demonstrated that the MP can facilitate proper cone alignment (e.g. cones orient their long axis toward the center of the pupil to maximize photon capture). Stringham & Hammond (2007) argue that the MP reduces the visual disability associated with glare, termed the Glare Hypothesis, which is, in principle, similar to an earlier idea by Wooten & Hammond (2002) who propose that the MP can improve visibility (detection and discrimination of distant targets) by absorbing blue light scattered by the atmosphere, termed the Visibility Hypothesis.[1] Since the MP is dietary in origin, it may be possible that improved seeing could be achieved through better diet and lifestyle. However, the Visibility Hypothesis has yet to be tested and the current data (Engles et al., 2007) evaluating the Acuity Hypothesis is insufficient as discusses later. Consequently, the goals of the present study are to fully test the Acuity hypothesis and provide a first empirical evaluation of the Visibility Hypotheses.

The Macular Pigment

The MP is composed of lutein, zeaxanthin and meso-zeaxanthin (e.g., Wald, 1945, Bone et al, 1985; Handelmann et al, 1988), which are obtained dietarily through carotenoid-rich (specifically xanthophylls which are deoxygenated carotenoids) foods (i.e., they cannot be synthesized de novo). MP possesses several interesting characteristics that are central to the Acuity and Visibility Hypotheses. For instance, the MP is concentrated anterior to the cone photoreceptors in the Henle fiber layer within and around the central fovea (Snodderly et al,

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[1]The Glare hypothesis deals with MP absorbing intraocular scatter whereas the Visibility hypothesis focuses on scattering outside of the eye. In both cases, MP is absorbing a veil created by scattered light and an object becomes more visible as a function of MP attenuating this intermediary.

1984a,b). This area of the retina has the highest density of photoreceptors (e.g., Osterberg, 1935; Curcio et al, 1990), and is comprised almost entirely of cones within 1.25° of the center (e.g., Curcio et al, 1990). Also, it is in this portion of the retina that one finds the highest visual acuity (Helmholtz, 1924).

The MP exhibits a broad spectral absorption profile occupying the short-wave region of the visible spectrum. It is a yellow filter and therefore the physical intensity of shortwave light is reduced before it reaches the photoreceptors as a linear function of its optical density. More specifically, the MP absorbs visible light between 400 and 550nm, with its peak absorbance at 460nm (Wyszecki & Stiles, 1982; Snodderly, 1984a,b; Pease et al, 1987).

The density of the pigment is highest in the central fovea and usually follows an exponential decay function with eccentricity reaching minimal concentrations at approximately 5º visual angle for most individuals (e.g., Snodderly et al, 1984b), although it has been measured in small amounts at eccentricities reaching 7º and even nearly 10º in some individuals (e.g., Werner et al., 2000). The peak concentration of the MP is highly variable across individuals, ranging for instance, from nearly 0.0 to 1.6 log optical density (OD) units (e.g., Hammond et al, 1997). In terms of light transmission this constitutes a range of nearly 100% transmittance to approximately 2.5% transmittance measured at 460nm. In other words, the foveal cones of a person with very little or no MP would receive the full brunt of the light energy impinging on the retinal tissue, whereas the cones of a person with very high MPOD would receive a severely reduced amount. This enormous variability in MPOD is due, in part, to the fact that lutein and zeaxanthin are diet derived compounds that come from green leafy vegetables (e.g. spinach, broccoli, etc.). During digestion, the compounds can be absorbed through the walls of the gut and enter the blood stream. Due to the wide variability across individuals in diet, weight, and lifestyle, as well as a multitude of other intermediate factors, there is a corresponding large variability in the concentration of the MP (as reviewed by Hammond & Johnson, 2002).

Taken together, the MP constitutes a variable density shortwave filter in a functionally significant region of the retina.

Experiment 1: The Acuity Hypothesis

The earliest hypothesis regarding the function of the MP, and more specifically the visual influence of the pigments, was proposed by Schültze (1866). Schültze proposed that the MP improved the quality of the retinal image by selectively removing the violet-blue penumbra of broadband targets produced by chromatic aberration (CA), thus improving visual acuity. CA is an optical phenomenon whereby the focal length for short-wave light is shorter than for long-wave light. The result of this phenomenon when viewing a broadband target is that the observer will always be myopic for the short wavelength light, and hyperopic for the long wavelength light, hence the violet-blue penumbra. In fact, CA is exaggerated in the short-wave region of the visible spectrum with up to -1.2 diopters of defocus at 460 nm (e.g., Howarth & Bradley, 1986). With regard to the effect of blurring, past studies have shown that with every additional diopter of achromatic blur an observer's acuity decreases by a factor of about 2 (e.g. Haegerstrom-Portnoy et al, 1997; Akutsu, Bedell & Patel, 2000; Radhakrishnan et al, 2004). Consequently, it is anticipated that with increased absorption by the MP the retinal image would become progressively less blurry. Nevertheless, it is unclear whether the relation between achromatic blurring and resolution is the same or similar to that for chromatic blurring across the contrast sensitivity function (CSF).

The idea that viewing a target through a yellow filter or only illuminated by narrow-band mid- or long-wave light would improve visual performance in a spatial task is an old one. For example, studies as early as König (1897) and Roaf (1932) reported poorer acuity when using predominantly short-wave light than when using predominantly mid- to long-wave light. More recently, Clark (1969) reviewed nearly 100 studies addressing visual performance while wearing colored sunglasses. It was concluded that there was no evidence to support the idea that the removal of short-wave light improved visual performance. In a recent study, Wolffsohn et al (2002) reviewed nine studies comparing contrast sensitivity (CS) in achromatic light and to CS in filtered light. The results of these studies are mixed and Wolffsohn et al, in their own study comparing a variety of filters, report no differences in CS at any of the spatial frequencies they measured.

A few caveats should be observed with regard to the variability of results to date. First, none of the above studies measured MPOD in their subjects. Second, increased filtration results in decreased luminance. It has been established that visual performance (e.g. resolution acuity) is related to brightness (König, 1897; Hecht, 1927; Wilcox, 1933). Third, in a quantitative report by Reading & Weale (1974) using known parameters related to CA and visual thresholds, it was predicted that an average amount of MP would be sufficient to reduce the violet penumbra of a white disc to subliminal levels. Additional levels of MP would be superfluous. That the findings of the above studies are mixed is not surprising when one considers these points. Assuming a normal variability of low to high MPOD in the collective subjects, those with low MPOD may be the ones exhibiting improvements, whereas additional filtration by sunglasses over-and-above the filtration already provided by mid or high MPOD may provide no additional benefit and may even impair vision by reducing light levels. Consequently, the aforementioned results are not necessarily in disagreement with the Acuity Hypothesis.

There may also be additional factors to consider. McLellan et al. (2002) argue that the various other ocular aberrations (mainly wavefront) tend to wash out the deleterious effects of chromatic aberration and, therefore, MP would not serve to improve acuity. The authors did not measure MP. Rather, they reached this conclusion by simply noting that when all of the ocular aberrations are considered together, they would have a general dampening effect on spatial vision. Although possibly true, and consistent with their data, their study in general was limited by several confounds. For example, McLellan et al. utilized a large (7 mm) pupil which would maximize the effects by other ocular defects (i.e., many aberrations arise from the edge of the lens normally covered by the iris). This is an unnatural situation. A more realistic pupil diameter that would apply to normal daylight vision is around 3mm. A pupil diameter of this size permits considerably less spherical and wavefront defects to be transmitted to the retina. It would also result in a smaller depth of field (approximately ±0.25 – 0.30 diopters; e.g. Campbell, 1957) with respect to the magnitude of effective chromatic aberration (> 1.0 D). Another issue complicating the interpretation of McLellan's (2002) result was the dosage used for the dilating agent, namely 0.5% tropicamide. It has been noted by Davies & Morland (2004) that this dosage was probably not sufficient to prevent accommodation despite the presence of an accommodation target in McLellan et al.'s study. Obviously, if subjects could focus on the individual wavelengths used during testing then the measured effects of CA would be reduced.

Other studies comparing visual performance in achromatic light to performance in narrow-band light have come to different conclusions. In a study conducted by Campbell & Gubisch (1967), for instance, contrast sensitivity was measured at 10, 15, 20, 25, 30 and 40 cycles/degree for two observers using broadband-achromatic and monochromatic (578nm) light. Campbell & Gubisch found slight improvements when using a moderate pupil size of 2.5mm, but no differences at pupil sizes of 1.5 and 4mm. Note that 2.5mm is a typical pupil diameter for normal daylight conditions. In a later study, Yoon & Williams (2002), also testing only two subjects, found that contrast sensitivity (2, 4, 8, 16, 24, and 32cycles/degree) measured when using narrow-band light was improved for both subjects by a factor of 1.2 – 1.5 for the higher frequencies beyond about 8cycles/degree.

Although these studies are relevant, they do not address the central predictions of the Acuity hypothesis. None of the above studies, for instance, have included the MP as a factor in their analyses. Since the MPOD of the observers in the studies by Campbell & Gubisch and Yoon & Williams are unknown it is not possible to attribute a lack of improvement at the low spatial frequency end of the CSF to a lack of influence of chromatic blurring for the same reasons as argued above. If the observer's MP levels are at least average, then according to Reading & Weale's modeling, no difference between the achromatic broadband and narrowband stimuli would be expected.

