Lens-Corrected Visual Field Sensitivity and Diabetes

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Purpose. To examine whether peripheral S-cone system and achromatic sensitivity was reduced in patients with diabetes compared to normal controls.

Methods. Perimetric measurements were obtained to study peripheral S-cone system and achromatic sensitivity in patients with diabetes and normal controls. Measures of individual lens absorption of short-wavelength light were used to correct visual field sensitivity values for attenuation of test light due to lens absorption.

Results. Both before and after correction for lens absorption of test spot light, peripheral field-averaged S-cone system and achromatic sensitivities were not significantly reduced among patients with diabetes compared to normals of the same age. However, localized sensitivity losses in the visual field were found in most patients with diabetes both before and after lens absorption correction, compared to age norms. The amount of localized loss (number of field locations with reduced sensitivity) was significantly correlated with the level of retinopathy. Statistical analysis showed that after the effects of age and duration were removed, field-averaged S-cone system sensitivity in patients with diabetes was also significantly reduced as a function of increasing severity of retinopathy.


Previous studies have reported changes in color vision with diabetes. Studies using the Farnsworth-Munsell 100-Hue (FM100-hue) test showed an association between overall increased error scores and the presence of a tritan axis with the development of diabetic retinopathy. Some studies have shown a correlation between increased FM 100-hue error scores and the presence of macular edema in patients with diabetes. Increment threshold techniques have also been used to study color vision changes with diabetes and have shown a reduction in short-wavelength-sensitive (S) cone system sensitivity compared to normals. All the above studies used foveally presented stimuli.

Reductions in achromatic sensitivity in the peripheral retina in patients with diabetes have been reported.11-13 The areas of reduced sensitivity in individuals with diabetes were associated with areas of retinal capillary nonperfusion. The above findings suggest that S-cone system changes might also occur in the periphery, and that these changes may be associated with features of diabetic retinopathy such as capillary nonperfusion.

Most of these previous studies have not corrected for lens absorption factors. Lutze and Bresnick14 have shown that the lenses of patients with diabetes are denser or "yellower" than controls of the same age. This finding indicates the importance of measuring individual lens absorption in patients with diabetes when studying color vision using short-wavelength stimuli. It is possible that the previously observed changes in color vision with diabetes were, at least in part, attributable to absorption of short-wavelength light by the lens.

In this study, we looked at S-cone system and achromatic visual field sensitivity in patients with diabetes and normal controls. Lens absorption was measured in each individual, and visual field sensitivities were corrected for absorption of test light by the lens.

MATERIALS AND METHODS

Equipment

A modified Humphrey Field Analyzer (perimeter; Allergan-Humphrey, San Leandro, CA) was used to obtain visual field sensitivities. The Humphrey 30-2 pro-
gram and test spot size V were used to obtain thresholds for blue test spots presented on a bright, yellow background (S-cone system condition) and for white test spots presented on a white background (achromatic condition).

Modifications made to the equipment to allow for color perimetry were similar to those reported by Johnson and coworkers.\(^1\)\(^5\)\(^1\)\(^6\) Two additional light sources (80 W Kodak quartz-halogen projector bulbs, Eastman Kodak, Rochester, NY) were attached to the front panel of the perimeter, which allowed brighter background luminances than provided by the original equipment. Broad-band yellow (Schott OG530) filters were used to modify light output, which created a uniform, bright yellow globe illuminance. A photocell and electronic circuit were used to provide background calibration information. The luminance of the yellow background was 200 c/m\(^2\). The broad-band blue filter original to the equipment (OCLI blue) was used to present blue test spots.

For the achromatic condition, standard Humphrey conditions were used for white test spots presented on a white background. The luminance of the white background (10 c/m\(^2\)) was set by the original equipment.

Measurements of near visual acuity (30 cm) were obtained for each subject, and large, rimless lenses were used to correct refractive error. All subjects were correctable to at least 20/30 near acuity.

