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Visual evoked potentials after photostress in newly diagnosed insulin-dependent diabetes patients

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Abstract ● Background: The study was performed in order to ascertain whether electrophysiological abnormalities in visual function exist in newly diagnosed diabetic patients. ● