Visual Dysfunction In Recent Onset Diabetes: A Clinical Report

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Abstract

A clinical report is presented of a 64 year old patient with recent onset diabetes. Simple in-office test procedures for the detection of subtle functional abnormalities in the visual system are presented. Diagnostic findings are expanded by results of electrophysiological testing, and complemented by an investigation of vascular structural integrity by fluorescein angiography. The importance of an examination routine consisting of an assessment of both functional and structural aspects of the visual elements typically affected by the diabetic condition is emphasized.

Introduction

The effects of diabetes on the visual system range from abnormalities in the structure and action of the extraocular muscles, abnormalities in pupil function, dark adaptation, and intraocular pressure, and anatomical alterations within the iris, crystalline lens, and retinal vasculature. Generally, changes in the morphology of ocular tissues are thought to occur only after the patient has been diabetic for many years. The alteration of ocular anatomy appears to occur independent of the degree of normalization and stabilization of blood-glucose levels. Although it is generally agreed that adequate control of blood-glucose levels will delay the onset of physical changes within ocular structures, there is insufficient clinical data to conclude that tight control of blood-glucose levels will prevent the onset of the most devastating consequence of diabetes on the eye, namely diabetic retinopathy. In fact, some preliminary clinical trials utilizing insulin pumps to accurately control blood-glucose levels have shown an acceleration of retinopathy in patients switched from traditional insulin injection procedures to the insulin pump (Begg, 1984). However, these findings are only preliminary and should not be interpreted as inevitable blindness for the patient regardless of the degree of control of the diabetic condition.

Woodruff et al. (1983) and Spafford and Lovasik (1986) have clearly demonstrated functional defects in the juvenile diabetic population prior to significant alterations in intraocular structures. The present report illustrates the utility of simple, but all too often underutilized, in-office techniques for the detection of functional abnormalities in the visual system, and their congruence with data provided by more elaborate electrophysiological testing as well as invasive procedures such as fluorescein angiography. In addition to the standard test procedures forming an oculo-visual assessment, tests of functional reserves can be administered to the diabetic patient in an effort to correlate these findings with anatomical changes observed in the visual system.

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Patient History

A 64 year old, Caucasian female was referred by a chapter of the Canadian Diabetes Association to the Electrodiagnostic Clinic at the University of Waterloo for an assessment of visual function. The patient was a diagnosed diabetic for three years and was medically managed by 32 units of insulin per day. The effectiveness of insulin in controlling blood-glucose levels was monitored by urinalysis. The patient was in generally good health and suffered only minor health problems related to arthritis. At the time of the examination the patient reported her blood-glucose levels to be normal.

The patient's ocular history indicated that she experienced somewhat impaired vision since her diagnosis of diabetes. A visual assessment some six months earlier by an optometric practitioner did not disclose any significant diabetic macular signs or age-related changes. However, vascular abnormalities typical of diabetes were found in more peripheral areas. The patient also reported fluctuating vision when blood-glucose levels were high.

Relevant visual and ocular findings at the patient's first visit were as follows:

Visual Acuity (Aided)

	OD	OS
6m	6/9	6/7.5
0.4m	0.5M	0.37M

Ocular Motility

Eye movements were unrestricted in all cardinal positions of gaze. The patient was non-strabismic.

External Findings

The ocular tissues and adnexa were considered normal for the patient's age. There were no signs of diabetic involvement in any of the tissues within the anterior segment of the eye.