The proper way to test the Acuity Hypothesis is as follows: Acuity or CS thresholds must be obtained in both achromatic and short-wave deficient light. MPOD should be correlated to the thresholds obtained using achromatic light, but not to the thresholds obtained using short-wave deficient light. To this end, Engles et al (2007) tested the Acuity Hypothesis using resolution acuity, which was defined as the detection of a gap between two thin dark bars, and hyperacuity, which was defined as the minimum offset required to detect a misalignment between two thin dark bars separated by a small gap. It was shown, using rigorous psychophysical procedures (a 2AFC task) that the MP does not affect these forms of spatial vision, or in other words, that the relative insensitivity of the visual system to shortwave light is sufficient to maintain optimal visual performance. One shortcoming of the Engle's et al. study, however, is that only the highest spatial frequencies of the CSF were evaluated. Although no significant results were obtained at high spatial frequencies, it should not be ruled out that improvements related to MPOD will not be found for lower spatial frequencies.

To date, testing of the Acuity Hypothesis is insufficient. The study proposed herein will measure MPOD and measure CS in both broadband-achromatic and shortwave-deficient light using a specially constructed three-channel optical system that will allow assessment of the entire CSF.

Experiment 2: The Visibility Hypothesis

Wooten & Hammond (2002) have recently proposed a new hypothesis for the function of the MP. It has been termed the Visibility Hypothesis and unlike the Acuity Hypothesis, which directly addresses optical distortion caused by the eye itself, the Visibility Hypothesis addresses the optics of seeing outdoors. More specifically, it deals with the aspects of light scattering by the atmosphere.

To the knowledge of the experimenters, this study represents the first attempt to evaluate the Visibility Hypothesis. The suggestion that the use of yellow filters would improve vision in the outdoors, or in general, has, however, existed for some time. As indicated above, Clark (1969) has reviewed a large number of studies evaluating visual performance while wearing colored sunglasses. The results were mixed, with some studies reporting improvements and others not. Nevertheless, Clark concluded that visual performance was not improved by filtering out short-wave light. Wolffsohn et al (2000) also performed a similar review of 9 studies and derived the same conclusion. An important consideration, however, is that roughly half of the studies reviewed by Clark and Wolffsohn et al reported improvements. Furthermore, even in the studies that produced overall null results, some observers demonstrated increased visual performance.

It is likely that there are many reasons for the mixed results. One reason may be the optical configuration of the task. Studies that have evaluated visual performance in optical configurations that mimic seeing distant targets in the atmosphere have consistently reported positive effects. For example, in a study by Luria (1972) the increment threshold to a yellow target suspended within a blue background was measured with and without the presence of a yellow filter worn by the observer. With this optical configuration, the filter would selectively reduce the brightness of the blue background without attenuating the brightness of the target. As would be expected it was determined that the increment threshold for the yellow target was lower when the observers wore the yellow filter. These results are directly predictable based on results of studies testing increment thresholds on backgrounds of varying brightnesses (e.g. Pirenne, 1958; Cornsweet & Teller, 1965; Westheimer, 1967; Westheimer & Liang, 1994; see also Bartley, 1963 for an excellent review of some early but important works). If the luminance of the background is selectively reduced, then the visibility of the target is enhanced. Although this study may appear too specific, a yellow target suspended within a blue background, it is in fact directly analogous to the viewing conditions experienced when viewing distant targets through the atmosphere.

Expanding on this finding, Wolffsohn et al (2000) measured achromatic CS while in the presence of a blue (450nm) background in 10 subjects. Measurements were made at six spatial frequencies (0.5, 1.0, 2.0, 4.0, 8.0, and 16.0 cycles/degree). Significantly higher CS values were obtained when subjects wore yellow tinted filters compared to spectrally flat filters at 0.5 and 2 cycles/degree but not at others. Testing the Glare Hypothesis of MP, Stringham & Hammond (2007) measured the visibility of a grating (nearly 100% contrast) and MPOD in 36 healthy subjects (age range = 18 – 41yrs) using a broadband-achromatic xenon light source. With their optical configuration, the target grating was obscured by the veil of scattered light from a bright annulus. Visual thresholds in their experiment were strongly related to MPOD ($r = 0.76$, $p = 0.0001$). In the Stringham & Hammond study light was projected through the pupil of the subjects and the intensity of the annulus was varied. This induced forward intraocular scatter which had the effect of veiling the central target. When wavelengths were used that were absorbed by MP, the target was made more visible as a direct function of MP amount (MP filtered the veil allowing the visibility of the target to be maintained). In the case of glare, light enters the eye and hampers vision. Of course, scattering veils can also be passive and obscure targets. The mix of target with the obscuring veil still enters the eye and the veil itself, depending on wavelength, can be absorbed by MP to improve visibility of a target. Hence, the Glare hypothesis and the Visibility hypothesis make similar predictions (albeit working at different light levels). Consequently, the results of the Stringham & Hammond study should hold with equal or greater magnitude when testing the Visibility hypothesis.

Overall, we argue that among the studies evaluating visual performance using optical configurations mimicking the conditions of seeing in the outdoors the evidence to support the Visibility Hypothesis is markedly positive. The predictions would only matter, however, if it were indeed the case that our vision in the atmosphere is often veiled by short-wave scattered light.

Air can contain a large variety of constituents from very small molecules (Oxygen and Nitrogen), to much larger particles. These particles are collectively referred to as aerosols (McCartney, 1976). Haze of any kind is the result of light scattering off of the various particles that comprise the atmosphere, and therefore, light scattering is the largest determinant of visibility in the outdoors. The magnitude and wavelength dependency of the light scattering is strongly dependent upon the size of the scattering particles and their concentrations in the atmosphere.

Incidentally, the small molecules of the atmosphere preferentially scatter short-wave bluish light, thus the sky is blue and hence the term blue haze. It is easily observable that distant objects, such as the features of mountain sides, etc., have a distinctively bluish appearance because of this phenomenon. Furthermore, distant objects, when viewed directly, will become "yellowed" and will simultaneously be covered by a bluish veiling haze. This phenomenon is apparent at sunset when the atmospheric path length between the sun and the observer has increased and the sun becomes reddish in color.

The theory of the effect of atmospheric light scattering on visibility was initially developed by Kochsmeider (1924) and later by Duntley (1948) with updates and revisions by Middelton (1952). Later models have been devised that combine the known optical characteristics of the atmosphere (atmospheric modulation transfer function) with the known optical characteristics of the human eye (ocular modulation transfer function). For example, one such model devised by Kaufman (1981) is referred to as the combined eye-atmosphere visibility model. Using this model, Kaufman argues that the mid spatial frequencies will be the ones most heavily attenuated by the atmosphere, whereas high spatial frequencies will be primarily attenuated by the eye. Though it is useful, one feature lacking in Kaufman's eye-atmosphere visibility model is a consideration of the spectrally dependent filters found in the human eye, namely the MP. The theoretical treatment by Wooten & Hammond is similar to Kaufman's theory, however, Wooten & Hammond take into direct account the spectrally dependent effects of the MP.

The study described herein will test the Visibility Hypothesis by measuring MPOD and CS in short-wave deficient light and with the addition of a blue haze carefully chosen to mimic sky light in the same observers.

CHAPTER 2: MATERIALS AND METHODS

Subjects

Sixteen subjects (age range = 21 – 32yrs; male = 6) were tested. Two subjects were Indian, one was Chinese and the rest were of European descent. All subjects reported normal ocular health and one subject was a dichromat. Informed consent was obtained (IRB#: H2004-10037-1) from all subjects and the nature of the task was thoroughly explained prior to testing. Fourteen of the subjects were inexperienced psychophysical observers and were naïve to the purpose of the experiment. All subjects were treated ethically and briefed prior to and following experimentation in compliance with the Tenets of the Declaration of Helsinki.

Apparatuses

The apparatus used to measure contrast sensitivity consisted of a three-channel optical system. See Figure 1 for a diagram of the system. A 1000-W xenon arc bulb served as the light source. Light from the bulb was routed through the three channels and re-integrated via a system of beam-splitters at the opposite end. Channel 1 provided a uniform circular field of light. Light in Channel 2 directly illuminated the test grating. The light from these two channels was integrated at beam-splitter 1 and could be independently regulated by a series of neutral density filters and wedges (reflection type). Consequently, the contrast of the grating, as seen by the subject, can be manipulated by varying the amount of light that back-illuminated the grating contrapositively with the amount of light that comprised the diffusing channel. In other words, the two channels were counterbalanced such that a range of contrasts from 0.0 to the maximum inherent contrast of the grating could be produced while maintaining a constant luminance.

Light from Channel 3 was passed through a chromatic filter (Schott glass Filter #BG34, UQG Optics Ltd., Barrington, NJ), which in conjunction with the spectral output of the xenon arc lamp very nearly reproduced the blue haze spectrum of sky light. See Figure 2 for a diagram of the blue haze spectrum used in this study. To simulate the “yellowing” of distant targets, two additional chromatic filters (long filter #2, Edmond Optics, Barrington, NJ) were placed in Channels 1 and 2. Light from Channel 3 was integrated at beam-splitter 2 with the light from Channels 1 and 2. A timed electronic shutter (Uniblitz AOX5; Vincent Associates, Rochester, NY) provided regulated exposure durations of 3 sec. Opening of the shutter was controlled by the experimenter. Care was taken to maintain a constant inter-stimulus interval.

The apparatus used to measure macular pigment consisted of a Macular Metrics Densitometer (Providence, RI). This devise uses heterochromatic flicker photometry to estimate macular pigment optical density and is described in detail and validated in Wooten et al, 1999.

