Sensitivities in Older Eyes With Good Acuity: Eyes Whose Fellow Eye Has Exudative AMD

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We compared several indices of foveal visual function between two groups of people aged 60 and older. One group was comprised of individuals who had good acuity in one eye, but had a history of exudative aging macular degeneration (AMD) in the other eye. We measured visual function in these individuals' good eyes only. The second group was a normative group; it was comprised of individuals who had good acuity in each eye. None of the eyes which we tested from either group had funduscopic evidence of macular pathology other than macular drusen and/or hypopigmentation. We found that eyes whose fellow eye had suffered from exudative AMD themselves suffered compromised foveal function, even when they retained 20/20 or better acuity. Losses of sensitivity mediated by blue-sensitive cones tended to be greater for 1° than for 3° diameter test stimuli. Absolute sensitivity losses at long test wavelengths were probably due to several factors, including decreased effective cone photopigment density. Slow rates of recovery during dark adaptation were associated with the presence of many macular drusen and/or macular hypopigmentation. Eyes whose fellow eye had suffered from exudative AMD had more macular drusen and hypopigmentation than eyes whose fellow eye had not suffered from exudative AMD. Invest Ophthalmol Vis Sci 28:1832–1837, 1987

The leading cause of new blindness among people aged 60 or older is aging macular degeneration (AMD).1 There are two forms of AMD, exudative and atrophic; most AMD-related blindness is due to the exudative form.2 Because exudative AMD may be treatable,3,4 we have elected to study visual function in eyes which may be at increased risk for developing future exudative AMD.5-8 Specifically, we have measured a series of visual functions psychophysically in eyes whose fellow eye has already suffered from exudative AMD.

Although the etiology of AMD is debated,9 there is no doubt that AMD affects the retinal pigment epithelium (RPE). The psychophysical functions that we chose to measure were among those likely to be especially sensitive to the integrity of the RPE, and which could be measured on a large naive population. These functions include sensitivity mediated by blue-sensitive ("S") cones,10 photopic dark adaptation,11,12 and color matching.12 In order to demonstrate that any functional deficits are due to RPE compromise, we have tested only eyes having good acuity and no obvious pathology except perhaps for macular drusen or pigmentary change, or both.

In this study we compare the results of psychophysical tests of visual function for two populations of eyes having good acuity: eyes whose fellow eye has suffered from exudative AMD, and eyes whose fellow eye has not suffered from exudative AMD. We also evaluate several aspects of fundus appearance for these two groups of eyes. In the preceding paper we analyzed age trends in psychophysical data obtained from the latter group of eyes.13

Materials and Methods

Criteria For Subject Eligibility

Individuals of age 60 or older were eligible for inclusion in the study as subjects if: (1) they had best corrected acuity of no worse than 20/25 in one eye and a history of exudative AMD in the other eye, and they otherwise met all relevant eligibility criteria for good ocular health detailed in the preceding paper13, or (2) for each eye they met the eligibility criteria detailed in the preceding paper.13

Nomenclature

Subjects with one eligible eye, ie, subjects with a history of exudative AMD in their other eye, will be called "Group I" subjects. Subjects with two eligible eyes will be called "Group II" subjects. The term
"Group I eyes" refers to the good eyes of Group I subjects.

Subject Recruitment

Group I subjects were recruited through the files of a retinal surgeon (MLK) or from individuals referred to a retinal surgeon because of active exudative maculopathy. Group II subjects were recruited from a number of sources described in the preceding paper.13

Subject Screening

Screening procedures were as described in the preceding paper.13 Written informed consent was obtained from all subjects.

Numbers of Subjects

Fifteen Group I subjects, nine males and six females, had 20/20 or better best corrected acuity. Six Group I subjects, five males and one female, had 20/25 best corrected acuity. A total of 122 Group II subjects, 38 male and 84 female, had 20/20 or better best corrected acuity in at least one eye. A total of 130 Group II subjects, 39 male and 91 female, had 20/25 or better best corrected acuity in at least one eye.

