Contrast Sensitivity in Obese Dyslipidemic Patients With Insulin Resistance

André A. Dosso, MD; Ferah Yenice-Ustun, MD; Jorg Sommerhalder, PhD; Alain Golay, MD; Yves Morel, MD; Peter M. Leuenberger, MD

Objective: To evaluate contrast sensitivity in insulin-resistant obese patients and in aretinopathic diabetic patients.

Methods: Contrast sensitivity was measured at 3 letter sizes (44 × 44, 9 × 9, and 5 × 5 mm) in mesopic (5 candela [cd]/m²) and low photopic (85 cd/m²) vision in 20 dyslipidemic obese patients with insulin resistance, 20 age-matched patients with type 2 diabetes mellitus, and 20 aged-matched healthy control subjects.

Results: Significant loss of contrast sensitivity at all 3 letter sizes was observed in low photopic vision (at 44 × 44-mm letter size, control vs obese, \( P < .002 \), and control vs diabetic, \( P < .001 \); and at 5 × 5-mm letter size, control vs obese, \( P < .05 \), and control vs diabetic, \( P < .005 \)) and mesopic vision (at 44 × 44-mm letter size, control vs diabetic, \( P < .005 \); at 9 × 9-mm letter size, control vs obese, \( P < .005 \), and control vs diabetic, \( P < .001 \); and at 5 × 5-mm letter size, control vs obese, \( P < .005 \), and control vs diabetic, \( P < .001 \)) in insulin-resistant obese and diabetic patients.

Conclusion: The results suggest that an early neurosensory dysfunction may occur without visible vascular involvement and without overt hyperglycemia.


Patients with diabetes mellitus, with or without clinically visible vasculopathy, exhibit reduced contrast sensitivity and color perception, alterations in the pattern electroretinogram, and changes in visual-evoked potentials. In patients with advanced disease, visual dysfunction correlates with the severity of the retinopathy.

The presence of visual pathway dysfunction in some diabetic patients with clinically normal retinas and in a number of patients with type 1 diabetes mellitus within weeks of diagnosis and the failure to find any correlation between visual pathway dysfunction and the duration of diabetes suggest that visual pathway dysfunction in diabetes mellitus may not be primarily a microvascular complication. Instead, it may be the result of reversible changes in retinal function, possibly at the level of the ganglion cells.

Therefore, a better understanding of the nature of these abnormalities of visual function, as well as the course of their development and progression, could provide insight into the mechanisms involved in visual loss in diabetic patients.

To evaluate whether contrast sensitivity changes are precursors to the vascular type of diabetic retinopathy, we studied a possible visual dysfunction in aretinopathic patients with diabetes mellitus and in obese dyslipidemic patients with insulin resistance by contrast sensitivity testing. Furthermore, we determined risk factors for contrast sensitivity deficits.

RESULTS

The fasting plasma glucose level was significantly higher in group 2 than in groups 1 and 3. No significant differences were found between groups 1 and 2 for systolic and diastolic blood pressure measurements and for body mass index and levels of total plasma cholesterol, high-density lipoprotein cholesterol, and total plasma triglycerides. The steady state plasma glucose concentration, a measure of the efficacy of insulin to dispose of the infused glucose load, was 10.0 ± 1 mmol/L (reference range, <8 mmol/L) in group 1.

The distribution of contrast sensitivity measurements in groups 1, 2, and 3 is shown in Figure 2 and Figure 3. Compared with those of group 3, the distribu...
PATIENTS, SUBJECTS, AND METHODS

PATIENTS AND SUBJECTS

We studied 20 insulin-resistant obese patients (group 1) and compared them with 20 age-matched patients with type 2 diabetes mellitus (group 2) and with 20 age-matched control subjects (group 3). None of the patients had visible retinal abnormalities. The median age (60 years) was identical in the 3 groups (range, 40-72 years), and the median duration of diabetes was 12 years (range, 9-37 years).

A body mass index exceeding 25 kg/m² served as the criterion of obesity. The cutoff fasting plasma glucose level was less than 6.0 mmol/L (108 mg/dL) in groups 1 and 3.

The current metabolic control status of the group 2 patients was estimated by hemoglobin A₁c concentrations (mean ± SD of the fasting glucose level, 0.09 ± 0.01) ranging between 0.07 and 0.11. The results of eye examinations, including corrected Snellen acuity, tonometry, slit-lamp examination of the lens and anterior chamber, and fundus biomicroscopy, 5-field fundus photographs, were normal in all patients and subjects. The absence of retinopathy was assessed by slitlamp biomicroscopy using a 90-diopter lens and by 5-field photographs. The fundus photographs were evaluated independent of the ophthalmologic and the psychophysical examinations.

