Altered Visual Sensitivity in Axial High Myopia: A Local Postreceptoral Phenomenon?

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PURPOSE. The present study investigated retinal integrity in high myopia using spatial psychophysical tasks.

METHODS. Ten axial high myopes (−8.5 to −11.5 D) and 10 age-matched control subjects (≤1.0 D) were recruited. All participants underwent clinical examination and ocular biometry and demonstrated no visible macular disease with visual acuities better than 6/12. Foveal summation thresholds were determined for white and S-cone-isolating spots of various diameters up to 5.4° and spatial contrast sensitivity to luminance sine wave gratings (0.5–9.7 c/deg) Data were analyzed after correction for the magnification induced by eye size and correcting lens power.

RESULTS. Spatial summation for both white and S-cone-isolating spots showed a generalized loss of sensitivity at all spot sizes in myopes relative to control subjects (P < 0.01). Critical areas at maximum summation were significantly larger in myopes, for S-cone isolating spots only, after image size correction (P = 0.048). Sensitivity at maximum summation correlated negatively with vitreous chamber depth for both targets (P = 0.005). Sensitivities for S-cone and luminance spots also correlated (P < 0.001), indicating widespread dysfunction. Myopes displayed contrast sensitivity losses at high spatial frequencies (P ≤ 0.006) with a normal peak contrast sensitivity.

CONCLUSIONS. These data can be interpreted to indicate that highly myopic eyes have either (1) a reduction in the number of receptors and/or a reduction in their sensitivity or, (2) a reduction in the sensitivity of postreceptoral processes. The presence of normal contrast sensitivity at low spatial frequencies indicates dysfunction at a postreceptoral level in high myopes. (Invest Ophtalmol Vis Sci. 2006;47:3695–3702) DOI: 10.1167/iovs.05-1569

Myopia is a common refractive condition, which occurs due to an excessive axial enlargement of the eye that is not coordinated with the power of the eye’s optical surfaces. The resultant visual image of distant objects is formed in front of the photoreceptor plane. This excessive axial enlargement is largely accounted for by increased vitreous chamber depth, as little abnormal change is found in anterior chamber depth or lens thickness in high myopia.1

High myopia is usually defined as myopia in excess of 6 D, equating to an eye length of between 25 and 26 mm. The prevalence of high myopia in the general population is approximately 3%; however, the prevalence is as high as 16% in certain Southeast Asian populations.3 One of the most important manifestations of high degrees of myopia is the increased prevalence of retinal degenerative disease, which is largely attributable to the increased stresses placed on the retina of the enlarging eye.4 The cause of these mechanical demands on the retina is probably twofold. First, the retina thins as it is stretched across the enlarging globe and, second, vitreous motion during eye movement places significant shear forces on the retina.5,6

There is increasing evidence to confirm that, in enlarging eyes, the retinal elements are stretched across the interior of the ocular globe. For example, anatomic studies in the chick model of myopia have shown that retinal pigment epithelial and photoreceptor densities are reduced in the enlarging eye.7,8 Furthermore, retinal amacrine and ganglion cells have shown increased dendritic field sizes.9,10 Psychophysical studies in humans confirm that retinal sampling, and therefore photoreceptor density, is decreased in larger eyes11 and suggest that this alteration in sampling density is, first, asymmetric12 and, second, greatest at the fovea.11 In addition, studies in the chick have shown that, despite outer segment disorganization, photoreceptor inner segment diameter increases as the eye enlarges,13 apparently contributing to increased photoreceptor sensitivity, under lower retinal illumination, as indicated by electroretinography.11 It has been suggested that this apparent anomaly is accounted for by improved waveguide14 and, presumably, light-capture properties.15 However, this phenomenon remains to be demonstrated in humans.

Despite this convincing anatomic and functional evidence of increased photoreceptor separation in the highly myopic eye, specific functional correlates of the spatial alterations to inner retinal structure are less easy to determine. Furthermore, it is unclear whether the changes in retinal structure are accompanied by altered sensitivity. For example, psychophysical and physiological studies in humans variously show normal or reduced spatial16–18 and temporal17,19 contrast sensitivity and normal or reduced function as implied from changes in various aspects of the full-field or multifocal ERG.20–22 The findings of such studies are complicated by uncertainty over, or failure to quantify, the nature of the stimulus on the retina, as the optics of the myopic eye result in altered retinal image size23 and presumably retinal illumination, relative to emmetropic eyes.