Visual Function Testing

Instrumentation: Two apparatuses were used for testing. All threshold measurements were obtained using a two channel Maxwellian view testing device. Rayleigh matches were made on a free viewing anomaloscope. Each instrument is described in more detail in the preceding paper.13

Procedure: Subjects were tested on a battery of tests by either of two examiners (AE or SAF). Group I subjects were tested in their good eye only. All other procedural details are as described in the preceding paper.13

Calibration

The details are described in the preceding paper.13

Fundus Photography and Evaluation

After visual function testing, subjects’ pupils were diluted with 1.0% tropicamide and 2.5% phenylephrine hydrochloride. Stereoscopic color fundus photographs of the posterior pole were then taken with ultraviolet and infrared light filtered out.

One of us (MLK) scored the photographs in the following way. The number of drusen within a one-disc diameter radius of the foveola were counted and on the basis of this count an integral score of from 0–4 was given. Zero represents no drusen, 1 represents 1–10 drusen, 2 represents 11–50 drusen, 3 represents 51–100 drusen, and 4 represents more than 100 drusen. Degree and extent of hypopigmentation within the same retinal area was scored with the same scale according to comparison with standard photographs. A score of 0 represents no atrophic change, and a score of 4 represents marked change.

Statistical Considerations

All functional testing was done with the examiner unaware of the appearance of subjects’ fundi or acuities. All grading of photographs was done without knowledge of any functional data. Statistical significance is according to Mann-Whitney U tests, except for evaluation of expected frequencies, which is according to chi² tests. All tests are one-sided. Unless stated otherwise, significance values are for eyes with 20/20 or better best corrected acuity only. Data from 20/25 eyes are presented in graphical and tabular form, however.

Statistical comparisons of psychophysical data between the good eyes of Group I subjects and the eyes of Group II subjects are comparisons of age-corrected data. The age corrections were made according to the best fitting linear regression lines through Group II subjects’ data. Linear regression slopes and other statistics derived from psychophysical data were computed using “mideye” rather than “single-eye” data when possible, as in the preceding paper.13 Age corrections were applied to a set of data pooled across sex only when no significant sex-dependent difference was found for Group II eyes.13 Unless specified otherwise, comparisons between Group I and Group II eyes are from data pooled across sex. Data from all eyes with 20/25 or better acuity are represented graphically.

Results

S Cone Sensitivities

S cone sensitivities were less for males in Group I (good acuity in one eye, history of exudative AMD in the other eye) than for males in Group II (good acuity in each eye, no history of exudative AMD). The significance levels were \( P < 0.00005 \) and \( P < 0.005 \) for 1° and 3° test stimuli respectively. The small number of Group I females may have precluded establishing an S cone sensitivity difference for females (Fig. 1).

For males, and also for both sexes combined, the difference in log S cone sensitivity between 3° and 1° test stimuli was greater for Group I eyes than for Group II eyes (\( P < 0.05 \)). That is, the loss of sensitivity to small test stimuli compared to large test stimuli was greater for Group I than for Group II eyes.
S Cone Sensitivity
Age 60-69

Absolute Sensitivity (660nm)
Age 60-69

Fig. 1. (A) Frequency histogram of S cone sensitivity (440 nm, 3°) for people aged 60-69. Hatched bars, females without a history of exudative AMD; open bars, males without a history of exudative AMD. Each closed and open circle represents respectively a female or male who has a history of exudative AMD in his or her non-tested eye. Acuity values represent best corrected acuities. Description of testing parameters are in the Materials and Methods section of the preceding paper.11 (B) Same as (A) except that the data are for people aged 70-79.

Photopic Dark Adaptation and Absolute Threshold

Sensitivity at absolute threshold was less for Group I eyes than for Group II eyes (P < 0.00001) (Fig. 2). Time constants of the recovery rate of log sensitivity were greater for Group I eyes than for Group II eyes (P < 0.005) (Fig. 3). Slow rates of recovery for Group I eyes were associated both with the presence of many macular drusen (P < 0.05)* and with the existence of much macular hypopigmentation (P < 0.01)* (Table 1).