Ophthalmoscopy

Direct ophthalmoscopy was employed to allow visualization of minute and subtle alterations of retinal vasculature. Indirect ophthalmoscopy lacks the optical magnification needed to see some of the finer alterations of structure found in diabetes. An overall impression of fundus changes associated with diabetes was obtained during fundus photography. Both eyes showed distinct background diabetic retinopathy. This consisted of numerous dot hemorrhages located primarily within the macular and paramacular areas. The right eye had numerous hard exudates in the macular area and a large serous exudate supero-nasal to the macula. Intraretinal microvascular anomalies (IRMA) were evident in both eyes. Both eyes showed venous beading. Significant

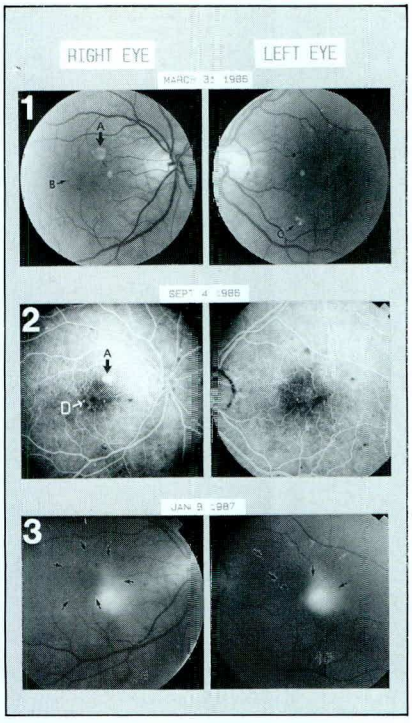

Figure 1:
Plate 1: Fundus appearance of right and left eyes at the posterior pole. Arrow A shows a large exudate at the one o'clock position referenced to the macula in the right eye. Many dot hemorrhages (for example, arrow B), as well as hard exudates (arrow C) are seen in both eyes.
Plate 2: Choroidal phase fluorescein angiograms taken about five months after the initial visit. Arrow A characterizes the lesion shown in Plate 1 as a retinal pigment epithelium detachment. Note the increased visibility and density of microaneurysms in the fluorescein angiograms compared to standard fundus photographs. Microaneurysms are seen as tiny hyperfluorescent lesions in the macular areas of both eyes (arrow D).
Plate 3: Appearance of the posterior poles two and a half months following laster photocoagulation treatment in the parmacular areas of both eyes. The small arrows point towards therapeutic focal argon lesions distributed in a roughly circular pattern in the right eye and less regularly in the left eye. Note the disappearance of the large circular lesion (Arrow A in plates 1 and 2) following treatment. Note also the occurrence of a new flame shaped hemorrhage in the right eye (arrow E) and IRMA in the left eye (arrow F). The diffuse grey spots near central maculae are artifacts of photography.

macular edema was not evident in either eye. The abnormalities seen on ophthalmoscopy are shown in Figure 1, plate 1.

The density of dot hemorrhages and exudative material in the macular area suggested a greater impairment of visual function than was measurable by the relatively small reduction in visual acuity in each eye. Several simple tests were selected to disclose further functional defects. These tests and results are summarized below.

1. Macular Photostress Test:

This test is primarily used to differentiate a maculopathy from a neuropathy as the cause for a reduction in visual acuity (Lovasik, 1983). Briefly, it involves measuring the time required to read two or more letters in the best acuity line after a macular dazzling period. The time for recovery from such a photostress period is dependent upon the structural and functional integrity of the macular area. Normal photostress recovery times are obtained for patients whose cause of