Stimulus

The target used to measure CS in the achromatic (ACH) condition was produced by using non-chromatically filtered xenon light in both Channels 1 and 2. To produce the short-wave deficient (SWD) condition, a glass chromatic filter (Corning 51300; Oriel, Stanford, CT) was inserted into the beam after the light from Channels 1 and 2 had been integrated. Light from Channel 3 was blocked during these two conditions. To produce the blue haze condition, Channel 3 was opened and chromatic filters (long filter #2, Edmond Optics, Barrington, NJ) were added to each channel.

CS in each condition was measured at 6 different spatial frequencies, specifically 2, 4, 8, 15, 22, and 43cycles/degree, thus allowing a nearly complete CSF to be measured. The stimulus was a circular target 0.5º in diameter. Subjects sat 4.35m from the target when measured at 4, 8, 15 and 43cycles/degree, and were moved to 2.2m from the target when measured at 2 and 22cycles/degree. A small aperture was placed over the target when subjects were nearer in order to maintain a constant target size of 0.5º.

The stimulus used to measure macular pigment is described in detail elsewhere (see: Wooten et al, 1999), however a brief description is as follows. Test stimulus was always a circular target (15-min, 30-min or 2-deg) superimposed onto and presented in the center of a 6°, 2.75-cd/mm^2, 470-nm circular background. The test stimulus was composed of a 458-nm measuring field (peak MP absorbance) alternating with a 570-nm, 3.0-cd/mm^2 reference field (no MP absorbance). Light for the measuring and reference fields and the background was produced by 20-nm half-bandpass LEDs (Nichia Corp., Mountville, PA). The radiance of the LEDs was controlled by constant-current, high-frequency electronic pulses. Measuring and reference fields were superposed and presented out of phase at an approximate alternation rate of 12 to 20 Hz in the foveal condition and 8 to 10 Hz in the parafoveal condition. This alternation rate was carefully optimized for each subject to create a narrow (e.g., equivalent to approximately 0.10 OD) null zone. Once optimized, subjects adjusted the radiance of the 458-nm measuring field (which was counterbalanced with the 570-nm reference to maintain constant luminance) until the perceived flicker was extinguished. This measurement was made in the fovea (where MP is most dense) and 7° in the parafovea (where light absorption by MP is negligible).

Calibration

Individual gratings were calibrated in the following way: Each grating was placed in Channel 2 of the optical system and the other channels were blocked. All filters were removed from the optical system and the wedges were set to their most transparent points to maximize light output. The two beam-splitters were removed and a radiometric detector with a pin-hole aperture (1mm diameter) was placed approximately 1mm from the final diffuser in Channel 2. The radiometric detector was mounted on an adjustable slide that was driven by a screw. This allowed the detector to be adjusted precisely. Minimum and maximum light intensity points were sought and recorded. After each minimum or maximum was recorded, the grating was removed and the unimpeded light intensity was recorded. This process was repeated 5 times for each grating.

Maximum inherent contrast, or inherent modulation, for each grating was calculated using the following formula:

$$M = \frac{T_{max} - T_{min}}{T_{max} + T_{min}},$$

where M is the percent inherent modulation of the grating, T_{max} is maximum transparency point of the grating, and T_{min} is the minimum transparency point of the grating.

The optical system used was calibrated daily prior to use. During calibration a radiometric detector with a diffuser was placed at the end of the optical system after the beam-splitters and all other sources of illumination were blocked. Each channel was active independently during calibration. A series of neutral density filters were added and wedges were adjusted in order to regulate the amount of light exiting the system. Random checks confirmed that light levels were remained constant during testing. To calibrate the system for the SWD condition, the corning filter was inserted in its testing location in front of the photodetector. Light levels in the SWD condition were calibrated to be the same luminance as the ACH condition. Calibrating the system for the blue haze condition was similar. The long filter #2 filters were added to channels 1 and 2 and the corning filter was removed. EACH channel was calibrated according to the above procedure.

Procedure

Subjects sat in a dark room separated from the room containing the optical system by a door with a hole cut through it (1.78º diameter). The electronic shutter covered the hole. When opened, the shutter made an audible click, which alerted the subject to view the target. The shutter remained open for 3sec.

A box mounted on a small cart containing an internally regulated light source served to maintain each subject's adaptive state. A head and chin rest assembly was mounted to the front of the cart. Subjects were asked to view the grating stimulus with their right eye only through an eye-piece mounted to the box with their chin placed comfortably in the chin rest. The far wall of the box had an aperture (4º diameter), through which, subjects viewed the target. Between judgments subjects were asked to fixate a small cross located on the far wall 5.5º below the center of the distal aperture. The inside of the light box was painted matte white and had an internal light source (24" warm white fluorescent bulb) to maintain a constant luminance of 90cd/m^2. Altogether, the subject's adaptive state was maintained at a constant level throughout the experiment.

Subjects were evaluated using a two-alternative forced choice staircase method. The initial trial sequence (10 consecutive presentations of the target at a given spatial frequency) began at a clearly visible level to allow the subject to adapt to and learn the task. After the subject had become comfortable with the task the contrast of the grating was dropped to 0.0 and incrementally increased (average minimum step size = 0.00015 contrast units; typical step size = 0.001) until at least 90% of the presentations were correctly identified for two consecutive experimental sets (set size = 10 consecutive trials). By starting at a low contrast level and progressively increasing the contrast, adaptation was avoided. This task was repeated until all spatial frequencies were assessed. On each trial the target grating was tilted clockwise or counter-clockwise 11.5º, and the orientation was chosen randomly. The task required the subject to identify the orientation of the grating (e.g. "left" or "right"). Feed-back was not provided. Following a total of 40 to 60 trials, a cumulative percent-correct for each contrast level was calculated.

Psychometric functions were generated using the graphing software Origins 7.0. The cumulative percent-correct value at each presented contrast setting for a given subject on a given grating was entered into a table and a best-fit psychometric function was rendered (Upper and lower bounds were 100% and 50% respectively; see Figure 3 for an example of a typical psychometric function). Thresholds were taken as the value that corresponded to the 75% correct point on the curve. In cases where multiple measures were made at the same spatial frequency in the same condition and in the same subject averages were used for the purpose of analysis.

Macular pigment was measured in the right eye only and on multiple days. The average MPOD was used for the purpose of statistical analysis. Judgments consisted of the subject viewing a small fixation spot at the center of the test stimulus and freely adjusting a dial until flicker was no longer perceived. Measurements were made in the fovea at 15' (30-min diameter target) and 30’ (1-deg diameter target) eccentricity, where MP absorption is highest, and one reference field in the parafovea at 7º (2-deg diameter target), where light absorption by MP is negligible. The difference between each foveal measure and the parafoveal measure provides an estimate of the optical density of the MP. Nine consecutive judgments were made for each of the three test stimuli.

CHAPTER 3: RESULTS

General Findings

Sixteen subjects were tested in this study. Granger & Cupury (1972) proposed a straight forward index of spatial processing ability that we used to characterize our overall CSF. These authors suggested that the area under the CSF could provide an overall summary for how well the visual system responds to the variety of spatial signals encountered in our visual environment. In our application, the "integrated spatial sensitivity" index, or total area under the curve (AUC), was calculated for each CSF and used as the dependent measure in all statistical tests. A summary of the descriptive statistics for the acuity experiment can be found in Table 1. A summary of the descriptive statistics for the visibility study can be found in Table 2. As can be seen in the Tables the measures varied widely across subjects in both studies. For example, MPOD ranged from 0.15 to 0.96 across all subjects representing the full spectrum from low to high values, and AUC for each condition varied by a factor of about 4.5 - 6.

Figure 4 is a plot of the average CSFs for the SWD (not absorbed by MP) and ACH (absorbed by MP) conditions. It is easily observable that the two curves are nearly identical. A Student's T-test confirms that the AUC averages for both conditions are not significantly different ($t(27) = -0.635$, $p > 0.05$). Since the SWD condition was common to both hypotheses, all 16 subjects were included in this initial comparison. According to the Acuity Hypothesis, MPOD should not be correlated to CS in short-wave deficient light (since the stimulus is not filtered by MP in this condition). As predicted and shown in Figure 5, MPOD is not correlated to CS in the SWD condition ($N = 16$; $r = -0.027$, $p > 0.05$). In contrast, the Acuity Hypothesis predicts that CS in the achromatic (white) condition should be proportional to one's MPOD (because this stimulus is absorbed by the pigments). The results (Figure 6), however, indicate that MPOD is not correlated to CS in the ACH condition ($N = 13$; $r = 0.0145$, $p > 0.05$). Taken together, the nearly identical curves, one filtered and one not filtered by MP, argues strongly that MP absorption does not influence either condition and that the effects of chromatic aberration does not influence task performance. Figure 7 is a plot of the average CSFs for the SWD and blue haze conditions (SWD, again, not being absorbed by MP, whereas MP does influence the blue haze, BH condition). Normalizing both functions to their peak and plotting them as an overlay demonstrates that the overall shape of the two functions is the same. The Visibility Hypothesis predicts that CS viewed through blue haze should be proportional to one's MPOD. In other words, one's CS in the BH condition should approach one's CS in the SWD condition with increasing MPOD. However, the results (Figure 8) indicates that MPOD is not correlated to CS in the BH condition ($N = 12$; $r = 0.181$, $p > 0.05$). This result, when all of the raw data is considered together, did not support the predictions of the Visibility hypothesis.