Color Matching

Group I subjects were more likely to have a color-match-area-effect of magnitude zero or less in their

Dark Adaptation Time Constant

Fig. 2. (A) Frequency histogram of sensitivity at absolute threshold to a 660 nm test for people aged 60-69. An arrow next to a symbol indicates that the symbol would lie off the graph in the direction of the arrow. Other details as in Figure 1A. (B) Same as (A) except that the data are for people aged 70-79.

* Since it was not decided at the outset of data collection what score would correspond to "many drusen," the significance level calculated for the most favorable score cannot be construed to be the true significance level for rejecting the null hypothesis that there is no association of large time constant with many drusen. However, since there are only four possible cutoffs, and the significance level is 0.01 for a cutoff score of ≥2 or 3, the null hypothesis can be rejected quite conservatively at the 0.05 level (since 4 X 0.01 < 0.05). (A Kruskal-Wallis one-way analysis of variance by ranks also yielded a significance level of P < 0.05.) Similarly, the null hypothesis of no association of large time constant with degree of atrophic change can be rejected conservatively at the 0.05 level given the 0.002 significance level associated with no notable change.
Table 1. Functional and fundus appearance scores for eyes with good acuity whose fellow eye has suffered from exudative AMD

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Time constant</th>
<th>Drusen score</th>
<th>Hypopigmentation score</th>
<th>SC 3°</th>
<th>SC 3°-SC 1°</th>
<th>Abs sens</th>
<th>CMAE</th>
<th>bca</th>
<th>AMD eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>86</td>
<td>M</td>
<td>67</td>
<td>2</td>
<td>4</td>
<td>3.06</td>
<td>0.35</td>
<td>4.71</td>
<td>—</td>
<td>20/20-3</td>
<td>CF 4'</td>
</tr>
<tr>
<td>72</td>
<td>M</td>
<td>101</td>
<td>1</td>
<td>0</td>
<td>5.16</td>
<td>0.53</td>
<td>6.36</td>
<td>0.060</td>
<td>20/25+2</td>
<td>disciform scar</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>107</td>
<td>3</td>
<td>0</td>
<td>4.34</td>
<td>1.00</td>
<td>5.59</td>
<td>0.000</td>
<td>20/25</td>
<td>CF 3'</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>110</td>
<td>1</td>
<td>0</td>
<td>4.84</td>
<td>0.29</td>
<td>5.69</td>
<td>0.060</td>
<td>20/20</td>
<td>disciform scar</td>
</tr>
<tr>
<td>76</td>
<td>M</td>
<td>116</td>
<td>2</td>
<td>0</td>
<td>4.67</td>
<td>0.35</td>
<td>5.89</td>
<td>0.005</td>
<td>20/20-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>68</td>
<td>M</td>
<td>139</td>
<td>1</td>
<td>0</td>
<td>4.93</td>
<td>0.48</td>
<td>6.23</td>
<td>0.075</td>
<td>20/50-2</td>
<td>large extrafoveal chorioretinal scar and hemorrhage, laser scar</td>
</tr>
<tr>
<td>67</td>
<td>F</td>
<td>139</td>
<td>2</td>
<td>0</td>
<td>4.74</td>
<td>0.59</td>
<td>5.95</td>
<td>0.040</td>
<td>20/20-1</td>
<td>disciform scar</td>
</tr>
<tr>
<td>74</td>
<td>M</td>
<td>144</td>
<td>1</td>
<td>0</td>
<td>4.95</td>
<td>0.27</td>
<td>5.66</td>
<td>0.015</td>
<td>20/25-2</td>
<td>disciform scar</td>
</tr>
<tr>
<td>64</td>
<td>F</td>
<td>147</td>