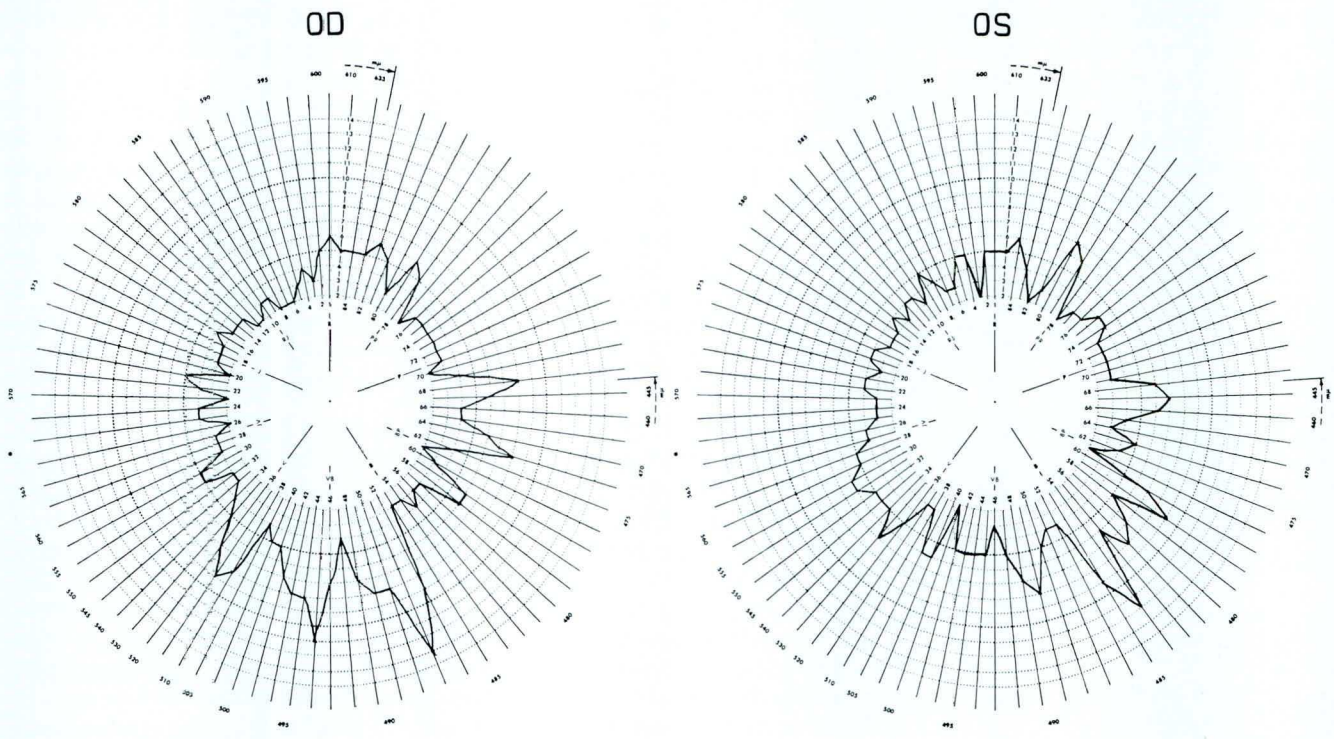

Figure 2:
FM-100 Hue error score recordings for the right and left eyes. Error scores were 214 and 218 for the right and left eye, respectively. Poor colour discrimination was inferred although no specific axis was indicated.

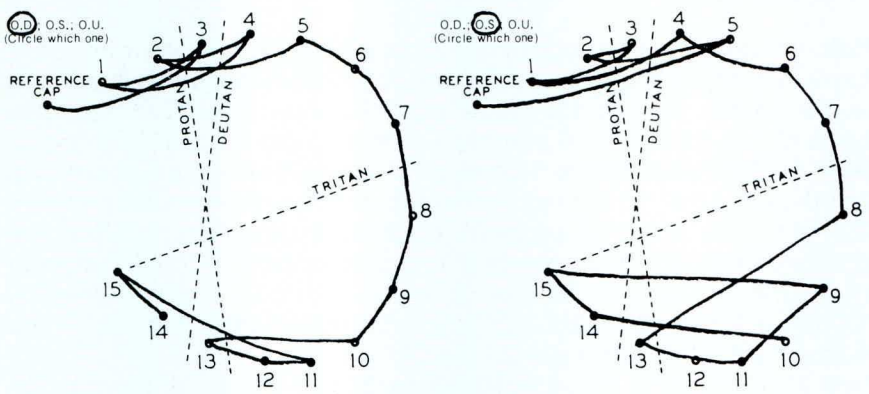

Figure 3:
Desaturated panel D-15 scoring for the right and left eyes illustrating frequent minor reversals with a tendency towards a tritanomalous defect.