None of the patients in groups 1 and 2 had earlier experience with the Gradual Contrast Sensitivity test (OPSIA, Ramonville, France). None of the group 3 subjects was receiving medication, none had a history of diabetes or eye disease, and none was known to have abnormal contrast sensitivity. Informed consent was obtained when the nature of the technique and the aim of our research were explained in detail.

CONTRAST SENSITIVITY

For all subjects and patients, visual acuity was measured for each eye on the day of contrast sensitivity testing by using projected Snellen optotypes at 6 m in standardized conditions (ie, a display of a minimum of 200 candela [cd]/m² and a maximum of 500 cd/m²). Optical correction was worn when necessary. All patients had a Snellen acuity of 20/20 or better.

Contrast sensitivity was measured with a Gradual Contrast Sensitivity test. This test consists of 11 rows of 10 Sloan letters engraved on a retroilluminated translucent chart with 3 levels of brightness (5, 85, and 700 cd/m²). The letters are set in 10 columns, and each column is numbered from C₁ to C₁₀ (Figure 1). As a result, the best and the worst performance for every line are marked with C₁₀ and C₁, respectively. The letters vary in size and in contrast. Optotype dimensions vary from 87 × 87 mm to 4 × 4 mm. The letters decrease in contrast by steps of approximately 0.15 log units, starting at a contrast of 93% on the left side of the screen. The test is administered like an ordinary acuity test. The subject names the letters, and the test continues until 2 or more errors are made in a line. The test is forced-choice; blank responses are not allowed. The test is administered at 3 m under controlled room illumination (0.5 lux). Contrast sensitivity was tested in each eye separately and determined at 3 letter sizes (44 × 44, 9 × 9, and 5 × 5 mm) and for mesopic (5 cd/m²) and low photopic (85 cd/m²) vision. Contrast sensitivity was recorded as log contrast sensitivity [log (1/contrast of letters at the threshold of visibility)].

OPACITY OF THE CRYSTALLINE LENS

The opacity of the lens was evaluated as described previously by using the Opacity Lensmeter 701 (Interzag, Zurich, Switzerland) that functions like a slitlamp. Briefly, a 1.5-mm–diameter light source (light-emitting diode at 700 nm) is projected into the eye. A fraction of the light, back-scattered by the lens, is sampled by a detector. The intensity of the sampled light is processed and displayed as a numeric value between 0 and 99, where 0 corresponds to a perfectly transparent lens. At opacity values between 25 and 30, the patients typically request surgery to remove cataracts. Within 0.5 second, 250 readings were taken and electronically stored as 1 single, averaged measurement. A series of 3 such measurements per eye were taken and averaged again.

INSULIN SENSITIVITY MEASUREMENT

Insulin sensitivity was measured by a modified insulin suppression test. This approach is based on the use of somatostatin to inhibit endogenous insulin secretion, simultaneous infusion of exogenous insulin to achieve an identical steady state plasma insulin concentration in all subjects, and determination of the steady state plasma glucose response to a continuous glucose infusion.

STATISTICAL ANALYSIS

All data are expressed as mean ± SD. An analysis of variance was used to assess the significance of the differences among groups 1, 2, and 3. The comparison of contrast sensitivity distributions in the 3 groups was made by using the χ² test. Multiple regression analysis was used to evaluate associations between deficits in contrast sensitivity and insulin resistance, age, duration of diabetes, and hypertension.
patients at the 9 × 9-mm and 5 × 5-mm letter sizes in low photopic vision (P < .3, P < .1, respectively), and mesopic vision (P < .05, P < .3, respectively).

At the time of the study, all 3 groups studied had similar opacity of the lens (15.1 ± 5, 14.9 ± 3.1, and 14.7 ± 3.3 for groups 1, 2, and 3, respectively).

Multiple regression analysis was performed with contrast sensitivity at the 3 letter sizes tested as the dependent variables, and age, duration of diabetes, and systolic and diastolic blood pressure measurements as the independent variables. We found a significant positive correlation between contrast sensitivity deficits of group 2 patients and systolic blood pressure measurements (P = .002) and age (P = .009) at the 44 × 44-mm letter size. In group 1, simple regression analysis was used to evaluate the relationship between age and insulin resistance and between contrast sensitivity deficits and insulin resistance. A significant positive correlation between age and insulin resistance was observed (P = .001); however, only a trend toward a positive correlation was found between contrast sensitivity deficits and insulin resistance.