A closer examination of Figure 8, however, is revealing. The regression line appears to bisect the data with one group above and one group significantly below. Indeed, when the individual CSFs are considered independently, the sample was clearly not normal but rather decidedly bimodal. For example, the CSF of five subjects (measured under the three conditions) appeared to be significantly suppressed (SWD: $N = 5$, $t(14) = -4.06$, $p < 0.01$; ACH: $N = 3$, $t(11) = -3.11$, $p < 0.01$; BH: $N = 4$, $t(10) = -4.25$, $p < 0.01$). When only these subjects with the suppressed functions are analyzed, the relation to MP is improved but still not significant (probably due to floor effects and the small sample size). In contrast, when only the data from the top eight subjects were analyzed (these subjects presumably having normal CSFs), MPOD was very highly correlated to CS in the BH condition ($N = 8$; $r = 0.903$, $p < 0.01$). See Figures 9-11.

Reliability Testing

To determine the reliability of the CS optical apparatus, 5 subjects underwent repeated testing. A correlation between first and second session CS using a perfectly reliable system should have a slope of 1.0 and an intercept of 0.0. A linear regression indicates that this is nearly the case (slope = 0.98, intercept = 10.04, $r = 0.963$, $p < 0.0001$), indicating that CSFs measured using our apparatus were highly reproducible.

CHAPTER 4: DISCUSSION

Overview

The goal of the above study was to test the Acuity and Visibility Hypotheses of the MP. Both were tested using a specially constructed apparatus with optimal optical arrangements and using a rigorous criterion-free psychophysical procedure. The results of Experiment 1 confirm the earlier findings by Engles et al (2007), in that, no significant relation between MPOD and the AUC-Ach CSF was found. The present data, when considered with the earlier study, modeling data, and ancillary evidence (e.g., McLellan et al., 2002), suggest that the Acuity hypothesis, while widely cited, is simply not valid. Our evaluation of the Visibility hypothesis, however, leads to a different conclusion. For subjects with normal CSF (eight subjects in our sample), MP appears to be very strongly related to improvements in the contrast sensitivity function under realistic conditions of blue haze. This effect was clearly specific to those stimuli affected by MP absorption. When testing grating stimuli that did not contain short-wave light and was therefore not influence by MP filtering, no relation was found.

Experiment 1: The Acuity Hypothesis

The human eye exhibits a significant amount of CA resulting in a severe blurring of short-wave light (approximately -1.2 D at 460nm). The Acuity Hypothesis, as originally proposed by Schültze in 1866, predicts that visual acuity (and CS) will be improved by the MP. This is because the MP absorbs short-wave light, and thus reduces the amount of optical distortion present in the retinal image. This hypothesis was tested by measuring the CSF from 2 to 43 cycles/degree in both broadband-achromatic light (subject to CA and filtration by the MP) and in short-wave deficient light (significantly less CA and no filtration by the MP). As can been seen in Figures 12 and 13, the results of this study do not support the predictions of the Acuity Hypothesis. No relation between MPOD and CS in the ACH condition was identified.

These results support the earlier findings of Engles et al (2007) who also used young healthy subjects similar to our own, an optimal optical arrangement, and a rigorous psychophysical procedure. As argued by Engles et al (2007), a null finding is not surprising. For example, Bradley & Fry (1991) modeled the effects of CA on the modulation transfer function (MTF) of the human eye and concluded that the resulting distortion would be small. Consequently, the expected effects due to absorption by the MP would be correspondingly small. Engles et al performed an analysis similar to that of Bradley & Fry on the spectral conditions used in their experiment. In agreement with Bradley & Fry's conclusions, it was determined that very little improvement in spatial vision due to MP would expected.

Our results would seem to be in apparent contradiction with other works aiming to evaluate spatial vision performance after CA and other higher-order aberrations have been removed. For instance, Liang & Williams (1997) corrected the higher-order monochromatic aberrations in their observers and found a 6-fold improvement in visual performance measured at 27.5cycles/degree with a 6mm pupil. Yoon & Williams (2002) also demonstrated substantial improvements after CA and other higher-order aberrations had been removed. Furthermore, their theoretical treatment predicts a 20-fold improvement in CS at 32cycles/degree if CA and most monochromatic aberrations could be corrected. That our results are in disagreement is most likely due to differences in pupil size. The average pupil size of our subjects was 2.5mm. The average pupil size of the subjects used in the above studies was 4.5-6mm. A large pupil permits a considerable amount of optical distortion due to higher-order aberrations to be transmitted to the retina. Consequently, it is not surprising that correcting them would improve vision, since having a smaller pupil nearly serves this function by minimized their influence. Our results indicate that when under normal viewing conditions with a typical pupil size the MP does not convey any additional improvement in achromatic contrast sensitivity.

To be certain that our null results are not due to noise, a test of the apparatus's reliability was conducted. It was determined that the reliability of our measure is quite high. Furthermore, our average CSFs did not differ from those reported in the literature using approximately the same luminance levels and stimulus sizes (Campbell & Gubisch, 1966). Consequently, we argue that our measure of CS is both reliable and valid.

Of course, our optical configuration and subject restrictions (only young subjects were admitted) limited our evaluation to apply only to the *optical* benefit that can be provided by the MP. Our results do not indicate that the MP cannot convey improved visual performance via a biological effect. For example, Richer et al (2004) conducted a double-blind placebo controlled study using 56 older subjects with age-related macular degeneration. After 12 months of supplementation with 10mg lutein or 10mg lutein + antioxidant, subjects' improved their acuity by 5.4 and 3.5 letters, respectively, on the Snellen letter chart. Subjects that received the placebo did not demonstrate improvements in visual performance. The findings by Richer et al are in agreement with an older but similar study conducted by Olmedilla et al (2003). Olmedilla et al asked cataract patients to regularly consume 15mg lutein 3 times a week for 2 years. It was shown that the visual performance of these subjects, as measured by a Snellen letter chart, improved relative to a placebo group. Lastly, in a recent double-masked placebo controlled study by Bartlet & Eperjesi (2008), 21 healthy subjects (age range = 22 – 73yrs; mean age =

50.1yrs ±15.1yrs) were given a 6mg lutein (plus additional vitamins and minerals) supplement for 9 months. Fifteen of these subjects continued to take the supplement for an additional 9 months. Bartlet & Eperjesi's measures included visual acuity and CS tested in white light conditions. No improvements in visual performance relative to the placebo groups were observed for either of the supplementation periods in any of their measures. Of course, once again, these authors did not measure MP so it is difficult to evaluate their findings (e.g., some subjects do not have increases in MP due to supplementation). Overall, however, improvements in visual acuity due to L supplementation or when related to MP increases appear to be specific to elderly or diseased subjects suggesting that the effect is biological and palliative. When young subjects are used with stimuli carefully characterized to test the predictions of the Acuity hypothesis (e.g., Engles et al., 2007), no relation is found.

Experiment 2: The Visibility Hypothesis

Atmospheric light scattering places limitations on visibility over great distances by reducing the contrast between the target and the background on which it is viewed. The small particles of the atmosphere preferentially scatter short-wave light, and so, the sky and distant targets are tinged blue. This bluish veil is termed Blue Haze. Wooten & Hammond (2002) argue that the natural short-wave filters of the human eye (e.g. the MP) will improve visibility by reducing the optical contribution of the background (blue haze) without significantly affecting the target. Consequently, CS measured in the presence of Blue Haze should be proportional to one's MPOD. To test this hypothesis, CSFs were measured from 2 to 43 cycles/degree in short-wave deficient light (no attenuation by the MP) and in the presence of simulated blue haze (attenuated by the MP). As can be seen in Figure 14, the results of this experiment for eight normal subjects (see the points raised later) strongly support the predictions of the Visibility Hypothesis.

This is the first known experiment to directly test the Visibility Hypothesis. Several studies, however, have evaluated visual performance in optically comparable configurations. For example, in the study by Luria (1972), the detectability of a yellow target on a blue background was evaluated with and without the addition of a yellow filter. With this optical configuration, the filter reduced the brightness of the blue background without significantly attenuating the brightness of the target. Luria's findings are directly predictable based on results of studies testing increment thresholds on backgrounds of varying brightnesses. As the background brightness is reduced, the target is just visible at a correspondingly reduced brightness. Wolffsohn et al (2000) measured achromatic CS while in the presence of a blue (450nm) background in 10 subjects. Measurements were made at six spatial frequencies (0.5, 1.0, 2.0, 4.0, 8.0, and 16.0 cycles/degree). Significantly higher CS values were obtained when subjects wore yellow tinted filters compared to spectrally flat filters at 0.5 and 2 cycles/degree. In a more recent related study, Stringham & Hammond (2007) measured the visibility of a grating (nearly 100% contrast) and MPOD in 36 healthy subjects (age range = 18 – 41yrs) using a broadband-achromatic xenon light source. Visual thresholds in their glare condition were strongly related to MPOD ($r = 0.76$, $p = 0.0001$). In a follow-up to that study, Stringham & Hammond (2008) supplemented 40 subjects with 12 mg of L and Z and measured changed in glare disability and MP that resulted. They found that this intervention directly reduced glare disability as a function of an individuals increase in MP density. As noted, their study is somewhat analogous to this study except using stimuli that were less ecologically valid (stimuli are normally never viewed, for example, in Maxwellian, i.e., projective, view). Taken together, however, the evidence that

MP can improve stimuli optically by reducing the interference of veiling short-wave light is accumulating. The data in the present study support this conclusion as well.