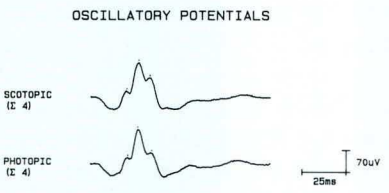

Figure 5:
The normal number of oscillatory potentials in our testing protocol were recordable for both eyes under scotopic and photopic conditions. Temporal and amplitude characteristics of these potentials were considered to be within normal limits. Recordings represent responses from the left eye. Dots identify the first, second, and third oscillatory potentials.

decreased acuity is optic nerve in origin since photochemical processes involved in the recovery of vision from bleaching are normal. Vascular or structural anomalies within the macula affecting vision also affect the photopigment regeneration process and consequently result in a prolonged photostress recovery time. For our patient the photostress times were OD 129 sec, OS 364 sec. Both values were far above the normal range of responses for the test as applied at our clinic. An upper normal value for the procedure used here is considered to be approximately 30 sec. The large difference in photostress recovery times between the two eyes highlights the fact that large functional deficits may exist between eyes with similar visual acuities and grossly similar fundus appearance.

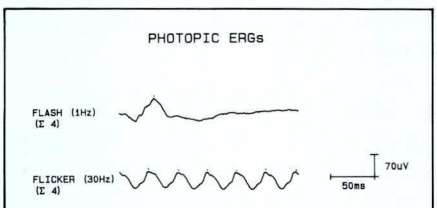

Figure 6:
Sample recordings of photopic ERGs to red flash and red flicker stimulation, indicating normal cone function. Records represent the average of 4 and 8, 200ms epochs, respectively. Identical responses were obtained from the two eyes. Peaks at which amplitudes were measured are denoted by dots (.).

2. Colour Vision Assessment:

Acquired ocular diseases frequently affect colour perception. With this in mind, both the FM-100 Hue and the desaturated panel D-15 were administered monocularly to the patient. The results of this testing are illustrated in Fig. 2 and Fig. 3 for the 100 Hue and the panel D-15, respectively. The patient made frequent colour reversals of a general nature with a tendency to show a tritanomalous colour defect, an anomaly frequently seen in various disease processes of the retina including diabetes (Adams et al, 1987).

3. Prism Competition Test:

This test is primarily utilized to identify and differentiate the laterality of a prechiasmal or post-chiasmal lesion (Mehdorn, 1980). Briefly, this test involves observing eye movements when base out and base in prisms (four prism diopters each eye), are quickly placed before the eyes as the patient views a distant fixation target. Normal responses include convergence, divergence, or alternate fixation when the total prism value before the eye exceeds fusional reserves. Positive responses include sustained dextroversion or laevoversion with prisms in place. Pre-chiasmal lesions result in the

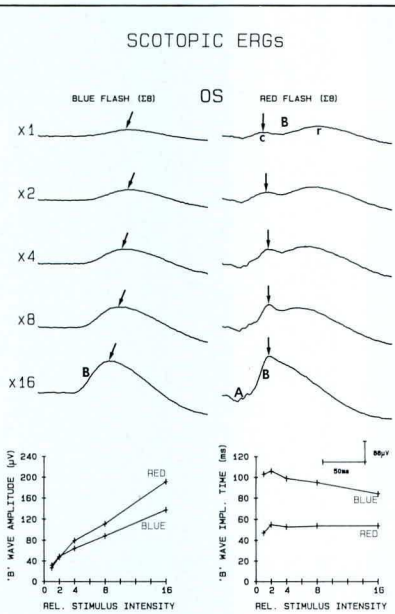

Figure 4:
Scotopic ERGs to graded relative intensities (×1 to ×16) of scotopically matched blue and red flash stimuli for the left eye. Each record represents the average of eight ERGs. Similar responses were seen for the right eye. Blue flash responses (rod isolated) demonstrated an increased amplitude and decreased implicit time of the b-wave component with increased flash intensity. The implicit times are identified by small oblique arrows. Red flash responses (rod dominated) demonstrated an increased amplitude and relatively constant implicit time for the cone component (c) of the biphasic b-wave with increased flash intensity. The implicit times for the cone component are shown by vertical inverted arrows. A rod/cone break is evidenced by the double peak within the b-wave at low flash intensities. The amplitudes of the b-wave component were measured from the trough of the a-wave to the peak of the b-wave. c = cone component, r = rod component in red flash ERG recordings.