<td>1</td>
<td>0</td>
<td>5.58</td>
<td>0.38</td>
<td>6.19</td>
<td>0.050</td>
<td>20/15-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>152</td>
<td>2</td>
<td>2</td>
<td>4.84</td>
<td>0.21</td>
<td>5.98</td>
<td>0.000</td>
<td>20/20-2</td>
<td>disciform scar</td>
</tr>
<tr>
<td>76</td>
<td>F</td>
<td>158</td>
<td>3</td>
<td>2</td>
<td>5.03</td>
<td>0.71</td>
<td>5.48</td>
<td>—</td>
<td>20/25-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>72</td>
<td>M</td>
<td>232</td>
<td>4</td>
<td>3</td>
<td>4.20</td>
<td>0.17</td>
<td>5.57</td>
<td>0.000</td>
<td>20/20-2</td>
<td>disciform scar</td>
</tr>
<tr>
<td>64</td>
<td>M</td>
<td>232</td>
<td>2</td>
<td>4</td>
<td>4.42</td>
<td>0.97</td>
<td>4.92</td>
<td>0.000</td>
<td>20/20-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>237</td>
<td>4</td>
<td>1</td>
<td>4.71</td>
<td>0.38</td>
<td>5.81</td>
<td>0.000</td>
<td>20/20-2</td>
<td>disciform scar</td>
</tr>
<tr>
<td>73</td>
<td>F</td>
<td>260</td>
<td>4</td>
<td>0</td>
<td>4.72</td>
<td>0.55</td>
<td>6.00</td>
<td>0.070</td>
<td>20/20-1</td>
<td>disciform scar</td>
</tr>
<tr>
<td>68</td>
<td>M</td>
<td>272</td>
<td>4</td>
<td>1</td>
<td>4.44</td>
<td>0.52</td>
<td>6.02</td>
<td>0.070</td>
<td>20/20-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>297</td>
<td>4</td>
<td>4</td>
<td>4.50</td>
<td>0.53</td>
<td>5.60</td>
<td>—</td>
<td>20/25-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>346</td>
<td>4</td>
<td>0</td>
<td>4.26</td>
<td>-0.04</td>
<td>5.65</td>
<td>0.050</td>
<td>20/25-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>60</td>
<td>F</td>
<td>349</td>
<td>4</td>
<td>1</td>
<td>4.89</td>
<td>0.30</td>
<td>5.81</td>
<td>0.050</td>
<td>20/20+2</td>
<td>disciform scar</td>
</tr>
<tr>
<td>81</td>
<td>F</td>
<td>369</td>
<td>3</td>
<td>2</td>
<td>4.32</td>
<td>0.32</td>
<td>5.15</td>
<td>0.040</td>
<td>20/25-3</td>
<td>disciform scar</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>376</td>
<td>4</td>
<td>1</td>
<td>5.29</td>
<td>0.66</td>
<td>5.98</td>
<td>0.080</td>
<td>20/15</td>
<td>disciform scar</td>
</tr>
<tr>
<td>74</td>
<td>M</td>
<td>397</td>
<td>1</td>
<td>3</td>
<td>4.64</td>
<td>0.43</td>
<td>5.68</td>
<td>0.050</td>
<td>20/20-3</td>
<td>disciform scar</td>
</tr>
</tbody>
</table>

Best corrected acuities and brief descriptions of fundus appearance of eyes which themselves have exudative AMD are also tabulated. Individuals are listed in order of increasing time constant of dark adaptation.

"SC X°" signifies log S cone sensitivity to an X° diameter test. "Abs sens" signifies log sensitivity at absolute threshold to a 660 nm test. In each case, units are in -log (Mw/deg 2). "CMAE" signifies the color-match-area-effect. "bca" signifies best corrected acuity. "AMD eye" signifies the eye with exudative AMD. Description of all testing parameters are in the Materials and Methods section of the preceding paper. The individual with the 297 sec time constant has a congenital deutan defect, but would otherwise meet all the criteria for entry into the study; his data are not included in graphs or statistical analyses of psychophysical or funduscopic data.