Future Directions

Perhaps the most unexpected result of our study was the fact that the CSF of our subjects was so clearly bimodal. A significant number of our sample (5 out of 16), although exhibiting normal Snellen acuity, had significantly suppressed contrast sensitivity. Our results indicate that much of the suppression in the CSF is in the mid-spatial frequency range. Subjects with normal visual acuity, like all of our sample, can exhibit suppressed mid-frequencies (Thomas, 1978; Zele et al, 2007). Consequently, screening subjects using best corrected visual acuity as the criteria, as was done here, was clearly inadequate. A somewhat exhaustive search of the literature did not reveal similar patterns in other larger CSF studies. A direct comparison with such studies is difficult, however. Often the CSF is measured using a wall-chart (e.g., in clinical settings) or a computer monitor. This allows a relatively rapid assessment of the CSF but, doubtless one with increased measurement error (an effect that would smooth out the distribution). In contrast, our CSF was measured using light that simulated sunlight (xenon-generated broad-band white) and, for some conditions, was filtered using specialized interference filters. This created a much more ecologically valid stimulus (a necessary condition given that we were testing, essentially, an ecologically-based visual hypothesis). Moreover, our psychophysical procedure was exceptionally involved (two-alternative forced choice) which required long and extensive testing (e.g., about 20 hours for each curve for each subject). Given the extreme difficulty in both setting up the optical system and testing the subjects, most analogous studies have only been done on very small samples (one or two subjects, usually the authors who tend to have good vision). Lastly, it is general practice to normalize each individual's CSF, a process that obviously obliterates individual differences in absolute sensitivity. It is difficult to say then just how commonly CSF curves are suppressed, when obtained under ecologically valid conditions.

We do know that CSF curves can be suppressed for a variety of reasons. For example, subtle refractive errors during development can create lasting amblyopic defects in the CSF of normal subjects (Thomas, 1978; Trobe et al, 1996; Hiraoka et al, 2007; Zele et al, 2007). Such subject refractive errors, particularly at the corneal level (e.g., astigmatic) can be relatively common and can even begin later in life and at that time suppress the CSF. Key studies (e.g., Thomas, 1978) have identified CS deficits in amblyopes between 2 and 15 cycles/degree, which agree with our findings (Figures 9-11).

The strong positive relation between MPOD and CS in the blue haze condition for the bulk of our sample suggests that visibility can be enhanced by increasing one's MPOD. It would be useful to expand the size of our current cross-sectional study in order to determine whether MP leads to improvements even for subjects with suppressed CSF. It could also be helpful to do an intervention. Past studies have already established that it is possible to increase one's MPOD via dietary modification or supplementation (Hammond et al, 1997; Landrum et al, 1997; Olmedilla et al, 2003; Richer et al, 2004). Consequently future studies should be directed toward establishing a stronger argument for a causal relation between MPOD and CS in the presence of blue haze by measuring their CS before and after supplementation.

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Table 1. Descriptive statistics for Experiment 1

	N	Minimum	Maximum	Mean	SD
ACH	13	2607.12	13835.47	7291.70	3166.75
SWD	16	2887.36	13277.99	8032.15	3090.21
MPOD	13	0.24	0.90	0.50	0.20

Table 2. Descriptive statistics for Experiment 2

	N	Minimum	Maximum	Mean	SD
BH	12	966.08	5929.17	4024.54	1420.67
SWD	16	2887.36	13277.99	8032.15	3090.21
MPOD	12	0.15	0.96	0.49	0.27

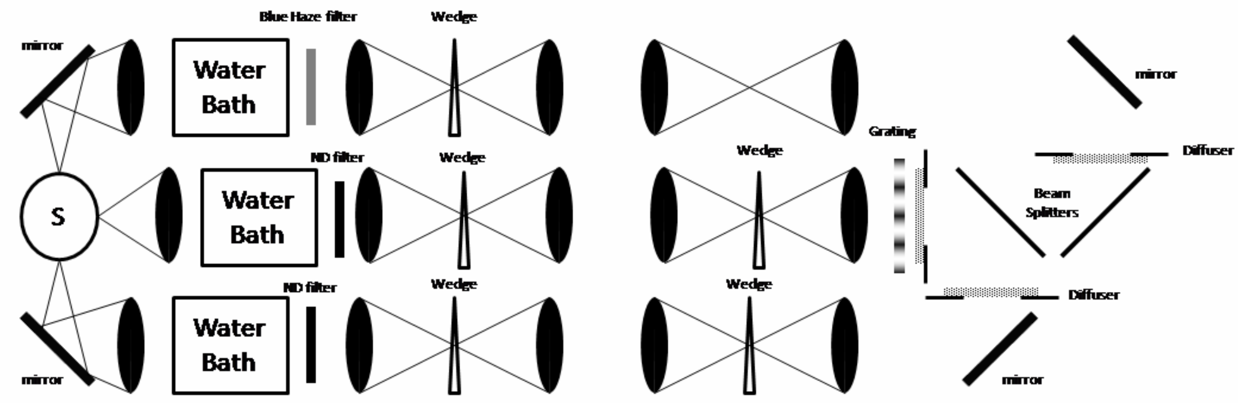

Figure 1. A diagram of the optical system used in this experiment. Channels 1 and 2 (lower and middle respectively) were used in all three conditions, however, Channel 3 (upper) was only active during the visibility experiment.

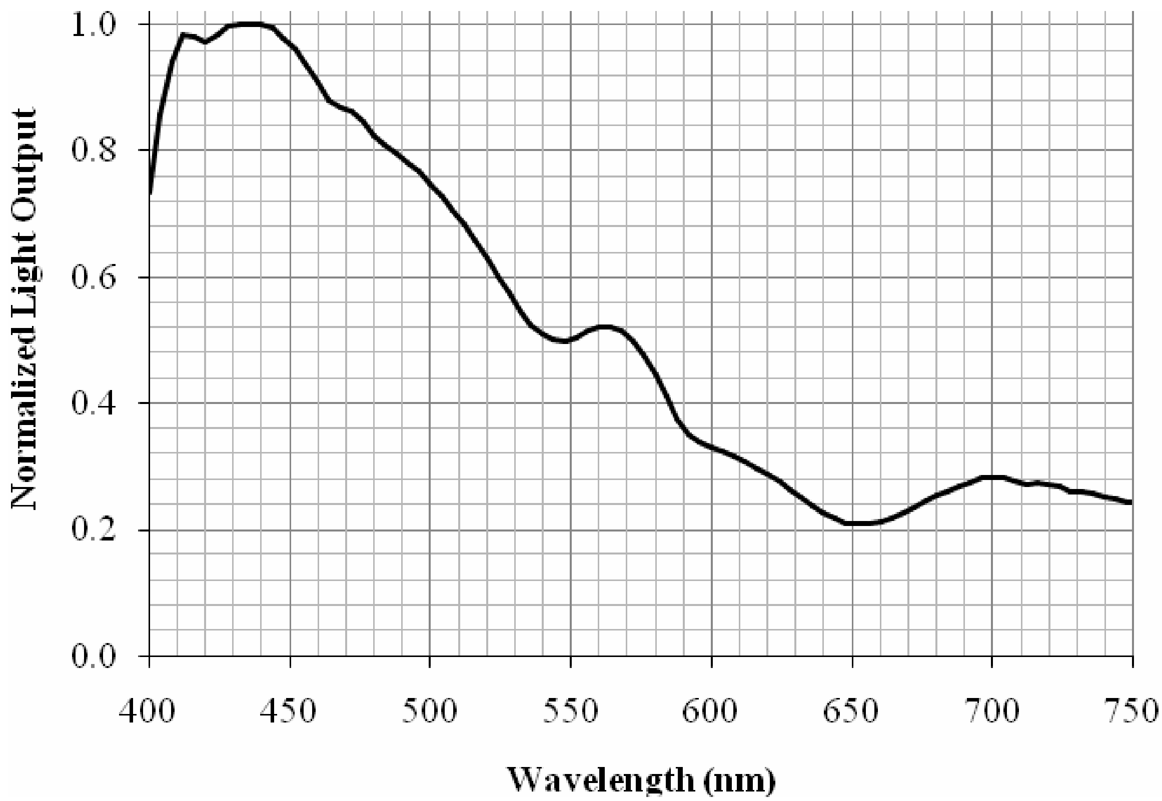

Figure 2. The normalized spectral content of the simulated blue haze used in the visibility experiment.

