TEMPORAL VISUAL MECHANISMS MAY MEDIATE COMPENSATION FOR MACULAR PIGMENT

by

NICOLE TRESSA STRINGHAM

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

ABSTRACT

Macular pigment (MP) is a pre-receptoral filter that is diet-derived and deposited in relatively high optical density in the foveal region of the retina. Due to its yellow coloration, MP absorbs short-wavelengths from 400-520 nm (which appear blue). Despite the spectral and spatial non-uniformity imposed upon the sensory retina by MP, perception appears to be uniform across the visual field. MP therefore offers an opportunity to determine experimentally potential mechanisms responsible for mediating this uniformity. After assessing, in 14 subjects, MP’s effects on the temporal sensitivity of both the short-wavelength- and middle / long-wavelength-sensitive visual pathways, it appears that the visual system compensates for absorption of short-wavelength light by MP by slowing short-wavelength-cone signals, and by increasing the processing speed of middle- / long-wavelength-sensitive cones. This mechanism could work via temporal summation or a temporal neural code, whereby slower response dynamics would amplify relatively weak signals.

INDEX WORDS: Color vision, Temporal processing, Compensation, Macular pigment
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CHAPTER 1
INTRODUCTION

Our conscious visual experience involves the precise amalgamation of many aspects of the physical world, including light intensity, wavelength distribution, and the form and location of objects. This considerable feat is exemplified by the uniform, stable appearance of the world across the visual field. Given the additional dynamics of photopigment bleaching and ocular media absorption, moving the eyes about the scene would seemingly disrupt any semblance of a seamless visual world. Nevertheless, the visual system renders for us what appears to be a uniform, stable percept. This most certainly involves dynamic processes, perhaps throughout the visual system, that serve to regulate and balance inputs for the purpose of maintaining uniformity. These dynamic processes begin at the level of the retina, where the visual system must first “normalize” its inputs, by maintaining relative balance between the three cone types (short-wave (S) cones, long-wave (L) cones, and mid-wave (M) cones) present in the human retina (e.g., von Kries adaptation; see West and Brill, 1982). Perceptual balance is maintained despite substantive changes in conditions that would seemingly distort receptor input balance. For example, age-related changes (i.e., yellowing) in the crystalline lens would tend to cause an overall yellowing of the visual field, and would greatly limit the perception of blue if there were no compensation for short-wavelength light loss. This, however, is not the case as color matches are found to be quite stable throughout the lifetime (Elsner et al. 1988). Further support for the visual system’s ability to compensate for relatively dramatic changes in the spectral content of the world was provided by Neitz et al. (2002). They artificially disrupted perceptual color
balance by use of an external color filter. In this instance, a subject’s estimation of “unique yellow,” (yellow without any hint of red or green) shifted roughly 2 nanometers in wavelength up or down after wearing either red, or green goggles continuously for two weeks. Induced effects persisted for up to 2 weeks post-goggle removal, during which the visual system slowly returned to normal.

Given the examples above, it appears that both external optical and internal ocular filters can induce visual compensation, over relatively short and long periods of time, respectively. The filters noted above, however, do not address the possibility of spatially local compensation in the retina; in other words, what if the retina were impacted not by a “global” filter, such as the crystalline lens or goggles (where the entire visual field is filtered), but by a spatially variable filter, where filtration was differential across the visual field? There is a naturally occurring filter known as macular pigment (MP) in the retina that, if not compensated for, could indeed disrupt the balance of cone inputs differentially across the retina. MP is obtained via the diet from leafy green vegetables, is made up of the carotenoids lutein (L) and zeaxanthin (Z), and is deposited in the retina, just anterior to the photoreceptors (Snodderly et al. 1984b). MP is most dense in the center of the retina, and declines rapidly in density out to roughly 7 degrees eccentricity, where it is optically undetectable (Snodderly, 1984b). Since MP is a yellow filter, it functions to selectively absorb visible, short-wave (blue) light (Snodderly 1984a). Additionally, given its location anterior to the sensory retina, MP screens light before it reaches the photoreceptors. Although MP is deposited in the retina in a normal distribution about the fovea, the actual density varies widely from person to person. The average MP optical density (MPOD) in the general population is approximately 0.35 log units near the foveal center (see table 1 for derivation), but can range from 0, indicating no MP, to over 1 log unit (Hammond et al., 1998);
at this level it absorbs approximately 90% of short-wavelength light before it reaches the photoreceptors. If there were no compensation for this naturally occurring filter, central color vision, specifically with respect to short-wave (blue) light, would be severely compromised.