**Lens Absorption Measurements**

Lens density measurements were obtained on all subjects. The procedure for measuring lens density was explained in detail elsewhere.\(^1\)\(^4\) Scotopic thresholds for 420 and 550 nm stimuli were determined. The difference between the thresholds for the two wavelengths was taken as the lens density index. Because these two wavelengths are equated on the rod spectral absorption curve,\(^1\)\(^7\) elevated thresholds for the 420 nm stimulus compared to the 550 nm stimulus indicated the amount of 420 nm light absorbed by the lens.

**Correction of Field Sensitivity Measures for Light Absorption**

A method was developed to correct visual field sensitivities for lens absorption of test spot light. With this method, individual lens density measurements were used to calculate the amount of test spot light absorbed by the lens for a field-average sensitivity value. This amount of light was then added to the field-average sensitivity value, which gave a lens-corrected sensitivity measure.

For our testing conditions, lens absorption correction was necessary only for the test spot light, not the background light. The yellow background used for S-cone measurements was created with a 530-nm cut-off filter, which removed wavelengths that would be preferentially absorbed by the lens. The achromatic testing condition background level was in the flat portion of the TVI curve; therefore, correction was not necessary.

Figure 1 shows a schematic of the method used to calculate the amount of light absorbed by the lens with our experimental design for measuring S-cone system field sensitivity. This method is similar to that used for calculating chromaticity coordinates\(^1\)\(^8\) with the lens as filter. The output of the light source (tungsten-halogen lamp) was multiplied by the spectral transmission of the filter used to create the blue test spots. This product was then multiplied by lens transmission for wavelengths 400 to 500 nm. (Lens transmission for an individual was measured at 420 nm,\(^1\)\(^4\) and this value was used to choose the proper spectral lens transmission curve for that individual.\(^1\)\(^4\)\(^1\)\(^9\) This assumes that the shape of the lens transmission curve for a given individual is the same as the family of curves described for different ages.) This product was then multiplied by the Zbar 1951 CIE color matching function\(^1\)\(^7\) for 400 to 500 nm. The area under the resulting curve gave an estimate of the amount of light absorbed by the lens.

A similar procedure was used to correct the white-on-white field sensitivity measures. The range of wavelengths used for the white-on-white procedure was 400 to 700 nm, and \(V_{x\ell}\) was used instead of the Zbar 1951 color-matching function.

**Data Averaging**

Overall field-averaged sensitivities were obtained by averaging all values for an individual field test except for two points, one above and one below the blind spot. These two points were eliminated from the analysis because of interindividual variation in blind spot locations. Seventy-four points were included in each field average.

The means and standard deviations for the lens-corrected sensitivity value for each test spot location were also obtained for 10 normal, control observers in each of five age decades.

**Subjects**

Thirty-one patients with diabetes participated in the study. All had insulin-dependent type I diabetes. Level of retinopathy ranged from none to proliferative (no retinopathy, \(n = 6\); mild nonproliferative, \(n = 10\); moderate nonproliferative, \(n = 4\); severe nonproliferative, \(n = 4\); proliferative, \(n = 7\)), and no tested eye received laser treatment or showed macular edema or vitreous hemorrhage. No eye had distance corrected visual acuity worse than 20/80. The ages of patients with
diabetes ranged from 19 to 59 years (median = 30 years). Seventeen men and 14 women participated in the study. Duration of diabetes ranged from 4 to 34 years (median = 21 years).

Fifty control subjects participated in the study; 10 subjects in each age decade (age range, 20 to 69 years; median = 42 years) were included in the study. Seventeen normal controls were men and 33 were women. Control subjects reported no history of diabetes or eye disease, and subjects older than 59 years were examined and assessed to be free from retinal pathology, glaucoma, and cataracts.