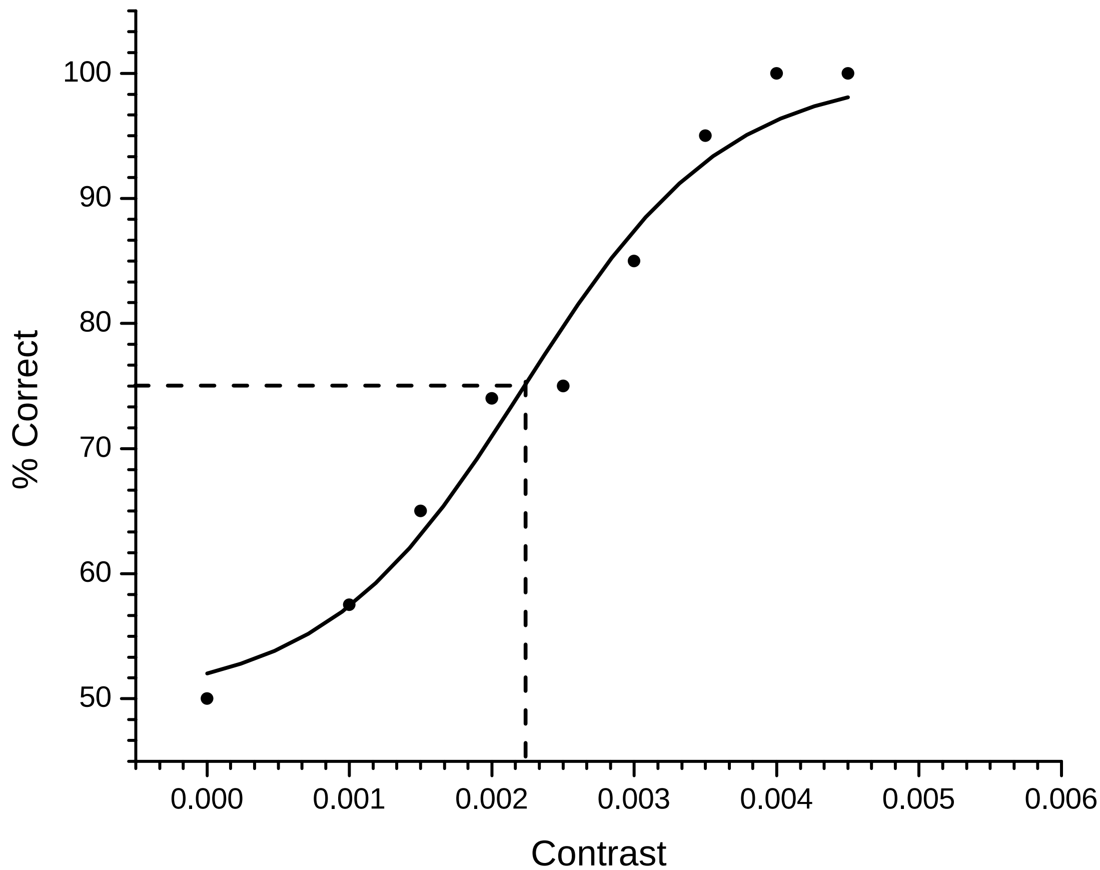

Figure 3. Typical psychometric function. Thresholds (75%) were derived mathematically from the best-fit curve.

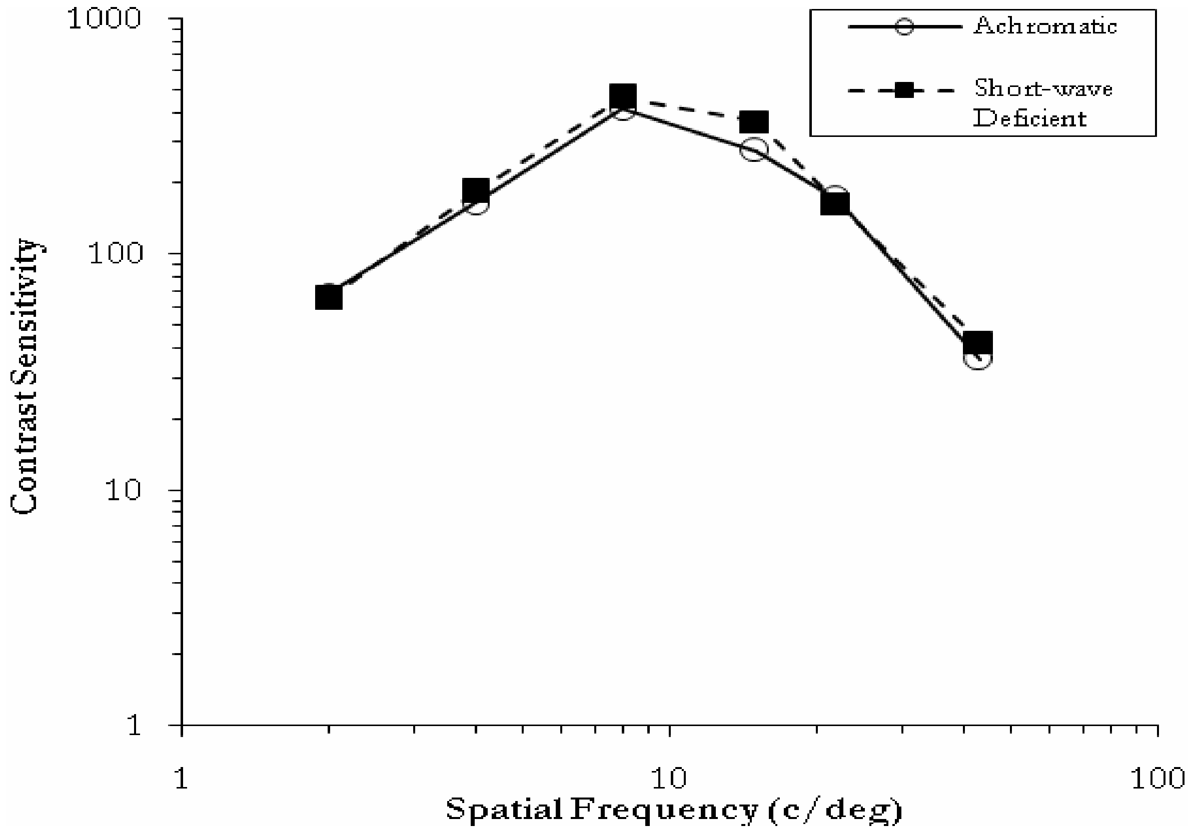

Figure 4. Overlay of the absolute achromatic and short-wave deficient contrast sensitivity functions. Note the near perfect correspondance between the two curves.

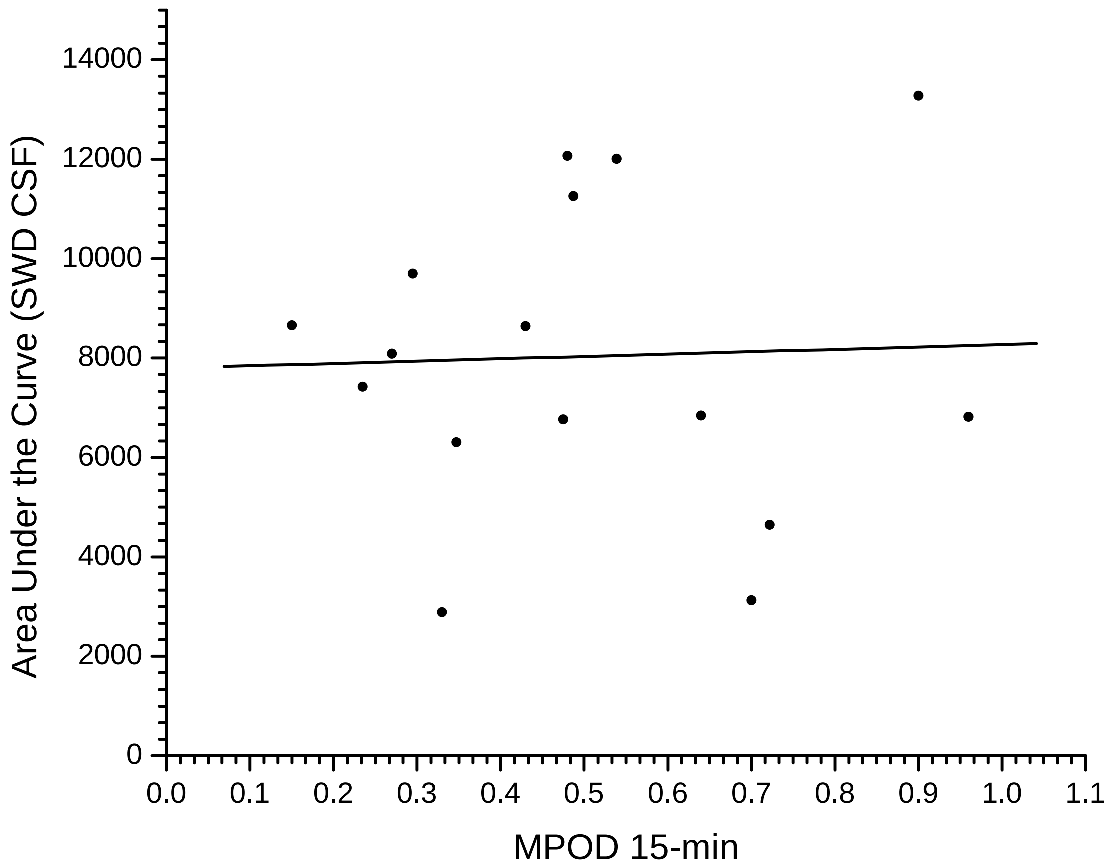

Figure 5. Relation between MPOD measured at 15-min eccentricity and CS measured in the SWD condition ($r = -0.027$, $p > 0.05$).