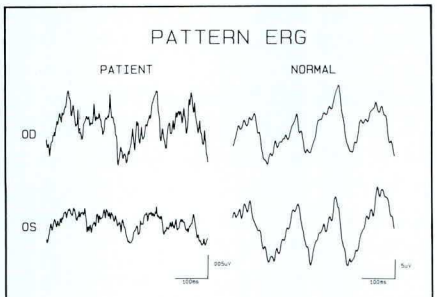

Figure 7
Pattern ERG recordings for the right and left eyes of the patient as compared with an age- and sex-matched non-diabetic subject. Each record represents the average of 100 epochs. Note the difference in the vertical scales for the patient and the normal subject. Note also the inferior response from the left eye of our patient.

superior eye determining the direction of the versional response according to whether base in or base out prisms are placed before the eyes. Post-chiasmal lesions result in sustained dextroversion or laevoversion when either direction of prisms are placed before the eyes, with the laterality of the version identifying the side with the post-chiasmal lesion. Thus, a post-chiasmal lesion on the right hand side results in a dextroversion with either base in or base out prisms. For our patient, the test results were positive for a pre-chiasmal lesion on the left hand side and were in agreement with a prolonged photostress recovery time for the left eye. Thus even though visual acuities were similar for each eye, there were demonstrable differences in neural conduction times between the two eyes.

4. Electrophysiological Tests:

In addition to these simple tests, an electrophysiological assessment of visual function was performed. Retinal function was evaluated by flash (fERG) and pattern (pERG) electroretinograms (Lovasik & Kothe, 1986). The integrity of the macular-cortical fibres were assessed by flash and pattern visually evoked responses (VERs) (Lovasik & Woodruff, 1983). The results of scotopic fERG testing for the left eye by scotopically matched blue and red flashes of increasing intensity are shown in Fig. 4. Although the implicit times of the b-wave component of the ERG were somewhat delayed and the amplitudes reduced, they were not diagnostic for diabetic retinopathy. The amplitude and implicit time characteristics of the b-waves were not out of range with those reported by Weleber (1981) for patients in the seventh decade of life. The oscillatory potentials (Speros & Price, 1981), an electrical index of the function of the inner plexiform layer of the retina, were present and not considered abnormal. Sample recordings for the left eye are shown in Fig. 5. Photopic flash and flicker ERGs indicated normal gross cone function in each eye. Sample data for the left eye are shown in Fig. 6. Similar responses were obtained for the right eye under these test conditions.

Pattern ERGs, elicited by a reversing checkerboard target, were obtained for each eye and compared to an age- and sex-matched non-diabetic subject. These results are presented in Fig. 7. The pERG morphology was relatively undisturbed but the amplitude of the signal was far below normal values in each eye, more so for the left eye than for the right. In as much as the pERG is thought by some to reflect the function of the retinal ganglion cell layer, our results pointed to a possible retinal dysfunction at the most vitread layer of the retina.

A detailed electrophysiological assessment of macular function was also performed by steady state (ssVER) and transient (tVER) pattern visual evoked responses. These were elicited by a checkerboard target reversing at 8 and 2 Hz, respectively. The results for ssVERs for the right and left eyes of the patient and an age-matched non-diabetic subject are shown in Fig. 8. The calibration scale for each record indicated a profound reduction in amplitude of our patient's ssVERs. This identified highly reduced reactivity of macular-cortical neurons tuned for spatial resolution. Given the ophthalmoscopic appearance of both maculae, the gross attenuation of the VERs was likely of retinal origin.