The cone photoreceptor class that is most strongly impacted by MP’s absorption of short-wave light is, of course, the short-wave sensitive (S) cones. S-cones account for roughly 8-10% of all cones (DeMonasterio et al., 1985) and differ from L- and M- cones in several different respects: morphology (Anhelt and Kolb, 2000), evolutionary origin (Nathans et al. 1986), neural pathway to cortex (“koniocellular” [Calkins, 2001]), and retinal distribution (Curcio et al. 1991). Perceptually, S-cones are responsible primarily for color perception (Rodieck, 1991; Gouras et al., 1993). Using long-wave adaptation to isolate the S-cone channel, Lee and Stromeyer (1989) obtained results that suggested S-cones contribute to luminance and motion pathways; however it was found to be only approximately 1/50th the amount that L and M cones contribute. Chatterjee and Callaway (2002) later corroborated this finding, but more recently in an experiment that accounted for absorption of short-wave light by MP, it was shown that S-cones most likely do not contribute to the L / M luminance pathway (Sun et al. 2006).

With regard to compensation for short-wave light absorption by MP, Stringham et al. (2006) used Stiles’s classic two-color threshold technique to show that S-cone sensitivity was nearly invariant across central retina. Additionally, Hibino (1992), and subsequently Stringham and Hammond (2007) used a hue-cancellation technique wherein subjects indicated how much blue light was needed to cancel a yellow light in order to perceive white (neither blue nor yellow), as a function of retinal eccentricity. If there were no compensation for short-wavelength light loss via MP, the expected outcome of this procedure would be that more blue light would be needed to cancel the yellow in the center of the fovea (where MP is dense) versus the
parafovea. Results indicated, however, that blue-yellow color vision is invariant across central retina. This was also true for a subject whose MP increased substantially via supplementation with lutein over 6 months. This subject’s hue cancellation values were assessed daily, and despite the changes in MP (and commensurate attenuation of short-wave light detected by the S-cones), the B / Y balance remained stable across the retina. These results suggest that an active compensatory mechanism is at work and the sensitivity of S-cones appears to be adjusted to compensate for MP.

A potential mechanism whereby the visual system could compensate for MP is one that involves temporal sampling of the S-cone. Bloch’s law (Brown, 1965) states that for detection of a light, there is a perfect tradeoff between time and intensity up to a critical duration. In other words, a light stimulus is equally detectable if the flash is fast and intense, or if it is relatively slow and dim. Much like a camera, the eye detects and encodes intensity by summing signals over time: Longer exposure times (i.e. slower sampling) leads to greater summation of light, at the expense of temporal resolution. Conversely, shorter exposure times (i.e., faster sampling) would lead to reduced summation of light, and greater temporal resolution. For example, within the visual transduction cascade, it has been shown that phosphodiesterase can be chemically modulated to produce changes in temporal integration times; this modulation results in changes in visual sensitivity (Stockman et al., 2007). Following this line of reasoning, the visual system could modulate the sampling rates of specific photoreceptor classes in order to maintain constant signaling intensity. The extremes of this constancy would be represented by: a) rapid sampling of a relatively bright stimulus, and b) slow sampling of a dim one. For L and M cones, the critical duration for temporal summation, measured using very brief flashes of light, is roughly 10-15 ms on average (Brown, 1965; Krauskopf and Mollon, 1971). S-cones, however, exhibit a
significantly longer critical duration, of approximately 50-100 ms (Brindley et al., 1966; Krauskopf and Mollon, 1971). If a filter, such as MP, decreases the luminance of blue light entering the eye, it would logically follow that, in order to normalize the sensitivity of the S-cone system across the retina, someone with more MP would have a greater summation period for S-cones in the fovea, relative to the parafovea, thus yielding the same effective visual intensity as someone with little MP. The positive correlation between luminance and CFF is well known (e.g., Hecht and Shlaer, 1936), and could certainly account for any effect of S-cone CFF reduction related to MPOD. In order to obviate this potential confound in our experiment, we implemented two controls. First, the intensity of the lights absorbed by MP was such that it placed CFF thresholds on the “plateau” first suggested by the data of Hecht and Shlaer (1936), and later carefully characterized by Brindley et al. (1966). The plateau represents S-cone activity, and is roughly 1 order of magnitude wide. By controlling the intensity of the flickering stimulus such that it was roughly in the middle of the plateau, luminance changes (brought on by MP’s absorption of short-wave light) deviating from that point would, theoretically, not impact CFF. To show that our conditions indeed yielded a target intensity that was on the S-cone plateau, results from an experiment of CFF-versus-intensity for three subjects are presented in Figure 1. Our second control involved obtaining S-cone CFFs for two wavelengths (410 and 440 nm) differentially absorbed by MP. This way, if our obtained CFFs were simply reflective of luminance differences produced via light absorption by MP, the slopes of the lines for CFF as a function of MPOD among subjects would be different. Indeed, due to greater absorption of 440 nm light by MP, for a group of subjects with a wide range of MP levels, the slope of CFF versus MPOD would be much steeper than that for 410 nm. Conversely, parallel slopes for these functions would indicate a common mechanism, independent of luminance, which slows the
temporal sampling rate of the S-cone. On this basis, we hypothesize that CFF values should be related to MP levels, such that subjects with higher MP levels exhibit lower foveal S-cone-mediated CFFs (i.e. slower temporal responses) indicative of greater temporal summation, whereas subjects with lower MPOD exhibit higher foveal S-cone-mediated CFFs (i.e. faster temporal responses) indicative of reduced temporal summation. For L- and M-cones, perhaps it is the case that temporal summation is reduced in order to aid in balancing the relative signal strength between S- and L/M-cone channels? There is empirical evidence to show that higher L- and M-cone-mediated CFF is positively correlated with MPOD (Hammond and Wooten, 2005). To explore this possibility, we obtained measures of both S- and L/M-cone CFFs, and compared these values in subjects with a relatively wide range of MPOD.
CHAPTER 2

METHODS

Subjects

Fourteen subjects, aged 19-42 years, with a wide range of MPOD, were studied. MPOD at the 30’ locus ranged from 0.04 to 0.95. All subjects were free of ocular pathology and had best corrected visual acuity of at least 20/25. Color vision was assessed with Ishihara Pseudoisochromatic Test Plates, and all subjects were normal trichromats. Informed consent was obtained from each subject and the study adhered to the tenets of the Declaration of Helsinki. This study was approved by The Institutional Review board of the University of Georgia.

Measurement of Macular Pigment

Measurement of MPOD was performed using the densitometer described by Wooten et al. (1999; Macular Metrics, Rehoboth, MA). Briefly, this device utilizes heterochromatic flicker photometry, by superimposing a short-wave (blue) disc of light (460 nm peak) on a middle-wave (green) light (550 nm peak), and alternating them in square-wave counterphase. When the luminances of the two lights are sufficiently different, a subject will perceive the stimulus to flicker. If, however, the two lights are equiluminant, the stimulus will appear stable (i.e. no flicker). The subject’s task is to adjust the relative energy of the lights in order to eliminate flicker from the test stimulus. In order to obtain a narrow range of settings and low response variability, adjustment of the alternation frequency for the different retinal loci is necessary (Stringham et al. 2008). Depending on the retinal locus tested, the alternation frequency ranges from 8 to roughly 20 Hz. Because MP absorbs the short-wave but not the middle-wave disc, an
equiluminant balance (no flicker) in the stimulus will require more blue energy, relative to green, for retinal loci that contain more MP, compared to those that contain less. To determine spatial profiles of MPOD across the central retina, this was done at several retinal eccentricities (10’, 15’, 30’, 1°, 1.75°, and 3°), with the reference measure at 7° (where MPOD is negligible). MPOD was calculated for each locus, and the average over the central 2° was used for comparison to the data from the temporal processing speed experiment (detailed below), which utilized a 2° test stimulus.

*Measurement of temporal processing speed: S-cones and L+M cones*

**Apparatus**

For this portion of the study, a two-channel Maxwellian-view optical system with a 1-kW xenon arc lamp source was used to present stimuli. Unless otherwise noted, both background and target stimuli were monochromatic, and made so by either interference filters (background fields; Edmund Scientific, Tonawanda, NY; 8-nm bandwidth at half peak) or via a 500-mm Bausch and Lomb (Rochester, NY) monochromator (target stimuli; 4-nm bandwidth at half peak). The first channel was used to present the 10°, circular background field. Within this channel was an opaque fixation point placed 6° from central fixation. This fixation point was used for measurement of temporal processing speed outside the spatial extent of appreciable absorption by MP. The second channel was used to present a 2° monochromatic target stimulus, concentric with and superimposed upon the background field. The stimulus was made to flicker by an optical chopper (Scitec Instruments LTD, Wiltshire, UK) with high-resolution frequency adjustment. For isolation and measurement of the S-cone channel, the following two conditions were employed: 1) 410-nm target; 4-log troland, 530 nm background, and 2) 440 nm target; 4-
log troland, yellow background (produced by a high-pass broadband filter that cuts-on at 510nm). The stimulus conditions for #1 above were chosen based on the ability of the intense 530-nm background to sufficiently suppress L/M-cone activity, coupled with the subjective feasibility of consistently performing the CFF task (detailed below). Conditions for #2 above were used to replicate those of Brindley et al. (1966). The L/M system was isolated and measured via the following condition: 550 nm target; 1.2 log troland, 442 nm background.

Procedure

The right eye of each subject was studied. A dental impression bite bar and forehead rest assembly was used to ensure subject alignment. Additionally, infrared LEDs were used in combination with a CCD camera to continuously monitor subject fixation. Upon familiarization with the visual task, the subject was aligned to the optical system, whereby the apex of the Maxwellian image was in focus in the plane of the pupil, and passing directly through the center of the pupil. The diameter of the aperture conjugate with the pupil was 1.5 mm.

The same experiment was performed for three separate conditions (listed above). The ascending method of limits was used to determine each subject’s critical flicker fusion frequency (CFF), the frequency at which the subject indicated that subjective flicker was no longer present in the target stimulus. The flicker frequency of the test stimulus was initially presented to the subject at a rate far below CFF (e.g., 8 Hz). The experimenter then gradually (roughly 1 Hz / second) increased the rate of flicker until the subject noted that the flicker had ceased. To avoid effects of perceptual fading, the test stimulus was shuttered, and repeatedly presented in the pattern: 2 seconds on, 0.5 seconds off. CFFs were determined in both the fovea (where MP is most dense), and the parafovea (where MP absorption is minimal; 6° eccentricity from the foveal
center). Data points for the figures were generated by averaging multiple measures for each condition.

In order to ensure that subjects’ thresholds for the S-cone isolating conditions were indeed mediated by S-cones, we set the target stimulus intensity near the middle of the S-cone “plateau” region (described by Brindley, 1966; see Figure 1). This plateau in S-cone response represents the target intensity zone over which the CFF for S-cones does not change. If the intensity of the target extends beyond the plateau region, the L/M system will begin to signal the presence of flicker (see Brindley et al., 1966). Three subjects, with relatively low (0.37), middle (0.55) and high (0.75) levels of MP at 30’ of retinal eccentricity were enlisted to determine an appropriate intensity level to use for all subjects during the main experiment. As noted above, an additional control (use of two S-cone target wavelengths, 410 and 440 nm, differentially absorbed by MP) was instituted. Therefore, if the CFFs obtained were determined by the luminance of the targets, then the functions for these two conditions would exhibit markedly different slopes, due to differential absorption (and hence target luminance) of the two target wavelengths by MP (see Figures 1 and 2).

Statistical analysis

Pearson product-moment correlations were conducted to determine correlation coefficients between subjects’ MP levels and CFF values for all conditions. A p-value of 0.05 was used as the level of statistical significance. To enable better visualization of the data, least-squares fits to data were made where appropriate. Linear equations corresponding to the fits are noted in the legends of applicable figures. Statistical analysis and curve fitting were conducted with Origin 8.0 (OriginLab; Northampton, MA).
CHAPTER 3
RESULTS

Subjects’ MPOD ranged from 0.04 to 0.95 at 30’ eccentricity from the foveal center. This spread of MPOD values enabled us to characterize, with relatively fine resolution, the effects of MPOD on temporal vision measures. As noted in the Introduction section, in order to ensure that our S-cone-isolating conditions produced results that were indeed reflective of S-cone, and not L/M-cone, activity, we conducted a control experiment that assessed the effect of stimulus intensity on CFF values for the 410-nm condition. Results for three subjects with MPOD values ranging from 0.37 to 0.75 at 30’ of retinal eccentricity are presented in Figure 1. Also shown in Figure 1 is the intensity level used for the actual 410-nm experiment. Data for our other S-cone-isolating condition (440 nm, not shown) exhibited a similar pattern.

S-cone-isolating temporal data indicate that subjects with higher levels of MP tended to have lower CFF values for foveal, relative to parafoveal, viewing (see Figure 2). The strength of this relationship was significant for both 410 nm (r = -0.88, p < 0.001) and 440 nm (r = -0.87, p < 0.001) stimulus conditions. It can also be seen in Figure 2 that the slopes of the best-fit lines to the two S-cone isolating conditions are nearly identical (-15.22 vs. -15.49 for 410 and 440 nm conditions, respectively). Because MP differentially absorbs 410- versus 440-nm light, equal slopes is not what would be expected if the mechanism for determining CFF was simply luminance. To the contrary, this result suggests that the S-cone system is slowed down in a general way, not simply because of a loss of luminance (MP would more strongly reduce the luminance of 440 nm light compared to 410 nm). To better visualize this idea, Figure 3 shows a theoretical, purely luminance-based result for 410 nm and 440 nm. The functions presented in
Figure 3 were generated using Brindley et al.’s (1966) S-cone data for CFF as a function of luminance, and the MP absorption coefficients for 410- and 440-nm light determined by Bone et al. (1992).

Perhaps the results of the S-cone isolating conditions were due to the temporal processing characteristics associated with the retinal locations tested (i.e. foveal vs. parafoveal), and not due to a compensatory adjustment of the short-wavelength visual channel? To test this hypothesis, we used a long-wavelength test stimulus that is not absorbed by MP. As can be seen in Figure 4, regardless of MPOD, the difference in CFF between foveal and parafoveal conditions is very small. In fact, the slope of the difference as a function of MPOD is virtually zero (-0.04).

For the L/M system, a significant relationship between MPOD and CFF was found ($r = 0.57; p = 0.03$; see Figure 5). This finding has been reported before (e.g., Hammond and Wooten, 2005), but, as far as we are aware, not for stimuli presented in Maxwellian view. The relationship between L/M system CFF, S-cone system CFF, and MPOD is presented in Figure 6. Here we see a systematic relationship whereby subjects with higher MPOD exhibit both higher L/M CFF and lower S-cone system CFF. This relationship was significant for both the 410 nm ($r = 0.74; p = 0.002$) and 440 nm ($r = 0.75; p = 0.002$) conditions.
CHAPTER 4

DISCUSSION

It is clear from the results of our study that MP has direct effects on the speed of visual processing for both S-cone and L/M-cone-mediated visual streams. With regard to the S-cone system, it appears that, as a function of MPOD, the difference between foveal and parafoveal CFFs becomes greater (see Figure 2). Conventional visual psychophysics wisdom would suggest that this difference could be explained on the basis of the luminance difference produced by the absorption of short-wave light by MP. In order to obviate the within-subjects luminance argument, we implemented two controls (described in the Methods section). Our first control involved setting the S-cone experimental conditions such that CFF thresholds were on the S-cone “plateau,” first described by Brindley et al. (1966). In this way, the luminance change brought on by foveal (MP) versus parafoveal (no MP) viewing would presumably not affect CFF thresholds. Indeed, as can be seen in Figure 1, the intensity level used in our 410 nm experiment allowed for an increase in luminance of 0.6 to 1 log unit, which was more than sufficient to account for the lack of MP in the parafovea. For example, based on the S-cone plateau data, the subject with 0.75 MPOD in Figure 1 (filled squares) would have a nearly 0.8 log unit “buffer” before appreciable CFF change. In other words, given the experimental conditions, the difference between foveal and parafoveal CFFs for this subject should, theoretically, be nearly zero. What was found for this subject, however, was a roughly 4 Hz difference (slower for foveal viewing; see Figure 2). Additional support for the effective isolation of S-cones, and placement on the S-cone “plateau” comes from the parallel functions produced in Figure 2, for 410 and 440 nm conditions. If our experimental conditions were not conducive to plateau
placement, the functions would have appeared somewhat like the theoretical functions shown in Figure 3, which are clearly not parallel.

The question then becomes, if not for a luminance change, why does the S-cone system appear to slow down for retinal areas that are affected by MP absorption? There are a couple of potential explanations. As suggested earlier in the manuscript, a slower CFF may simply be indicative of increased temporal summation, which would serve to amplify the S-cone signal. In this scheme, the S-cone system pools energy into relatively slow bursts of higher intensity, in order to offset the loss associated with MP’s absorption of short-wave light. Another potential explanation involves the idea that compensation for short-wavelength light loss may involve a change in neural code; in other words, the reduction in temporal sampling of the S-cone channel, relative to the L/M-cone channel, could form the basis for perceptual compensation in the brain. This idea is based on recent neurophysiological and neuroimaging findings that appear to indicate differential neural response between B/Y and R/G color systems with regard to stimulus frequency. For example, Mullen et al. (2008) measured hemodynamic activity in LGN and V1 during color perception tasks and found that LGN showed a robust response to red / green (R/G) color contrast, and a relatively weak response to blue / yellow (B/Y) contrast. At low presentation frequencies (2 Hz), however, the activation of the B/Y color pathway increased dramatically in V1 relative to LGN. The effect was found to be selective for temporal frequency – at 8 Hz, the B/Y signal change in V1 (compared to LGN) was much weaker. They attributed this to an amplification of S-cone signals between LGN and V1 when lower stimulus frequencies are used. Another fMRI study by Mullen et al. (2010) extended the findings of their previous work to demonstrate the same slow frequency - high activation relationship in more ventral areas in the visual stream, namely V4 and the ventral areas of V2 and V3. Again, this result suggests
an amplification of blue channel pathway signal at some point between LGN and V1 (perhaps via geniculo-cortical feedback) or early in V1. Although a reasonably clear relationship between stimulus frequency and neural signal strength was determined for the B/Y channel signal, Mullen et al. did not ensure isoluminant stimuli to account for between-subject differences in pre-retinal absorption by MP. This could have possibly resulted in R/G signals being generated during presentation of ostensibly B/Y modulating stimuli, and misinterpreted as B/Y signals in cortex. A recent study by D’Souza and colleagues (2011), however, did account for interindividual differences in MP, and report very compelling data, similar to Mullen et al.’s (2008; 2010). Importantly (perhaps due to cleaner neural signals afforded by custom-tailored isoluminant stimuli), the relationship between stimulus frequency and blood oxygen level dependent (BOLD) signal strength was demonstrative: from 12 Hz down to 2 Hz, lower-frequency modulation of the B/Y channel evoked a strongly significant, linear increase in V1 activity as well as ventral and temporal visual regions. It may be the case, therefore, that the visual system uses temporal sampling rate as a neural code that signals compensation for the spatially non-uniform absorption of short-wave light by MP, thereby maintaining a uniform balance of S- and L/ M-cone input. Temporal summation and neural code-based compensation may both have explanatory power for the results we have generated. Based on principles of the physiology of neural systems, both seem plausible.

With regard to the L/M-cone system, it appears as though MP produces very little difference in CFF (see Figure 4). This makes sense in terms of the luminance argument: MP absorbs none of the 550 nm light that was used for this condition, and therefore moving from central to 6° retinal eccentricity would produce no effective luminance change due to MP absorption. In absolute terms, however, the temporal sampling rate of the L/M-cone system is
significantly increased as a function of MPOD (see Figure 5). In sum, therefore, as a function of MPOD, the S-cone system decreases its temporal sampling rate, and the L/M-cone system increases its temporal sampling rate. Perhaps the L/M-cone system increases its sampling rate in order to reduce temporal summation? Based on the principle of Bloch’s Law (described earlier), this could be the case, given that the increased sampling effectively “chops” the incoming light intensity into a relatively fast, lower intensity stream of visual input. In terms of neural code-based compensations, data from Mullen et al. (2010), similar to their S-cone system data, support the view that faster signals in the L/M-cone system yield less intense activation in regions of the brain that are associated with color and luminance.

When the combined temporal effects of S-cone and L/M-cone pathways are considered as a function of MPOD, the result is striking. Figure 6 is a plot of the difference between foveal CFFs for L/M-cone (550 nm) data and both S-cone conditions (410 nm and 440 nm), as a function of MPOD. The resulting, positively-sloped functions are suggestive of a temporal ratio between L/M- and S-cone systems whereby (as noted above) the temporal sampling rate of the L/M- and S-cone systems are increased and decreased, respectively, as a function of MPOD. As with the data in Figure 2, the functions in Figure 6 are linear, and roughly parallel, which is suggestive of a general increase in temporal sampling rate for the L/M-cone system, and a decrease in temporal sampling rate for the S-cone system.

Taken together, the available data suggest that, by virtue of either temporal summation or neural code mechanisms, the visual system uses temporal processing to compensate for loss of light due to absorption by MP. This same compensatory mechanism could be responsible for the neural plasticity seen in compensation for neural loss in the normal aging retina, and may also have implications for better understanding of how the brain deals with aging and injury.
REFERENCES


Table 1. Sampling of recent investigations of MPOD. Total number of subjects = 1820; calculation of grand mean is based on average MPOD, weighted by number of subjects. All studies utilized HFP to assess MPOD. For investigations where separate group values were reported, multiple subject cells in the table are used.

<table>
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<td>Kirby et al (2010)</td>
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<td>42±13</td>
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<td>Renzi and Hammond (2010)</td>
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<td>Connolly et al (2011)</td>
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<td>Yu et al (2012)</td>
<td>China (Beijing)</td>
<td>281</td>
<td>17-85</td>
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<td>Grand mean</td>
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Figure 1. “Plateau functions” plotted for three subjects. Critical flicker fusion thresholds for a 2.20, 410-nm stimulus on an intense 530 nm background, as a function of log relative radiance. MPOD at 30’ of retinal eccentricity for each subject noted in legend.
Figure 2. Subjects’ foveal CFF minus parafoveal CFF for 410 and 440 nm stimuli, plotted as a function of central 2-degree averaged MPOD. Pearson’s $r = -0.88$ (p < 0.001) for 410 nm data, $r = -0.87$ (p < 0.001) for 440 nm data. Slopes of best-fit lines to data: 410 nm= -15.22; 440 nm= -15.49.
Figure 3. Theoretical slopes of data from Figure 1. Because 440 nm light is absorbed more strongly by MP than 410 nm, the slope is steeper as a function of MPOD. Brindley et al.’s (1966) data for CFF as a function of luminance was used as a basis for the functions; MP absorption coefficient used for 440 nm: 0.84 relative to peak at 460 nm; for 410 nm: 0.38 (Bone et al. 1992).
Figure 4. 550 nm (L/M-cone) CFF data. Foveal CFF minus parafoveal CFF, as a function of 2-degree averaged MPOD. Pearson’s $r = -0.008$; $p = 0.98$. Slope of best-fit line to data: -0.04.
**Figure 5.** Subjects’ CFF, as a function of MPOD for the L/M system condition (550 nm target, dim blue background). MPOD averaged over the angular subtense of the target stimulus (2°).
Figure 6. Foveal CFF for L+M cone condition (550 nm) minus foveal CFF for two S-cone isolating conditions (410 nm & 440 nm), as a function of central 2-degree averaged MPOD. Pearson’s $r = 0.74$, $p=0.002$ (550-410 nm); $r= 0.75$, $p=0.002$ (550-440 nm). Slopes = 15.75, 13.73, respectively.