The research followed the tenets of the Declaration of Helsinki, informed consent was obtained from each subject after the nature and possible consequences of the study were explained, and the research was approved by the institutional human experimentation committee.
RESULTS

Averaged-Field Sensitivity

Patients With Diabetes Versus Normal Controls With Age. S-Cone System Condition. Figure 2a shows results for averaged, S-cone system visual field sensitivities before correction for lens absorption. There is an apparent difference in the slopes of the regression lines for sensitivity with age between our sample population with diabetes and normal controls; however, this difference was not statistically significant at the $P < 0.05$ level. Figure 2b shows averaged, S-cone system visual field sensitivities after correction for lens absorption. The difference between the two groups was reduced such that the difference in sensitivity between groups at all ages appeared to be similar, and the slopes of the regression lines for sensitivity with age were not significantly different (F-test, $P < 0.05$). Additional statistical evaluation showed that the means for patients with diabetes and normals for age decades 20 to 29, 30 to 39, and 40 to 49 were not significantly different for either the lens-corrected or the lens-uncorrected data sets (analysis of variance, $P < 0.05$). There was no statistically significant difference in the variances (F-test, $P < 0.05$) for either the lens-corrected or lens-uncorrected S-cone condition between normals and patients with diabetes, although after lens absorption correction the variances for the two groups appeared more similar.

Achromatic Condition. Figure 3 shows results for both the lens-uncorrected (Fig. 3a) and lens-corrected (Fig 3b) white-on-white condition. The apparent difference between the two groups seemed slightly reduced after correction for lens absorption of test spot light; however, the difference in slope between the two best-fit lines was not significantly different (F-test, $P <
0.05) for either the lens-uncorrected or lens-corrected data sets. A significant difference was not found between the means for patients with diabetes and normals (analysis of variance, $P < 0.05$) for age decades 20 to 29, 30 to 39, and 40 to 49 for either the lens-corrected or lens-uncorrected data sets.

**Patients With Diabetes Only: Age, Duration of Diabetes, and Level of Retinopathy. S-Cone Condition.** Stepwise regression analysis, including age, duration of diabetes, and level of retinopathy, showed that after the effects of age and duration were removed, retinopathy level was significantly correlated ($P < 0.05$) with lens-corrected S-cone system sensitivity. In our data, there was no significant improvement in predicting S-cone system sensitivity by including age and duration in the analysis.

**Achromatic Condition.** Stepwise regression analysis, including age, duration of diabetes and level of retinopathy, showed that there was no significant correlation at the $P < 0.05$ level between lens-corrected achromatic sensitivity and these variables.

**Localized Visual Field Loss**

Sensitivities for 10 normal, control observers in each of five decades were determined for each of the 74 points tested, and average sensitivities and standard deviations per decade were determined for both lens-corrected and lens-uncorrected S-cone system and achromatic visual field points. The pattern of these values represents the “hill of vision” for normals of a particular age decade for each condition. Lens-corrected sensitivities were compared point-by-point between each patient with diabetes and the age norms. A reduction in sensitivity $>2$ SD from the normal mean for each point was taken as localized loss for that diabetic patient.

Table 1 shows results from this analysis for lens-corrected data for each test condition. Most patients with diabetes (20 of 31, S-cone system; 27 of 31, achromatic) had at least one point that was reduced compared to normal controls. Simple regression analysis showed that for each lens-corrected condition (S-cone system and achromatic) the number of localized-loss points was significantly correlated with level of retinopathy ($P < 0.01$), with a greater number of localized-loss points correlating with greater retinopathy.

Analysis of sensitivity measures before lens absorption correction showed that there were greater numbers of localized-loss points (reduction compared to age norms) per patient with diabetes for the lens-uncorrected data compared to the lens-corrected data. With the S-cone condition, 30 of 31 patients with

