Diabetic Short-Wavelength Sensitivity: Variations With Induced Changes in Blood Glucose Level
Vicki J. Volbrecht,* Marilyn E. Schneck,* Anthony J. Adams,* John A. Linfoot,† and Everett Ar‡

Purpose. To investigate variations in diabetic short-wavelength sensitivity with acute, induced changes in blood glucose level.

Methods. Increment threshold measures were obtained for short-wavelength–sensitive and middle/long-wavelength–sensitive cone pathways after an induced, acute change in blood glucose level in diabetic observers.

Results. Diabetic observers showed an increase in short-wavelength sensitivity, but no change in middle/long-wavelength sensitivity, with a rapid drop in blood glucose level.


It is well documented that individuals suffering from diabetes display color vision losses. This color vision loss is substantiated by spectral sensitivity measures that show diabetic short-wavelength (SW) sensitivity lower than that of nondiabetics.1–3 Furthermore, SW sensitivity fluctuates across days of measurement, whereas middle- and long-wavelength (M/LW) sensitivity remains relatively stable.4 Others have demonstrated similar color vision variations with the FM 100-hue test. For example, Harrad et al5 administered the FM 100-hue test at three different blood glucose levels. When subjects with diabetes were hypoglycemic (low blood glucose level), their performance on the SW test stimulus either above the black line or below the black line was approximately 1° of visual angle. A Watten 47B broad-band filter defined the spectral properties of the SW test stimulus; the dominant wavelength as specified by the manufacturer’s guidelines for a tungsten source used in this optical system was 452 nm. The spectral composition of the M/LW test stimulus was the same as the adapting background.

The current study systematically investigated the relationship between blood glucose level and SW sensitivity in subjects with diabetes. Measurements of SW sensitivity and M/LW sensitivity were made under conditions of induced hyperglycemia (high blood glucose level) as well as during a 2-hour period in which blood glucose level was rapidly decreased. Diabetic SW sensitivity was directly affected by changes in blood glucose level, whereas M/LW sensitivity was not.

MATERIALS AND METHODS. Subjects. Eighteen patients with diabetes at the Diabetes and Endocrine Institute of Providence Hospital in Oakland, California, participated in this study. The volunteers were either recently diagnosed as diabetic or had a history of poor metabolic control under conventional treatment. Table 1 summarizes the characteristics of these patients. Mean visual acuity as assessed with the high-contrast Bailey-Lovie eye chart was 0.0 log MAR (range: −0.24 to 0.19 log MAR). All but one observer, a congenital deutan, were color normal according to the FM 100-hue test, D-15 test panel test, and the Adams desaturated D-15 test, and thus showed no evidence of a tritan color loss.

Informed consent was obtained from all subjects with diabetes after information was provided as to the nature and purpose of the experiment. The experimental methods followed the guidelines established by the Declaration of Helsinki, and was approved by the University of California and Providence Hospital human subject committees.

Stimulus and Apparatus. A portable, two-channel, rear-view projection optical system interfaced with a Macintosh SE computer (Apple, Cupertino, CA) was used to make threshold measures. One channel of the optical system projected a 6°, 200 cd/m² yellow adapting background (λd = 586 nm; x = 0.55, y = 0.45) onto the viewing screen. This adapting background was divided into two equal parts by a narrow horizontal black line. The second optical channel randomly presented a 1.5°, 300 millisecond test stimulus either above the black line or below the black line. The distance from the edge of the test stimulus to the black line was approximately 1° of visual angle. A Watten 47B broad-band filter defined the spectral properties of the SW test stimulus; the dominant wavelength as specified by the manufacturer’s guidelines for a tungsten source used in this optical system was 452 nm. The spectral composition of the M/LW test stimulus was the same as the adapting background.

Procedure. Threshold measures were obtained for diabetic subjects at varying blood glucose levels.

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The specific methods used to measure threshold and to manipulate blood glucose level are outlined below.