### Physical and Biochemical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 20)</th>
<th>Group 2 (n = 20)</th>
<th>Group 3 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose, mmol/L (mg/dL)</td>
<td>5.1 ± 1.0 (92 ± 18)</td>
<td>9.5 ± 3.0 (171 ± 54)</td>
<td>4.9 ± 0.7 (88 ± 13)</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>132 ± 12</td>
<td>138 ± 21</td>
<td>129 ± 10</td>
</tr>
<tr>
<td>Diastolic</td>
<td>90 ± 9</td>
<td>83 ± 11</td>
<td>82 ± 5</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>30 ± 3</td>
<td>28 ± 5</td>
<td>23 ± 3</td>
</tr>
<tr>
<td>Cholesterol, mmol/L (mg/dL)</td>
<td>6.6 ± 0.6 (255 ± 23)</td>
<td>6.3 ± 1.0 (243 ± 39)</td>
<td>5.0 ± 1.0 (193 ± 39)</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol, mmol/L (mg/dL)</td>
<td>1.1 ± 0.1 (42 ± 4)</td>
<td>1.0 ± 0.3 (39 ± 12)</td>
<td>1.4 ± 0.5 (54 ± 19)</td>
</tr>
<tr>
<td>Triglycerides, mmol/L (mg/dL)</td>
<td>2.3 ± 1.0 (203 ± 88)</td>
<td>3.3 ± 2.6 (292 ± 230)</td>
<td>2.1 ± 1.3 (186 ± 115)</td>
</tr>
</tbody>
</table>

*For a description of the groups, see the “Patients and Subjects” section. Values are given as mean ± SD.
†Group 1 vs group 2, P < .001.
‡Group 3 vs group 2, P < .001.
§Group 3 vs group 2, P = .01.
∥Group 3 vs group 1, P = .01.
and insulin resistance at the 5 × 5-mm letter size at photopic and mesopic vision (P = .2).

**COMMENT**

Impaired insulin sensitivity is a common feature observed in obese patients. An increased plasma free fatty acid concentration and accelerated lipid oxidation, commonly associated with obesity, induce impairment of glucose metabolism, in particular storage and uptake of glucose and modifications of insulin sensitivity, eventually leading to insulin resistance. A number of studies have documented that diabetes develops in a large proportion of obese patients with glucose intolerance (for review, see Golay and Felber). The insulin-resistance state in patients with obesity is associated with abnormalities in carbohydrate and lipid metabolism, and no changes in the retinal vessel architecture could be clinically detected in these patients.

The contrast sensitivity method applied in the present study detected a decrease of visual function in obese insulin-resistant patients, before hyperglycemia occurred and before microvascular abnormalities in the retina could be recognized. The deficits were more severe in group 2 than in group 1. Many authors have shown that contrast sensitivity is abnormal in diabetic patients without retinopathy, and, recently, alteration of visual function was described in patients with impaired glucose tolerance. These data and the observation of contrast sensitivity deficits in insulin-resistant obese patients with no vascular retinal damage strengthen the concept that visual pathway dysfunction is likely to be the result of changes in retinal function secondary to carbohydrate metabolism alteration rather than a microvascular complication. Moreover, our results suggest that the retinal parenchyma is very susceptible to the modification of carbohydrate metabolism.

Impaired visual pathway function might be the result of preretinal factors, such as refractive error, anterior segment disorders, and media opacities, that impede the passage of light to the photoreceptors. Any type of lens opacity is associated with a progressive decrease of contrast sensitivity, but the association is greatest for nuclear lens opacity. The contrast sensitivity method applied in the present study detected a decrease of visual function in obese insulin-resistant patients, before hyperglycemia occurred and before microvascular abnormalities in the retina could be recognized. The deficits were more severe in group 2 than in group 1. Many authors have shown that contrast sensitivity is abnormal in diabetic patients without retinopathy, and, recently, alteration of visual function was described in patients with impaired glucose tolerance. These data and the observation of contrast sensitivity deficits in insulin-resistant obese patients with no vascular retinal damage strengthen the concept that visual pathway dysfunction is likely to be the result of changes in retinal function secondary to carbohydrate metabolism alteration rather than a microvascular complication. Moreover, our results suggest that the retinal parenchyma is very susceptible to the modification of carbohydrate metabolism.