The present study was designed to test two hypotheses, formulated on the basis of the literature just mentioned: (1) that in highly myopic eyes, the enlarged retinal area and altered inner retinal connectivity result in reduced contrast sensitivity and altered spatial processing, and (2) that despite their altered spatial distribution and morphology photoreceptors retain their sensitivity. These hypotheses were tested by psychophysical comparison of a population of highly myopic eyes, which showed no overt clinical signs of disease, to a sample of normal non ametropic eyes.

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Supported by National Health and Medical Research Council (NHMRC) Project Grant 145700 (NAMcB), and Australian Research Council (ARC) Linkage Grant LP0211474 (AJV).

Submitted for publication December 9, 2005; revised February 6, March 20, and April 3, 2006; accepted May 31, 2006.

Disclosure: A. Jaworski, None; A. Gentle, None; A.J. Zele, None; A.J. Vingrys, None; N.A. McBrien, None.

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MATERIALS AND METHODS

Participants
Ten axial high myopes with an ocular refraction of −8 D or more were recruited through the records of a major public health optometry clinic, Ten age-matched, nonmetropic control subjects (refraction, ±1 D) were recruited from the Department of Optometry and Vision Sciences of the University of Melbourne. Exclusion criteria were a visual acuity of 6/12 or worse, tritan color vision defects (D15 desaturated panel), and the presence of clinically visible central retinal disease on dilated fundus examination. No participants exhibited significant lenticular changes, as assessed with the Wilmer grading system.24

Participants meeting the subject criteria attended a single experimental session (2.5 hours) that comprised both clinical evaluation and visual psychophysical testing. Clinical evaluation confirmed participant suitability and determined ocular biometric parameters. Psychophysical tests consisted of luminance and S-cone spatial summation assessment, and estimation of luminance spatial contrast-sensitivity functions.

As pilot studies showed that contact lens wear actually reduced contrast sensitivity in nonregular wearers, consistent with previous studies,25 spectacle corrections were used during all testing procedures.

All procedures were approved by a National Health and Medical Research Council of Australia–authorized Human Ethics Committee and were in compliance with the tenets of the Declaration of Helsinki.

Clinical Evaluation
A full clinical history was documented to identify any confounding conditions accounting for the refractive error. Ocular health, eye movements, and intraocular pressure were assessed according to standard clinical protocols.

Refraction and Keratometry. Nont Cycloplegic subjective refraction was performed on each participant. The end point of all subjective refractions was maximum positive sphere consistent with best vision. The back vertex distance was recorded for the right eye only. Refraction was reported as the mean spherical equivalent at the corneal plane. Visual acuity was assessed monocularly using a LogMAR (logarithm of the minimum angle of resolution) chart and corrected for spectacle magnification by using back vertex distance and distance refraction.

Corneal power was measured in the two principal meridians of each eye using a one-position keratometer (Bausch & Lomb Australia Pty. Ltd., North Ryde, Australia). Mean values were determined from three meridional measurements.

A-Scan Ultrasonography. Ocular axial length, vitreous chamber depth, lens thickness, and anterior chamber depth were measured by A-scan ultrasonography (Axis II Ophthalmic Echograph; Quantel Medical, Chiang Mai, Thailand). All measurements were made through a dilated pupil (tropicamide 0.5%; Alcon, French’s Forest, Australia). Ocular component lengths comprised the mean of at least three satisfactory measurements, as indicated by maximum separation and similar heights of the anterior and posterior lens surface echoes.

The percentage contribution of the vitreous chamber length to the final refractive status of high myopes, relative to control subjects, was estimated using the BASIC schematic eye program,26 using either measured values or, when measures were not taken, those determined from standard schematic eyes (i.e., media refractive indices, posterior corneal curvature, and anterior and posterior lens surface curvatures).

Psychophysical Testing
Psychophysical tests were performed in eyes with pupil dilation, with additional mydriatic drops instilled hourly. Testing did not commence until pupil size exceeded 6 mm. As nont Cycloplegic refraction determined correcting lens power for testing, systematic focusing errors may have been present after use of the mydriatic, particularly in our presbyopes.22 However, the literature indicates that these would have been small and similar in magnitude in our control subjects and high myopes.22 All testing was performed monocularly on the most myopic eye of high myopes and the least ametropic eye of control subjects. If refractive error was similar in both eyes, the eye with the best visual acuity was selected.