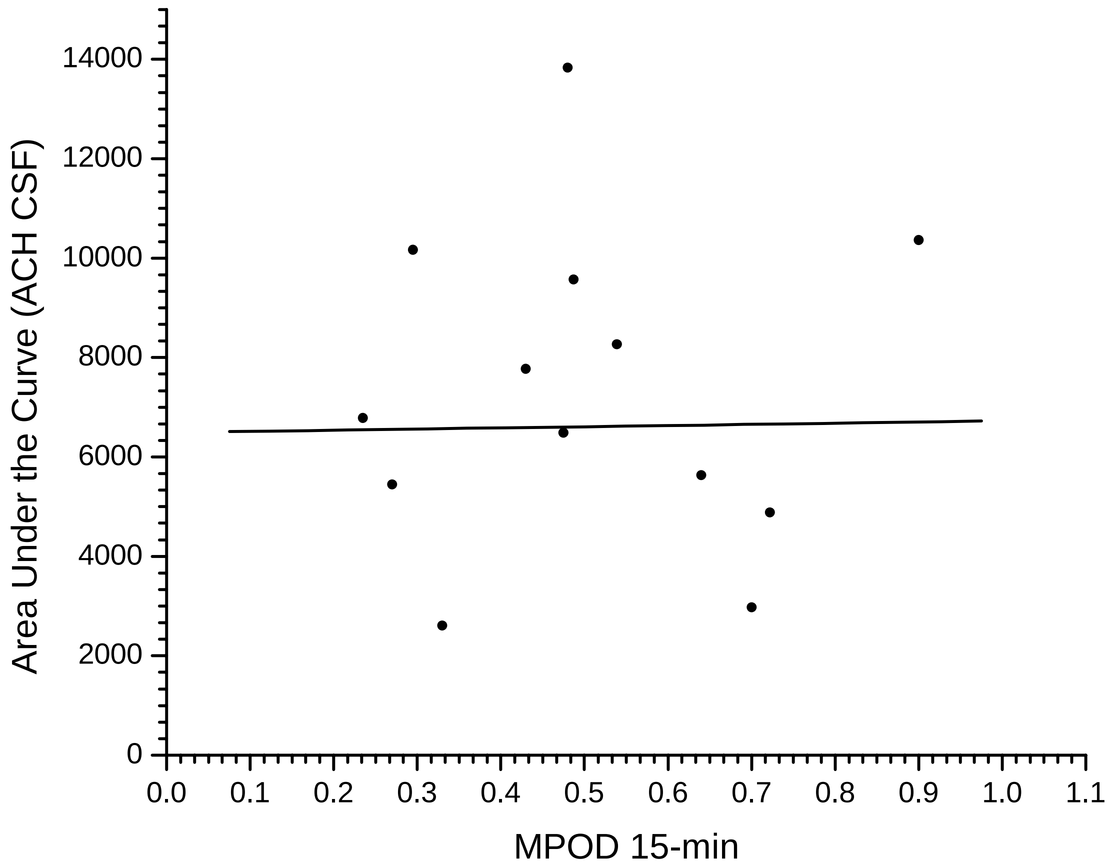

Figure 6. Relation between MPOD measured at 15-min eccentricity and CS measured in the ACH condition ($r = 0.015$, $p > 0.05$).

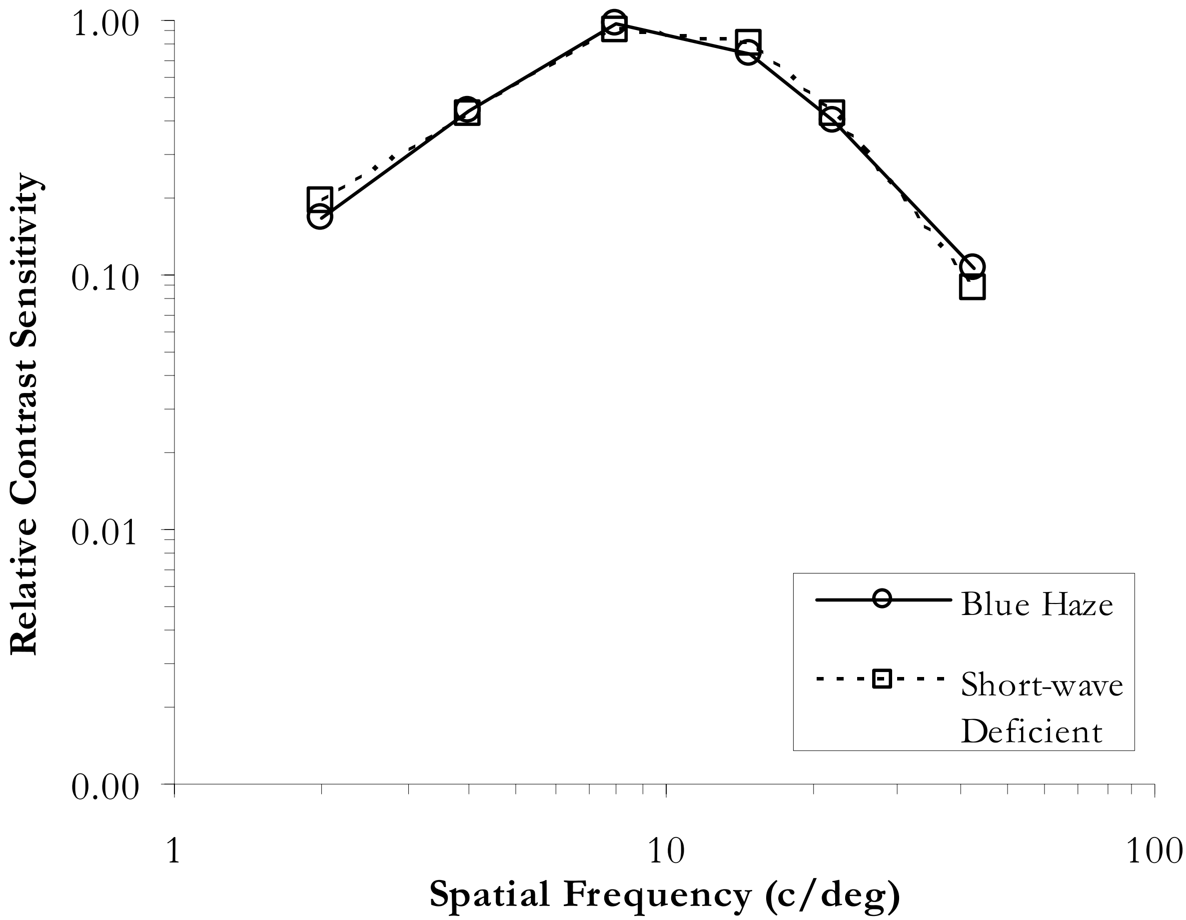

Figure 7. Overlay of the normalized blue haze and short-wave deficient contrast sensitivity functions. Note the near perfect correspondance between the two curves.

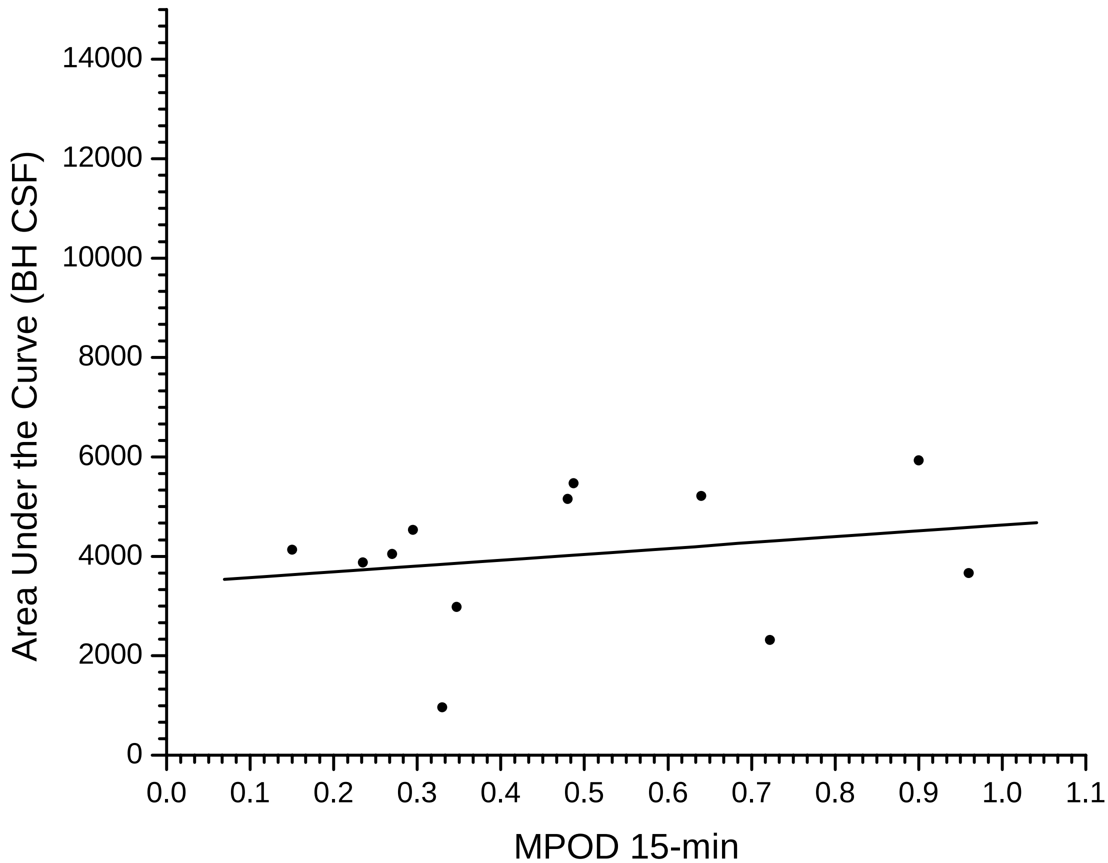

Figure 8. Relation between MPOD measured at 15-min eccentricity and CS measured in the BH condition ($r = 0.181$, $p > 0.05$).