**Threshold Measures.** Observers monocularly adapted for 1 minute to the yellow background. After this initial adaptation, a single-staircase, two-alternative, forced-choice procedure was used to measure the M/LW threshold, followed immediately by a measurement of the SW threshold. Because each threshold measurement took approximately 2 minutes, at least 3 minutes of adaptation to the yellow background preceded measurement of the SW threshold. Adams et al,\(^6\) using a variant of this procedure, demonstrated that this particular adaptation period successfully isolated the short-wavelength-sensitive (SWS) mechanism. Initial step size for stimulus intensity in the staircase was 1 log unit, and was continuously decreased by one half over a series of reversals to the smallest step size of 0.125 log unit. At the larger step sizes (1.0 and 0.5 log unit), one correct answer decreased the stimulus intensity and one incorrect answer increased the stimulus intensity. At the smaller step sizes (0.25 and 0.125 log unit), three correct answers made the test stimulus dimmer, and one incorrect answer made the test stimulus brighter.

Observers were instructed to fixate on the center of the horizontal dividing line on the adapting field and respond whether the test stimulus appeared above or below the black line by pressing the appropriate button. The staircase continued until four reversals were obtained at the smallest step size. A mean threshold was computed from the four threshold values ascertained at the last four reversals. A mean value was accepted only if the standard deviation was less than 0.25 log unit. Whenever possible, the staircase was repeated for standard deviations greater than or equal to 0.25 log unit; however, time constraints sometimes precluded repeated testing.

The same procedure was repeated to obtain SW and M/LW thresholds for the other eye. Only data from one eye of an observer were used in the analyses. Whenever possible, data from the right eye were used; however, data from the left eyes of four diabetic subjects were used because the standard deviations of the critical measurements of the right eye exceeded the criterion for inclusion (standard deviation > 0.25 log unit), only the left eye was tested, or technical problems occurred during testing of the right eye.

**Insulin Administration.** Twenty-four hours before an experimental session, the observers with diabetes refrained from taking their medication, maintaining their restricted diet, or both, thereby inducing hyperglycemia. At the start of the experimental sessions, the diabetic subject’s hyperglycemic blood glucose level was determined, followed by measurements of M/LW and SW thresholds.

After these measurements, insulin administration commenced. Each diabetic subject received a bolus injection of insulin and a continuous, intravenous infusion of insulin for up to a 2-hour period. The amount of insulin varied for each individual, depending on his or her high blood glucose value at the start of the session, known sensitivity to insulin, and past
medical history. The amount of insulin received by injection ranged from 6 to 25 units of insulin. The amount of insulin received by infusion ranged from 4 to 25 units per hour. Diabetic subjects were monitored continuously by medical personnel, who determined when the subject's blood glucose level had reached a level sufficiently low to terminate infusion.

Ten minutes after insulin injection and commencement of infusion, a blood glucose measure was taken, followed by M/LW and SW threshold measurements for each eye. This procedure of blood glucose and threshold measurements was repeated 20, 30, 45, 60, 90, and 120 minutes after the initial insulin administration.

RESULTS. To examine the effect of acute, rapid changes in blood glucose on visual function in subjects with diabetes, the SW and M/LW sensitivity values obtained at the highest blood glucose level were compared to the corresponding measures obtained at the lowest blood glucose level, which, depending on the individual, occurred 30 to 120 minutes after insulin administration. The high and low blood glucose values are specified in Table 2. For inclusion in the data analysis, the high and low blood glucose values needed to differ by at least 100 mg/dl, or the low blood glucose value needed to fall below 150 mg/dl, a blood glucose level considered to be the upper limit of the normal range for nondiabetic people. It was expected that if either criterion was not attained, a significant physiological change would not occur, and subsequently visual sensitivity would not be influenced. As a result of these criteria, the data from one observer (patient No. 5) were excluded from this analysis.