Epidemiological Findings

All subjects were asked if they had ever smoked. A comparison of fundus appearance scores for eyes with good acuity whose fellow eye has suffered from exudative AMD (P < 0.05) (Fig. 4). This finding implies that the foveal cones in eyes whose fellow eye has suffered from exudative AMD are more likely to have substantially reduced effective photopigment density than are the foveal cones of eyes whose fellow eye has not suffered from exudative AMD. Group I eyes having color-match-area-effects of less than 0.2 or 0.3 were found to have lower sensitivities at absolute threshold than those Group I eyes having greater color-match-area-effects (P < 0.05), when 20/25 eyes were admitted into the comparison.

Small-field anomaloscope matching ranges did not appear to differ between Group I and Group II eyes (P > 0.5).
Table 2. Normative fundus appearance scores

<table>
<thead>
<tr>
<th>Hypopigmentation score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drusen Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>44 (5)</td>
<td>2 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>1</td>
<td>118 (10)</td>
<td>4 (3)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>2</td>
<td>27 (6)</td>
<td>7 (0)</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>3</td>
<td>3 (1)</td>
<td>1 (1)</td>
<td>2 (0)</td>
<td>2 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>4</td>
<td>3 (0)</td>
<td>0 (0)</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Number of eyes whose fellow eye has not suffered from exudative AMD, as a function of fundus appearance scores. Non-parenthetical entries represent number of eyes with 20/20 or better acuity. Parenthetical entries represent number of eyes with 20/25 acuity.

Discussion

We found that those eyes whose fellow eye has suffered from exudative AMD have themselves suffered compromised foveal function, even though they may still retain 20/20 or better acuity and not have any macular lesions which are detectable with direct ophthalmoscopy or fundus photography. We found also that those eyes tend to have more macular drusen and/or atrophic change than do eyes whose fellow eye has not suffered from exudative AMD. The deficits of visual function probably reflect RPE dysfunction. We found that the eyes with the most drusen and/or atrophic change were the eyes with the slowest rates of sensitivity recovery during dark adaptation. While this finding was not unexpected, the association of many drusen with slow recovery need not be causal. The lack of a significant relation between fundus appearance and function for the other visual functions that we measured may reflect (1) less dependence on RPE integrity; (2) dependence on aspects of RPE integrity not evident ophthalmoscopically; or (3) relatively greater dependence on processes proximal to the photoreceptors.

The existence of negligible color-match-area-effects for some eyes suggests that losses of sensitivity at absolute threshold, and probably S cone sensitivity losses as well, are sometimes due to decreases in the effective photopigment density, ie, the quantum catching ability, of the foveal cones. Conversely, the existence of appreciable color-match-area-effects found for the majority of eyes suggests that not all the loss of sensitivity is due to decreased effective photopigment density of the cones. When a decrease in effective photopigment density does exist, the decrease may be due any of several factors: decrease in concentration of photopigment within the cones, misalignment of the cones due to photoreceptor dropout or to local traction on the retina,19 or change of refractive index in the outer retina.19

The losses of absolute sensitivity at long wavelengths which we found tended to be less than those found by Sunness et al20 for a similar population. The quantitative discrepancy between our results and those of Sunness et al exists probably because the subjects whom we tested met relatively strict eligibility criteria, and because we evaluated losses against age-matched norms. Sunness et al found that absolute sensitivity losses are greatest in the central retina. We did not measure absolute sensitivity at different retinal loci, but we did find greater losses of S cone sensitivity for 1° than for 3° diameter foveal tests. This finding may mean that the greatest losses of S cone sensitivity occur in the central fovea. Alternatively, the greater losses of S cone sensitivity for 1° versus 3° tests may reflect a compensatory increase in spatial integration area associated with diffuse photoreceptor compromise, rather than greater pathology in the central fovea.
Red/green color discrimination (as defined by the Rayleigh match width) did not appear to be any worse for eyes whose fellow eye had suffered from exudative AMD than it did for eyes whose fellow eye had not suffered from exudative AMD. Therefore, it appears that measuring visual sensitivity at threshold may be more effective than measuring color discrimination of suprathreshold stimuli for detecting macular pathology.

Key words: aging, exudative, macular degeneration, drusen, retinal pigment epithelium

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References