Impaired visual pathway function might be the result of preretinal factors, such as refractive error, anterior segment disorders, and media opacities, that impede the passage of light to the photoreceptors. Any type of lens opacity is associated with a progressive decrease of contrast sensitivity, but the association is greatest for nuclear lens opacity. The contrast sensitivity method applied in the present study detected a decrease of visual function in obese insulin-resistant patients, before hyperglycemia occurred and before microvascular abnormalities in the retina could be recognized. The deficits were more severe in group 2 than in group 1. Many authors have shown that contrast sensitivity is abnormal in diabetic patients without retinopathy, and, recently, alteration of visual function was described in patients with impaired glucose tolerance. These data and the observation of contrast sensitivity deficits in insulin-resistant obese patients with no vascular retinal damage strengthen the concept that visual pathway dysfunction is likely to be the result of changes in retinal function secondary to carbohydrate metabolism alteration rather than a microvascular complication. Moreover, our results suggest that the retinal parenchyma is very susceptible to the modification of carbohydrate metabolism.

Loss in contrast sensitivity also can be considered as the consequence of functional disturbances at the level of the retina or of the postretinal neuronal pathways. It seems to be related to the involvement of the ganglion cells, although more generalized effects at every retinal neurosensory cell could not be ruled out. Moreover, abnormalities of higher cerebral function also may be important, particularly during moderate or severe hypoglycemia.

A positive correlation between the loss of contrast sensitivity and the systolic blood pressure measurement and advanced age was found in group 2 at the largest letter size but not at the 2 other letter sizes. Our results are consistent with the observations of others that high blood pressure is a risk factor for the development or progression of diabetic retinopathy. The duration of diabetes is the strongest variable correlated with the risk of diabetic retinopathy. However, no correlation between the duration of diabetes and contrast sensitivity was found in the present study. This could be explained by the difficulty of evaluating the exact duration of type 2 diabetes mellitus, as the precise beginning of the disease is impossible to determine. However, the failure to find any correlation between visual pathway dysfunction and the duration of diabetes, as observed in other studies, suggests that visual pathway dysfunction in diabetes is not a complication of abnormal microvasculature. No correlation was observed between insulin resistance and contrast sensitivity in group 1. This result may be explained by the small number of obese patients included in this study, but it also may suggest that the severity of contrast sensitivity deficits is not directly dependent on the seriousness of insulin resistance. Indeed, the assessment of insulin resistance is only an indirect indication of alterations of the carbohydrate metabolism, which may be influenced by several factors, such as autonomic nervous system dysfunction and abnormal levels of free fatty acid, lectin, and glycogen.

The results of the present study show that contrast sensitivity testing may detect early changes of visual function in insulin-resistant obese patients and in diabetic patients before the appearance of microvascular retinal damage and the presence of overt hyperglycemia. The follow-up of these patients in a longitudinal study must be considered to evaluate whether contrast sensitivity testing may help to identify obese patients at risk of developing diabetes mellitus and diabetic patients at risk of developing clinically detectable retinopathy. It also remains to be studied with a larger cohort of obese patients whether a correlation between contrast sensitivity deficits and levels of free fatty acid, lectin, and glycogen or autonomic nervous system dysfunction can be observed. Moreover, it would be interesting to evaluate the reversibility of contrast sensitivity deficits after lessening of the insulin resistance.

Accepted for publication May 22, 1998.

Reprints: Andre A. Dosso, MD, Clinique d’Ophtalmologie, 22 rue Alcide Jenster, 1211 Geneva 14, Switzerland (e-mail: dosso-andre@diogenes.hcuge.ch).

**REFERENCES**


5. Di Leo MAS, Caputo S, Falsini B, et al. Nonselective loss of contrast sensitivity in...

**Archives Web Quiz**

Be sure to visit the Archives of Ophthalmology’s World Wide Web site (http://www.ama-assn.org/ophth) and try your hand at our new Clinical Challenge interactive quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month’s print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the first correct answer wins an Archives of Ophthalmology CD-ROM and will be recognized in the print journal and on our Web site. A full discussion of the case featured in the quiz can be found in the following month’s print edition of the journal.

**Archives Web Quiz Winner for September 1998:**
Our congratulations to the winner of our Clinical Challenge, Ann M. Bajart, MD, Boston, Mass.