The amplitude of the tVER was also severely reduced and the implicit time of the P-100 component for the left eye was delayed relative to the right eye. However, both implicit times were considered to be within a normal range. Transient pattern VERs for our patient are shown in Fig. 9 and compared with an age-matched non-diabetic subject.

The ability of the macular-cortical pathways to relay information related to simple light detection was tested by the determination of the cortical critical frequency of photic driving (CFPD) (Celesia & Daly, 1977). The VER amplitude-flash frequency function is graphically illustrated in Fig. 10. Normal CFPD values exceed 40 Hz. For our patient, both eyes

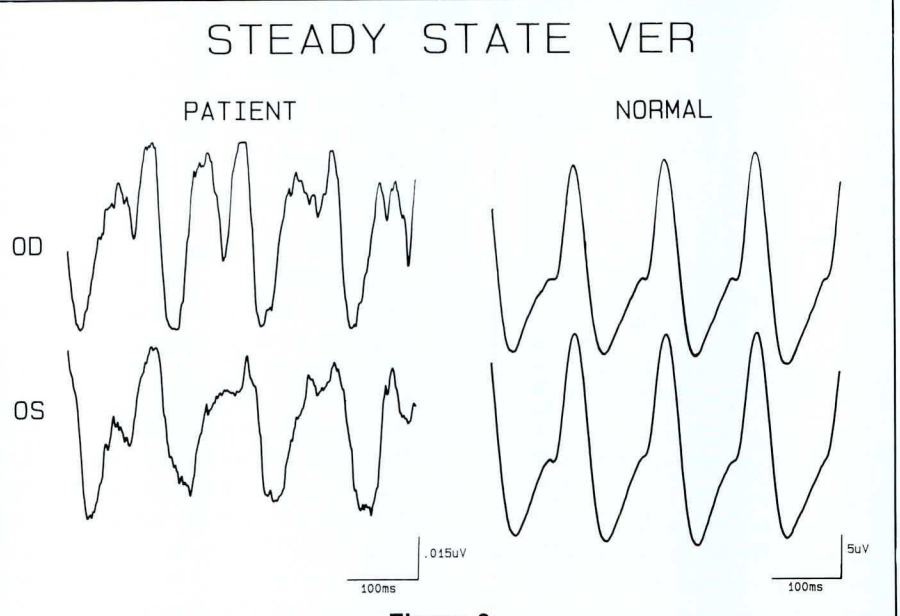

Figure 8:
Steady state VERs to a 6 degree diameter reversing (B Hz) checkerboard composed of high contrast 14 minutes of arc black and white checks. Each waveform is the average of 30 epochs. The VERs of the patient are compared to those for an age- and sex-matched non-diabetic subject. Whereas the waveforms are not significantly different, the patient's responses are many times smaller than those for the visually normal subject. Note the difference in the vertical calibration scales.