When more than one sensitivity measure was taken at a given time, a mean was computed from those values with a standard deviation less than 0.25 log unit. The mean standard deviations across observers was 0.13 log unit (range: 0.02 to 0.23 log unit). The log sensitivity differences are specified in Table 2, and the results are presented in Figure 1; differences are plotted on the left side of the figure and M/LW sensitivity differences are plotted on the right. Positive values indicate higher sensitivity at the low blood glucose level than at the high blood glucose level, whereas negative values indicate higher sensitivity at the high blood glucose level than at the low blood glucose level. For the diabetic observers, most of the SWS differences fall above the horizontal line, indicating an increase in sensitivity with a decrease in blood glucose. These SW sensitivity differences are statistically significant as determined by a one-tail, paired t test ($t_{16} = 3.92, P < 0.0005$). The M/LW sensitivity differences show no systematic change in sensitivity with changes in blood glucose, as demonstrated by an approximately even number of points falling above and below the horizontal line ($t_{16} = -0.28, P > 0.39$). The familywise error for the two multiple tests was 0.05, with a significance level of 0.025 for each individual test.

DISCUSSION. This study demonstrates that the SWS cone pathway of the visual system is dynamically responsive to transient changes in blood glucose level. To our knowledge, this is the first reported selective increase in diabetic SW sensitivity with an acute reduction in blood glucose level.

### TABLE 2. Blood Glucose Levels of Diabetics

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Blood Glucose Levels (mg/dl)</th>
<th>Log Differences</th>
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<tbody>
<tr>
<td></td>
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</table>

The high blood glucose readings of two of the patients exceeded the maximum reading (500 mg/dl) of the glucometer used in this study. Their values are denoted as >500.
Although it is now well established that a variety of ocular and systemic diseases, including diabetes, are harmful to the SWS cone pathway, causing a decrease in SW sensitivity, the site(s) of the loss is not well known. The loss in SW sensitivity in diabetes has been variously attributed to changes in the lens, loss of SWS cone receptors due to their greater vulnerability to insult, the reduced response range of normal SWS cones relative to LWS cones, and postreceptoral SWS functional losses either at the opponent site or beyond the opponent site.

The acute and reversible nature of SW sensitivity observed in this study constrains the choice of potential sites and mechanisms to explain this effect. Clearly, the current results imply that at least part of the SWS loss in diabetes cannot be ascribed to increased lens density or photoreceptor loss, because neither of these events is likely to be reversible. The current results, however, may reflect functional changes at the receptor level or at a postreceptoral site(s) at or beyond the opponent site, but the exact locus still needs to be isolated. The results do suggest that the changes in SW sensitivity are directly related to the transient metabolic state of diabetes and immediately tied to diabetic blood glucose levels, rather than to structural damage of vascular or neural tissues presumed to be involved in the SWS pathway loss in a variety of retinal diseases.

Key Words
diabetes, blood glucose, short-wavelength sensitivity, metabolic control

Scotopic Optokinetic Nystagmus Thresholds in 10-Week-Old Infants
Ronald M. Hansen and Anne B. Fulton

Purpose. To compare psychophysical and reflexive optokinetic nystagmus (OKN) estimates of dark-adapted scotopic thresholds mediated by the posterior retina in 10-week-old infants and adults.

Methods. A staircase procedure was used to determine the stimulus intensity needed to produce an OKN response to a moving 19° X 19° grating. In the same subjects, a two-alternative, forced-choice procedure was used to obtain thresholds for detecting 10° diameter, 50 ms duration stimuli.

Results. Both OKN and psychophysical thresholds of infants are 0.9 log unit higher than those of adults.

Conclusion. The infant–adult difference in thresholds mediated by retina at the posterior pole is greater than the infant–adult difference in thresholds for full-field stimuli. It is possible that delayed maturation of the posterior retina is the primary determinant of infants’ high OKN and psychophysical thresholds. Invest Ophthalmol Vis Sci. 1994; 35:1246–1249.

The dark-adapted, rod-mediated thresholds of young human infants are significantly higher than those of adults. However, the magnitude of the threshold elevation is not constant across procedures. At age 10-weeks, dark-adapted infants’ scotopic ERG and VEP thresholds for full-field stimuli are only about

References