| TABLE 1. Number of Field Points Showing Localized, Lens-Corrected Sensitivity Loss for Each Patient With Diabetes for Each Condition, With Level of Retinopathy (Total Points Tested = 74) |
|---|---|---|---|---|
| | No Retinopathy (n = 6) | Mild NPDR* (n = 10) | Moderate NPDR (n = 4) | Severe NPDR (n = 4) | Proliferative Retinopathy (n = 7) |
| S-Cone System | 0 | 0 | 0 | 0 | 2 |
| 0 | 0 | 1 | 0 | 8 |
| 0 | 0 | 8 | 0 | 23 |
| 0 | 1 | 19 | 16 | 30 |
| 10 | 5 | | | 38 |
| 39 | 5 | | | 61 |
| 5 | 5 | | | 66 |
| 9 | 9 | | | |
| 14 | | | | |
| Mean | 8.2 | 4.8 | 7 | 4 | 32.6 |
| Achromatic | 1 | 0 | 0 | 0 | 17 |
| 1 | 0 | 2 | 1 | 21 |
| 1 | 1 | 5 | 9 | 35 |
| 1 | 2 | 11 | 32 | 39 |
| 1 | 6 | | | 45 |
| 5 | 7 | | | 53 |
| 9 | | | | 58 |
| 13 | | | | |
| 18 | | | | |
| 32 | | | | |
| Mean | 1.7 | 8.8 | 4.5 | 10.5 | 38.3 |

* NPDR = Nonproliferative diabetic retinopathy.
diabetes had a greater number of localized-loss points before lens absorption correction. With the achromatic condition, 28 of 31 showed a greater number of localized-loss points before lens absorption correction.

DISCUSSION

The results of our study indicated that averaged visual field sensitivity in insulin-dependent type I patients with diabetes was not significantly reduced compared to normals of the same age. However, lens-corrected S-cone system field sensitivity was significantly reduced with greater levels of retinopathy. Localized S-cone system and achromatic visual field losses (compared to age norms) were found for most patients with diabetes, with more localized loss occurring in patients with greater retinopathy.

Studies have demonstrated foveal reductions in S-cone system sensitivity for patients with diabetes compared to normal controls (see introduction). Our findings of localized sensitivity loss in most patients could be considered consistent with the previous foveal studies. Perhaps the fovea is one localized site of vulnerability to sensitivity loss. Whether the fovea is particularly vulnerable to sensitivity loss versus peripheral sites requires further study.

In a previous study of lens yellowing in patients with diabetes and normal controls, we showed that persons with diabetes had yellower lenses than normals of the same age. Our results in the present study before lens absorption correction did not show a significant reduction in S-cone sensitivity compared to normals, even though our previous work showed that lenses of patients with diabetes have increased density compared to normals of the same age. Viewing Figure 2a, most of our observers with diabetes were younger than 40 years of age. Inclusion of more subjects older than 40 years may be necessary to uncover a possible difference in sensitivity with age over the life span.

The study reported by Lutze and Bresnick (1991) suggests that increased lens yellowing may contribute to an apparent reduction in S-cone system sensitivity in subjects with diabetes. One report in the literature that considered the lens found supporting evidence that lens factors contribute to the difference found between normals and patients with diabetes in color vision measurements. Daley and coworkers found that 10 of 12 subjects with diabetes tested showed an "absorptive" type deficit of blue-flicker discrimination, which was consistent with a lens-absorption effect.

Other studies in the literature have provided evidence that a true reduction in foveal S-cone system sensitivity can exist with lens yellowing factors ruled out. Zwas and colleagues used an increment thresh-

old technique to study sensitivity in patients with diabetes and found a reduction in sensitivity in some subjects even after correction for lens absorption. Adams and coworkers did not find a relative reduction in achromatic flicker sensitivity in the short-wavelength region for patients with diabetes compared to normals, but they did find a reduction for chromatic sensitivity in this region. Greenstein and coworkers did not measure lens transmission in their subjects; however, their method of comparing π1 and π2 system sensitivity using a single test wavelength excluded lens transmission factors as an explanation for their finding that S-cone system sensitivity was selectively reduced.

Our study showed that lens-corrected, S-cone system, averaged-field sensitivity was reduced with the increasing level of retinopathy, and most of the patients with diabetes we tested showed localized reduction in sensitivity both for the S-cone system and achromatic testing conditions. Further study is needed to determine whether localized reduction in field sensitivity correlates with areas of the retina that have or will soon develop retinopathic changes such as reduced capillary perfusion, localized blood-retinal barrier breakdown, or the presence of vascular lesions such as microaneurysms.

Key Words
S-cones, retinopathy, perimetry, lens, diabetes

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