Total time taken to complete the psychophysical tests was approximately 90 minutes, and both the paradigm and stimulus size presentation orders were randomized to control for any fatigue effects.

General Setup. Visual stimuli were presented on a gamma-corrected monitor (HMD-22471 RGB CRT; Hitachi, Tokyo, Japan) driven by a 12-bit video card (Visual Stimulus Generator, VSG2/3; Cambridge Research Systems, Rochester, UK)22 and a software program (Psycho for Windows, ver. 2.33; Cambridge Research Systems) was used to generate all stimuli.

 Participants were positioned 67 cm from the monitor. Forehead and adjustable chin rests minimized head movements and fixed the viewing distance. The monitor was bordered by a white surround, illuminated (illuminance 600 cd m⁻²) to approximately match screen luminance (19.5 cd m⁻²).

Participants were corrected appropriately for the target distance (67 cm) and the fixed vertex distance (26 mm) with spectacle lenses placed in a trial frame attached to the forehead rest. The observer’s head position was adjusted to ensure that the center of the target would be viewed through the optical center of the lens. A translucent occluder was placed in front of the untested eye to prevent Ganzfeld ‘blackout.’29 Crosses delineated the inferior and superior aspects of the central presentation zone of the monitor (approximately 6°) to aid fixation.

Psychophysical Testing Paradigm. Spatial contrast sensitivity and spatial summation were tested separately. Contrast thresholds were determined with a 30-step, yes/no BestPest paradigm.20 False-positive and -negative responses were monitored, with runs having more than 10% false responses repeated. An auditory tone marked stimulus presentation, and observers responded to the stimulus presentation via a response box (Cambridge Research Systems). Trials were conducted in two separate runs, to minimize fatigue and improve observer reliability. Stimulus presentation order was randomized in each run, and the order of psychophysical test was systematically varied between participants.

General Stimulus Characteristics. Stimuli were presented for 1 second with a ramped attack and decay of 200 ms and a presentation plateau of 600 ms that ensured temporal independence of the response.29 Stimuli were presented at 1-second intervals to eliminate the effects of visual persistence and variable response times.32 The starting contrast was approximately 15 dB above threshold, which allowed observers to familiarize themselves with the task.

Contrast thresholds were determined for stimuli set against an achromatic background (1931 CIE; x = 0.299, y = 0.318, Y = 19.5 cd m⁻²). Stimulus chromaticity coordinates were either designed to stimulate the luminance (achromatic) channel (x = 0.299, y = 0.318) or to be located along the blue–yellow opponent axis to stimulate the S-cone pathway selectively (x = 0.267, y = 0.252).55

Spatial Summation. Spatial summation was determined by using six spot sizes ranging from 0.2° to 5.4° diameter, using previously reported methodology.34 In brief, spot sizes were chosen to span the critical area, which is given by the transition from noise-limited processes (slope, 0.5) to complete summation (slope, 0). A two-component model was fit to each participant’s thresholds.34

Spatial Contrast Sensitivity. Achromatic contrast detection thresholds were determined for contrast-modulated (Michelson contrast), horizontal, sinusoidal luminance gratings of six spatial frequencies (0.5–9.7 c/deg). The contrast sensitivity function was modeled with the difference of two Gaussians.59 A detection paradigm was used, as resolution and detection tasks yield similar sensitivities at the fovea in most individuals.11
Calculation of Retinal Image Size of Each Stimulus.
Retinal image sizes of stimuli were calculated for the participants, using a ray trace spreadsheet kindly provided by David A. Atchison (Queensland University of Technology, Australia). This allowed spatial summation and contrast sensitivity to be assessed in terms of stimulus image size at the retinal plane. For this calculation, the measured values of anterior and vitreous chamber depths, lens thickness, anterior corneal radius, and distance spectacle correction (including the vertex distance of the trial frame) were used. The Gullstrand-Emsley relaxed schematic eye provided values for refractive index of the aqueous, distance between the anterior lens surface and the lens first principal plane, and the distance between the posterior lens surface and the second principal plane of the lens.

Statistical Analyses
Statistical analyses and modeling were performed on computer (Minitab software, Minitab Inc., State College, PA; Prism software, GraphPad Inc., San Diego, CA; or the solver module of an Excel spreadsheet, Microsoft Corp., Redmond, WA). Group data were analyzed with nonparametric tests, in cases of non-normal data, or two-way RM-ANOVA (factors: refractive error and spot size) and data are expressed as the mean ± SEM. An α-level of 0.05 was used, except in cases of multiple comparisons where a Bonferroni correction was applied. Spearman’s rank correlation and Deming’s linear regression were used to evaluate associations. Relative differences between high myopes and control subjects were expressed as the percentage change after image size correction (based on axial length and corrected refractive error).

RESULTS

General Characteristics of Participants
Table 1 presents the general characteristics of our participants. There was no significant difference between the ages of high myopes and control subjects (mean ± SD 43.2 ± 12.1 years vs. 37.7 ± 13.9 years; P = 0.40). LogMAR visual acuities of tested eyes also were not significantly different, after correction for spectacle magnification (0.03 ± 0.03 vs. 0.00 ± 0.01; P = 0.47), and there was no significant difference between magnification-corrected acuities of tested and nontested eyes of high myopes (P = 0.57). One high myope and one control were diagnosed with a congenital deuteranomalous defect. Thresholds for the deuteranomalous participants were not significantly different from their respective groups and are included in the subsequent analyses.

Table 1. Clinical Profile, Refractive Error, and Ocular Dimensions of High Myopes and Age-Matched Control Subjects
<table>
<thead>
<tr>
<th>Parameter</th>
<th>High Myopes</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td>43.2 ± 12.1</td>
<td>37.7 ± 13.9</td>
</tr>
<tr>
<td><strong>Gender (female/male)</strong></td>
<td>3♀/7♂</td>
<td>6♀/4♂</td>
</tr>
<tr>
<td><strong>Visual acuity</strong> (LogMAR)</td>
<td>0.03 ± 0.09</td>
<td>0.00 ± 0.01</td>
</tr>
<tr>
<td><strong>Refractive error</strong>† (D)</td>
<td>−10.12 ± 1.12</td>
<td>−0.18 ± 0.57</td>
</tr>
<tr>
<td><strong>Corneal radius (mm)</strong></td>
<td>7.57 ± 0.24</td>
<td>7.65 ± 0.24</td>
</tr>
<tr>
<td><strong>Anterior chamber depth (mm)</strong></td>
<td>3.55 ± 0.17</td>
<td>3.19 ± 0.35</td>
</tr>
<tr>
<td><strong>Lens thickness (mm)</strong></td>
<td>4.14 ± 0.57</td>
<td>3.98 ± 0.32</td>
</tr>
<tr>
<td><strong>Vitreous chamber depth (mm)</strong></td>
<td>19.20 ± 0.71</td>
<td>15.85 ± 0.59</td>
</tr>
<tr>
<td><strong>Axial length (mm)</strong></td>
<td>26.88 ± 0.74</td>
<td>23.03 ± 0.75</td>
</tr>
<tr>
<td><strong>Vitreous chamber depth contribution to myopia (%)</strong></td>
<td>97.4 ± 4.3</td>
<td>21.86 to 24.19</td>
</tr>
</tbody>
</table>

Data are the mean ± SD. Where relevant, the average and standard deviation are specified, and the range enclosed within brackets.

† Corrected for back vertex distance.

Role of Vitreous Chamber Elongation in Refractive Error
Table 1 also presents the ocular refractive and biometric data for high myopes and control subjects. The ocular axial length was significantly longer in high myopes (26.88 ± 0.74 mm vs. 23.03 ± 0.75 mm; P < 0.001), as was the vitreous chamber depth (19.20 ± 0.71 mm vs. 15.85 ± 0.59 mm; P < 0.001). Approximately 87% of the difference in axial length between high myopes and control subjects was attributed to elongation of the vitreous chamber. The remaining difference was mostly attributable to the anterior chamber depth (3.55 ± 0.17 mm vs. 3.19 ± 0.35 mm; 9%). Predictions based on the participants’ ocular parameters demonstrated that approximately 97% of the refractive error of our high myopes was attributable to vitreous chamber elongation.

Abnormal Spatial Summation in High Myopes
Pupil size, measured before the commencement of psychophysical testing, was not significantly different between high myopes and control subjects (7.0 ± 0.5 vs. 6.8 ± 0.4 mm respectively, P = 0.21). The data in Figure 1 show contrast sensitivity as a function of stimulus area. Each data point is the average of 10 observers (circles, luminance data; squares, S-cone data; filled symbols, high myopes; open symbols, control subjects). The vertical lines represent the 95% confidence limits around the critical area of the control group and the dashed gray lines the models for high myopes when corrected for image magnification. The luminance and S-cone summation curves (Fig. 1) displayed significant downward displacement for high myopes for all spot sizes (maximum summation: luminance −0.12 log units, P = 0.01; S-cone −0.18 log units, P = 0.01). These reductions represented a 23% and 31% loss in luminance and S-cone contrast sensitivity, respectively.

The increased critical area of high myopes, evidenced by the rightward shift of both the luminance and S-cone spatial summation curves relative to the control group (Fig. 1), was expected on the basis of eye size and spectacle magnification. The S-cone critical area remained significantly (P = 0.048) enlarged after correction for magnification factors (Fig. 1, dashed gray line). The luminance and S-cone critical areas were increased by 43% and 55%, respectively, after correction. The lack of statistical significance for the critical area of the luminance process reflects the limited power (P = 0.61) of our experiment, due to the sample size.

Association of Sensitivity with Increasing Eye Size
The data in Figure 2A show sensitivity to the S-cone stimulus as a function of stimulus area. Each data point is the average of 10 observers (circles, luminance data; squares, S-cone data; filled symbols, high myopes; open symbols, control subjects). The critical area for stimulus area. Each data point is the average of 10 observers (circles, luminance data; squares, S-cone data; filled symbols, high myopes; open symbols, control subjects). The critical area for each stimulus size is the maximum sensitivity, whereas the limits of summation are the smallest stimulus areas that produce a 75% increase in sensitivity. The critical area for each stimulus size is the maximum sensitivity, whereas the limits of summation are the smallest stimulus areas that produce a 75% increase in sensitivity.
show luminance and S-cone contrast sensitivity as a function of vitreous chamber depth. Each data point represents a single individual (filled circles, high myopes; open circles, control subjects). The dotted lines represent the lower (Fig. 2A) or upper and lower (Figs. 2B, 2C) 95% confidence limits of the control subjects. Contrast sensitivity at maximum summation did not correlate with spectacle correction, age, or duration of myopia, demonstrating that the losses measured in high myopes were not related to the lenses used to correct the refractive error (luminance, \( r = 0.59, P = 0.09 \) and S-cone \( r = 0.34, P = 0.15 \)), or the length of time that the patient had been myopic (age: luminance \( r = 0.58, P = 0.09 \), S-cone \( r = 0.32, P = 0.37 \); duration: luminance \( r = 0.52, P = 0.13 \), S-cone \( r = 0.27, P = 0.44 \)). In contrast, sensitivity decreased with increasing vitreous chamber depth (luminance \( r = -0.59 P < 0.01 \); S-cone \( r = -0.60 P < 0.01 \)), as illustrated in Figures 2B and 2C. As shown in Figure 2A, the losses in luminance and S-cone sensitivity correlated highly \( (r = 0.83, P < 0.001) \). These data support the proposal that excessive axial length is the major contributor to the visual processing anomalies found in the present study.

Contrast Sensitivity and Spatial Frequencies in High Myopes

The data in Figure 3 show contrast sensitivity as a function of spatial frequency. Each data point is the average of 10 observers (filled circles, high myopes; open circles, control subjects). The gray area represents the lower 95% confidence limits of the control group, and the dotted curve represents the high myopes when corrected for image magnification. The two x-axes give spatial frequency in object space (cyc/deg) and the approximate equivalent on the retina (cyc/mm). High myopes had normal sensitivity at spatial frequencies <4.2 cyc/deg (Fig. 3). The loss at higher spatial frequencies (≥4.2 cyc/deg) remained significant \((P = 0.006, \text{Bonferroni adjusted})\) even after correction for magnification factors, as indicated by the deviation of the corrected curve of high myopes (dotted line) from the 95% confidence interval of control subjects (Fig. 3, gray area).

**Figure 1.** Spatial summation sensitivity was reduced and critical area increased in high myopes, relative to control subjects, for a luminance (top plots, circular symbols) and S-cone (bottom plots, square symbols) isolating stimulus. Data were fit with a two-component linear model (slopes, 0.5 and 0). Filled symbols connected with solid black lines and open symbols connected with dashed black lines represent the findings for high myopes and control subjects respectively, before correction for image magnification. Vertical shaded areas define the 95% confidence limits of the luminance and S-cone critical areas of control subjects. Dotted gray lines: position of the spatial summation curve for high myopes, after correction for the image size relative to control subjects. The critical area was significantly larger in high myopes in response to the S-cone-isolating stimulus, after correction for image size \((P = 0.048)\), as evidenced by the fact that it remains outside the 95% confidence limits. \( n = 10 \) in each group. **\( P = 0.01 \).

**Figure 2.** Sensitivities to luminance and S-cone isolating stimuli in the spatial summation tasks correlated significantly \((P < 0.02)\) and showed that high myopes had low sensitivity to both targets, indicating widespread dysfunction. (●) High myopes; ( ○) control subjects. Dotted lines: lower (A) or upper and lower (B, C) 95% confidence limits of control subjects. (A) Correlation between sensitivity to S-cone and luminance stimuli. (B) Correlation between sensitivity to the luminance stimulus and vitreous chamber depth. (C) Correlation between sensitivity to the S-cone isolating stimulus and vitreous chamber depth. The correlation was established using a Spearman rank order coefficient.
light-capture properties. Indeed, the small, nonsignificant sensitivity increases as a result of improved waveguide and contradict previous suggestions that, in animal models, coneceptoral processing. Collectively, these findings are indicative of S-cone-isolating stimulus is further evidence of altered postreduction at all spatial frequencies. Third, given this normal or spatial summation deficits arise from postreceptoral dysfunc-
tion, as photoreceptor losses would produce a generalized spatial summation deficits result from postreceptoral elements remodeled sufficiently to maintain the same neural contacts. No change or reduction in critical area would have implied loss of neural contacts. Sec-
ond, we reasoned that the lower redundancy S-cone mosaic would be more sensitive to spatial changes and relatively im-
mune to optical limitations at the central fovea. Therefore, critical area changes in spatial summation would be more prominent in the S-cone task. Third, we reasoned that remodel-
ing of postreceptoral elements may result in reduced sensi-
tivity; however, this would be indistinguishable from reduced photoreceptoral sensitivity when using the spatial summation task alone. Finally, we reasoned that if a spatial contrast sensitiv-
ity function were also determined, reduced photoreceptor sensitivity would be revealed as a uniform decrease in sensi-
tivity across the entire function, albeit with slightly greater loss at the highest spatial frequencies, given the increased photoreceptor spacing. Normal sensitivity at any spatial fre-
quency would indicate normal receptor function.

Spatial summation curves were well fit with a bilinear model, where one line has a slope of approximately 0.5, re-
presenting the zone of neural noise, and the other has no slope, representing the zone of total summation for the detecting mechanism. The good fit of our data to a slope of 0.5 indicates that the function is noise limited by a postreceptoral detector. Furthermore, sampling has occurred through a single detector, rather than recruiting multiple detectors which should give a slope of 0.25. It follows that, given the critical area of the stimulus on the retina (achromatic, 0.025 mm²; and S-cone, 0.055 mm²) and the much smaller extent of ganglion cell receptive fields in the foveal region, the detector in question must invoke higher-order (extraretinal) visual pro-
cesses. Significant decreases in sensitivity were demonstrated in highly myopic eyes, both at partial and maximum summa-
tion, to achromatic and S-cone-isolating stimuli, demonstrating a loss of sensitivity in both the luminance and S-cone systems. This loss of sensitivity correlated with increasing eye size in both systems. Although the detector isolated in these studies is extraretinal, we argue that the most likely site of these sensi-
tivity deficits is retinal and either receptoral or postreceptoral and that these deficits are subsequent to enlargement of the globe. How retinal remodeling can be evaluated with spatial summation has been addressed previously, as this should yield a change in the critical area with differential sensitivity losses in the regions of partial and total summation. Data from the present study show such trends for both the luminance and S-cone targets (Fig. 1), although they were only significant for S-cone findings, and we interpret these findings as consistent with a generalized remodeling in the myopic eye. Such a conclusion is consistent with previous reports of retinal remodel-
ing in highly myopic eyes of animal models, and extends the literature by showing that this remodeling is not sufficient to maintain sensitivity as the retinal area increases in myopic eyes.

Direct evidence of retinal stretching is present in the differ-
ent critical areas of highly myopic individuals and control subjects. The critical area for S-cone mechanisms increased by 55%. Such a finding supports previous reports of increased photoreceptor spacing, and suggests that the receptive field size of the detector is increased in myopic eyes. This would mean that inner retinal neurons remodel and enlarge their receptive fields to maintain their connections, as found in animal models. Indeed, our estimates are consistent with modeling in which an increase of 36% in retinal area is pre-
dicted between control subjects and high myopes. Given that
this model assumes a uniform overall increase in eye size in myopia and that a recent report shows that ocular surface enlargement is likely to be greatest at the posterior pole.\textsuperscript{12} We suggest that the difference between the observed (55\%) and predicted (36\%) values reflects the relative prolate nature of the highly myopic eye.\textsuperscript{41} The lack of statistical significance of this finding in the luminance mechanism (43\% increase) is possibly attributable to increased noise associated with reduced sensitivity,\textsuperscript{42} which decreases the power of our experiment.

Contrast sensitivity functions were well fit with a difference of Gaussians with a significant loss of sensitivity found for grating periodicities $\approx 4.2$ cyc/deg in highly myopic eyes. The contrast sensitivity function is thought to reflect the response of a number of spatially tuned band-pass filters, which reside postreceptorially and most likely in the cortex.\textsuperscript{13} It can be assumed that a general decrease in photoreceptor input would result in reduced contrast sensitivity at all spatial frequencies.\textsuperscript{38}

This is similar to the disability produced in photoreceptors by a light-scattering diffuser which is known to reduce contrast sensitivity at all spatial frequencies.\textsuperscript{44} Hence, the preservation of sensitivity at low spatial frequencies, found in the present study, is interpreted as indicating losses of postreceptoral processing. Thus, it appears that cone sensitivity is preserved or enhanced, as suggested by previous studies in animal models,\textsuperscript{14} offsetting some of the postreceptoral losses. It may be argued that the roll-off at higher sensitivities is related to reduced retinal sampling, explaining the additional sensitivity losses found in the contrast sensitivity function task relative to the spatial summation task.\textsuperscript{35} However, several factors may influence this particular conclusion, and these are discussed in the following text.

Among the factors that potentially influenced the conclusions of this study are the following: (1) actual stimulus size on the retina, due to assumptions regarding magnification effects; (2) altered retinal illumination/retinal stimulus contrast during transmission through the correcting lenses and ocular media; and (3) optical limitations on the quality of the foveal image.

The physical size of the retinal image of the target is reliant on several factors, such as the correcting lens power, the power of each of the refracting components of the eye, the physical separation of these refracting components and their position relative to the retinal photoreceptors. Although the present study incorporated no methodology whereby the retinal image size was measured directly, the ray trace performed through the optical system of our corrected observers, which provided an image magnification factor for each individual, makes few assumptions. The well validated Gullstrand-Emsley schematic eye model was used, which meant that only three assumptions were required, as detailed in the Methods Section. We argue that these assumptions would only affect our comparisons if corneal curvature, anterior chamber depth and/or lens thickness were different in our high myopes. The data clearly shows this is not the case (Table 1).

Several factors may affect the number of quanta from the stimulus reaching the photoreceptors in our two groups of participants, thus potentially affecting the validity of our comparisons. These factors are reflection/scatter by the correcting lenses; altered area of the entrance pupil of the eye due to correcting lens; absorbance and scatter in the ocular media/the inverse square law of illumination; and retinal image size altering light condensation. High myopes were on average corrected with one more trial lens than control subjects; thus, light energy lost to reflection is estimated to be 9\% greater for the myopes (see the Appendix). On the basis of a previous report,\textsuperscript{45} the negative lenses used to correct the high myopes in the present study were estimated to cause a reduction in the area of the entrance pupil of the eye of approximately 23\%, relative to control subjects (see the Appendix). Our calculations indicate that the increased length of the myopic eye; thus, the greater distance traveled by light through the vitreous, will further reduce retinal illumination by 27\% relative to control subjects, given the evidence that light scatter in the vitreous of myopic eyes is no different from that of control subjects (see the Appendix).\textsuperscript{46} The calculations also showed that the decreased retinal image size in high myopes would produce a 27\% increase in retinal illumination (i.e., more photons per unit area) relative to control subjects, partly counteracting the decreases mentioned earlier. Therefore, a conservative estimate of the overall change in target illumination of the retina in our highly myopic subjects is a 32\% decrease (0.17 log units). Our background luminance was chosen to be high on the Weber slope for contrast detection (approximately 0.6--1.0 log unit beyond the transition). Thus, given that the luminance decrease applies to both target and background, we conclude that the contrast sensitivity losses reported herein are not attributable to altered stimulus transmission through the lens/eye system. The most parsimonious explanation is that they arise from neural dysfunction.

There is evidence to suggest that the density of the retinal sampling array does not limit the performance of resolution tasks at the center of the fovea and that the limiting factor is aberrations of the eye’s optical system.\textsuperscript{11} Indeed, some studies suggest that these aberrations may differ between myopic and emmetropic eyes,\textsuperscript{39} although other studies suggest otherwise.\textsuperscript{46,47} Furthermore, as we have asked participants to perform a detection task, rather than a resolution task, we are unable to extrapolate contrast sensitivity changes to direct estimates of photoreceptor separation. The main limitation that this places on the interpretation of the current data set is that we cannot determine the exact contribution of altered sampling density versus altered postreceptoral sensitivity to the decline in the contrast sensitivity function at higher spatial frequencies in highly myopic eyes. Despite this fact, sensitivity losses in performing the spatial summation and contrast sensitivity tasks are unlikely to reflect only reduced sampling density, as this should yield normal sensitivity at larger spot sizes,\textsuperscript{39} and our spatial summation data do not show this.

In summary, the present study found that sensitivity to a spatial summation task is significantly reduced in some highly myopic eyes, and that contrast sensitivity functions demonstrate that this loss of sensitivity involves postreceptoral elements. These findings suggest that postreceptoral deficits are present before the onset of clinically observable disease in highly myopic eyes, which is probably consistent with previous reports of remodeling of lateral elements of the inner retina as the retinal area increases.

\section*{Appendix}

\subsection*{Reflected Light from Extra Lenses in Myopes}

Using equations from Smith and Atchison\textsuperscript{50}

\[ \text{Transmittance} \times 100 \]

\[ \text{Transmittance} \times 100 = \frac{4 \times n' \times n}{(n' + n)^2} \times 100 \]

\[ \text{Reflectance} = 100 - \text{Transmittance} \]

where \( n' \) is 1.523 (spectacle crown glass), \( n \) is 1.000 (air), \( k \) (number of air-lens interfaces) = 2 (i.e., 1 extra lens in myopes). Substituting these values into the equations yields a value for increased light loss in myopes relative to control subjects of 8.4\%.
Reduced Entrance Pupil Area in Corrected Myopes

Campbell et al., determined that a myope wearing a spectacle lens of −9 D has a magnification relative to a control eye. Entrance pupil area change from control is therefore given by

\[
\text{percent change in entrance pupil area} = \frac{(\pi r_{\text{HM}}^2) - (\pi r_{\text{C}}^2)}{(\pi r_{\text{C}}^2)} \times 100
\]

Substituting values of \( r_{\text{HM}} = 0.88 \) and \( r_{\text{C}} = 1.00 \) for high myopes and control subjects respectively (12% linear reduction) returns a reduction of 22.6% in entrance pupil area in myopes.

Reduced Illumination Due to Increased Axial Length

Using equations from Rudnicka and Edgar, Retinal illuminance \( \propto \frac{1}{(k')^2} \times A \times T \times L \)

Assuming pupil area (A), media transmittance (T) and source luminance (L) similar in myopes and control subjects

Retinal illuminance (RI) \( \propto \frac{1}{(k')^2} \)

and

Reduced RI in myopes relative to controls (% of control)

\[
\text{Reduced RI} = \frac{R_{\text{HM}} - R_{\text{C}}}{R_{\text{C}}} \times 100
\]

The \( k' \) of our myopes (2.50 mm) was 1.2 times that of our control subjects (2.13 mm). Substitution of these values gives an RI for myopes of 0.16 and for control subjects of 0.22. This equates to a reduced RI in high myopes of 27.3%.

References