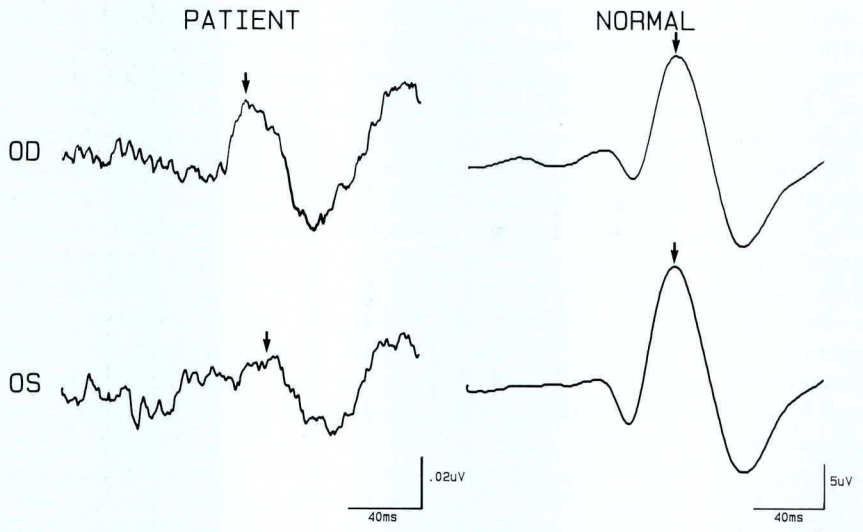

Figure 9:
Transient VERs to a 6 degree reversing (2 Hz) checkerboard composed of high contrast 14 minutes of arc black and white checks. Each waveform is the average of 30 epochs. The right and left eyes of the patient are compared with those of an age and sex-matched non-diabetic subject. As for the ssVERs, there was a very large difference in the amplitude of the evoked potential in relation to a non-diabetic subject. Note the difference in the amplitude scales for the patient and the normal subject. The implicit times for the P-100 component of the pattern VER are shown by small inverted arrows. The left eye of the patient showed a slightly delayed response when compared with the right eye. This difference was not considered diagnostically significant.

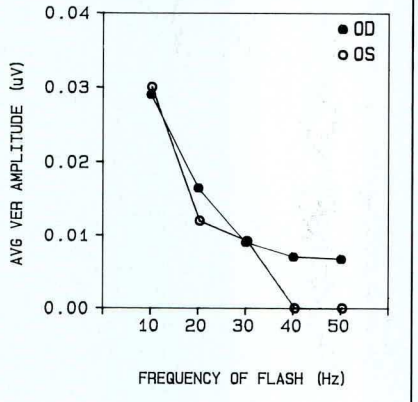

Figure 10:
Cortical CFPD amplitude-flash frequency relationship for the right and left eye of the patient. The flash VER amplitude is far below normal. A normal observer would continue to respond up to those flash frequencies establishing the psychophysically measured critical fusion frequency.

failed to conduct flash information much beyond 40 Hz. Furthermore, the response amplitude was exceptionally low, a finding consistent with all other test results signalling a significant maculopathy.

5. Ophthalmological Diagnosis/ Treatment:

An ophthalmological evaluation performed about three months after our initial assessment also concluded with a diagnosis of moderately severe non-proliferative background diabetic retinopathy. Fluorescein angiography done two months later revealed abnormal choroidal and retinal vascular filling phases for both eyes, with multiple tiny hyperfluorescent lesions located throughout the posterior pole. Both eyes exhibited mild macular edema. The right eye was generally better than the left but showed an area of retinal pigment epithelium detachment supero-nasal to the macula. The fluorescein angiograms are shown in Figure 1, plate 2. Focal argon laser therapy was carried out one and a half months later on both eyes in an attempt to minimize the progression of the diabetic retinopathy.

6. Followup Examination:

On a return visit approximately two and a half months after laser therapy, visual performance was assessed by visual acuity, VERs, colour vision and the photostress recovery test.

Aided visual acuity had improved in the right eye from 6/9 to 6/7.5 while the left eye gained two letters yielding 6/7.5 +2. The patient felt that her vision in the left eye was notably better than that for the right eye even though measured acuities were similar.

While the morphology of all pattern evoked potentials was unchanged from the initial evaluation and conformed to VERs recordable from a visually normal patient, the amplitudes had increased some ninety times. Flash evoked cortical potentials showed an even greater increase in amplitude but the associated cortical CFPD remained unchanged from that found prior to laser therapy.

Colour vision, as assessed by the desaturated panel D-15 remained unchanged from the previous visit. A tendency for a blue-yellow defect was still evident in both eyes.

The photostress recovery time for the left eye showed a dramatic improvement (first visit 364 sec, post-laser therapy 134 sec). Curiously, the right eye, that showed improved visual resolution, now showed reduced functional reserves (first visit 129 sec, post-laser therapy 215 sec). These latter observations indicated continued sub-clinical disturbances of the macula when the photochemical processes of vision were stressed by bleaching. The need for continued monitoring of this patient was strongly indicated.