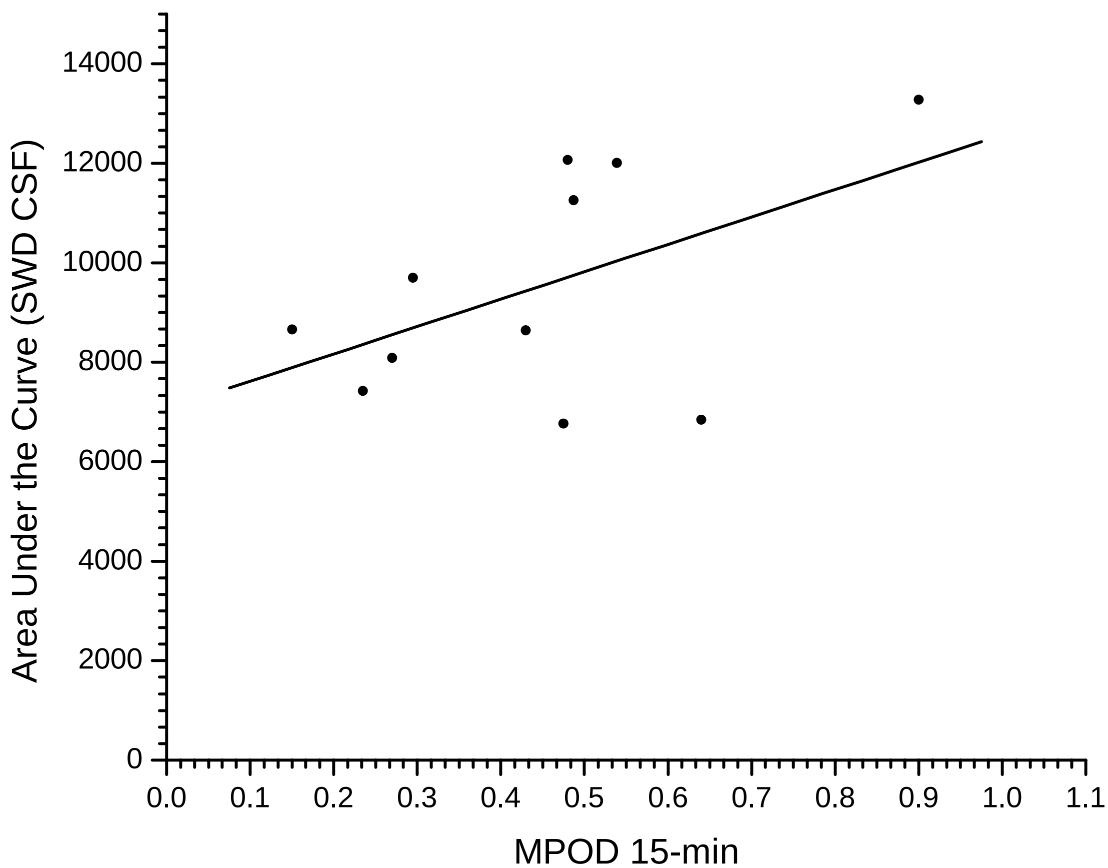

Figure 9. Relation between MPOD measured at 15-min eccentricity and CS measured in the SWD condition ($r = 0.440$, $p > 0.05$).

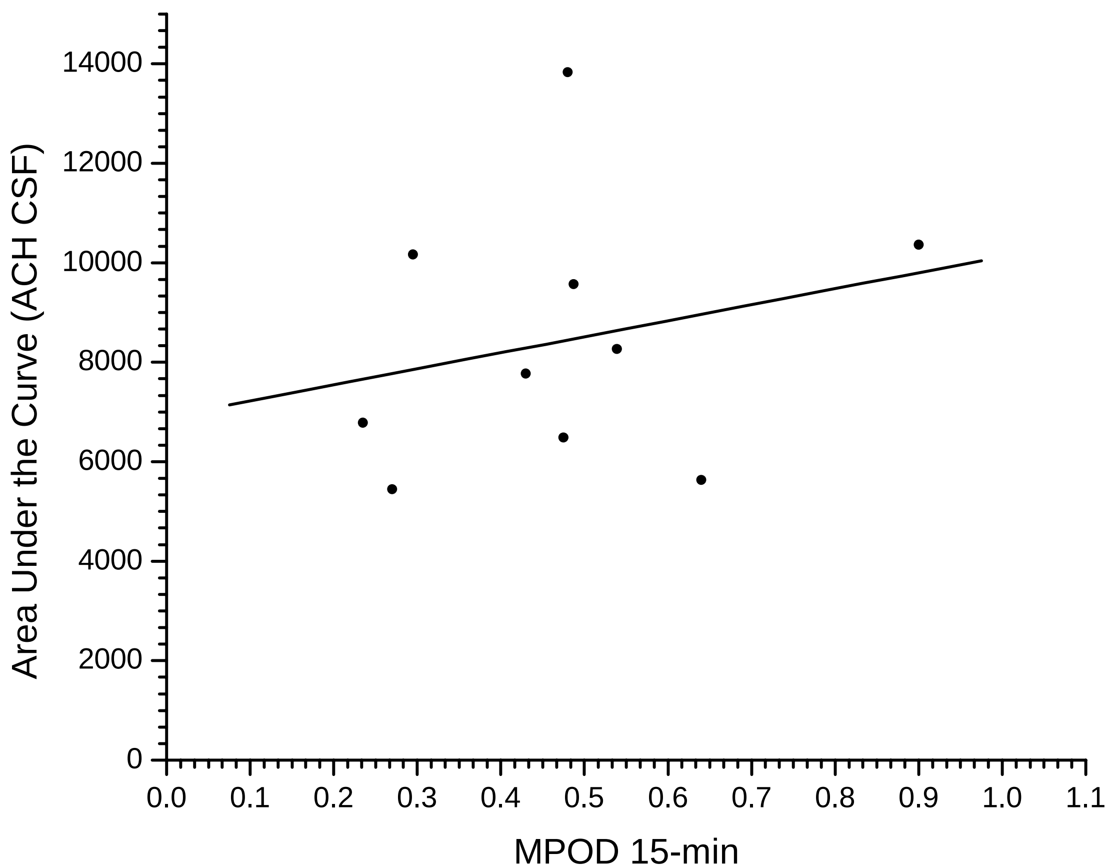

Figure 10. Relation between MPOD measured at 15-min eccentricity and CS measured in the ACH condition ($r = 0.258$, $p > 0.05$).

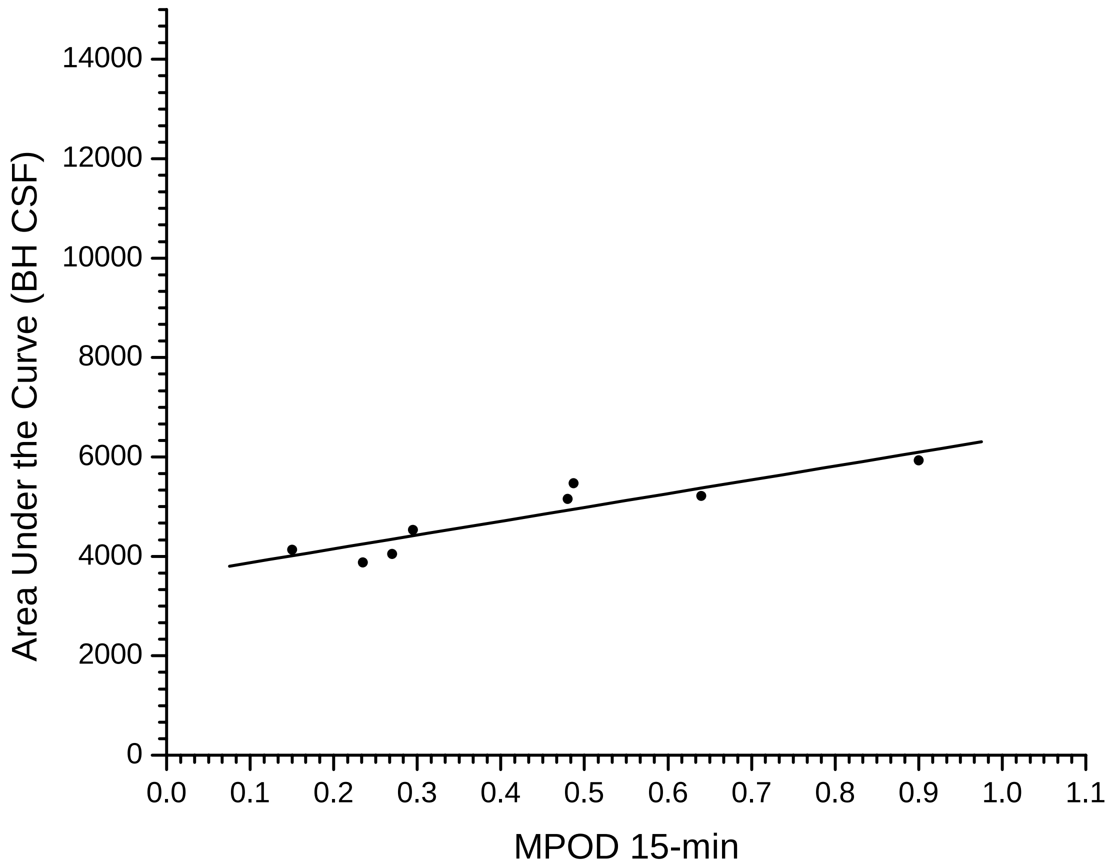

Figure 10. Relation between MPOD measured at 15-min eccentricity and CS measured in the BH condition ($r = 0.903$, $p < 0.01$).