Discussion

This clinical report is presented to emphasize the optometrist's role in managing the diabetic patient. Several simple in-office procedures are presented to demonstrate their use in the detection of subtle functional abnormalities in the diabetic visual system. Their proper application can lead to the required referral and management of the often hidden deficits.

Eye practitioners are reminded that appropriate colour vision testing should be routinely employed with diabetic patients. Kollner's 'rule' predicts that blue-yellow defects result from lesions of the outer retinal layers while red-green defects develop from lesions of the inner

retinal layers and optic nerve. Changes in colour vision with retinopathy have been reported in diabetics, particularly blue-yellow defects (Adams et al, 1987), which may worsen or improve as the underlying pathology progresses or undergoes remission. The FM-100 Hue test, although time-consuming, is especially effective in detecting acquired colour vision defects. However, the desaturated D-15 panel is much quicker to administer and is sensitive in detecting mild acquired colour vision defects, more so than the commonly used standard D-15. Optometrists are therefore encouraged to administer tests specific for detecting mild colour vision defects to all their diabetic patients on a routine basis.

The photostress recovery test is also a simple procedure which can be administered to all diabetics. The recovery time of this test is dependent on the rate of photopigment resynthesis and the functional integrity of the outer retinal layer and retinal pigment epithelium (Lovasik, 1983), giving additional diagnostic information in a case of suspected maculopathy.

These tests can be further complemented by the prism competition test and careful funduscopic examination and photodocumentation. In-office monitoring of blood-glucose levels can identify those patients who erroneously or falsely report good control of blood-glucose levels. In this regard it should be noted that more accurate estimates of blood-glucose levels are obtained from blood samples by simple pin prick than by measures based on urinalysis (Begg, 1984). Furthermore, since many diabetics experience their disease-related colour vision defects, it is advisable to utilize digital glucometers rather than colour matching of diagnostic sticks to colour coded reference standards in order to establish blood-glucose levels (Shute & Oshinskie, 1986).

Although more commonly utilized in group practices, hospitals and educational institutions, electrophysiological tests often provide clinically useful information concerning neural function in the diabetic patient prior to any ophthalmoscopically visible alterations in structure. The oscillatory potentials have been shown to be useful in predicting the rate of progression of diabetic retinopathy (Bresnick, 1984; Speros and Price, 1981). Others (Arden et al, 1986) maintain that the pattern ERG is even more useful clinically in the management of diabetics since it is apparently attenuated at the stage of diabetic retinopathy when referral for laser treatment becomes necessary. Pattern VERs are specific in detecting functional abnormalities in the macular-cortical pathways (Sokol, 1976; Sherman, 1979) and may be affected when retinopathy encroaches onto the macular area or when diabetic ischemic processes have affected retrobulbar components of the visual system.

In addition to drawing the reader's attention to the testing resources available for the clinical care of diabetic patients, the authors wish to dispel the notion that diabetes does not affect the visual system until the patient has been diabetic for many years. Current research indicates that functional changes in the visual system of the diabetic patient may occur in as little as five years in either juvenile or adult populations (Spafford & Lovasik, 1986). The present case is that of a patient who experienced visual abnormalities and incurred structural damage after being diagnosed diabetic for as little as three years. Structural changes were best visualized by fluorescein angiography. As is frequently the case in age-onset diabetes, compared with the rather abrupt onset of juvenile diabetes, our patient may unknowingly have been diabetic for a considerably longer period of time. However, it is also possible that diabetes acquired later on in life results in an acceleration of age-related changes in the visual system.

In summary, this report emphasizes the special role of the optometrist in the provision of eye care to the diabetic population. Vision testing should include tests routinely performed in an oculo-visual assessment, as well as those measuring functional reserves. With the exception of fluorescein angiography, the tests described here can be readily performed in the optometric office and will enhance the diagnostic capabilities so important in the management of diabetic patients.

Acknowledgements

Drs. Kothe and Lovasik were supported by a COETF award during the course of this clinical investigation. Dr. Lovasik was also funded by Canadian Medical Research Council grant No. MA-9264.

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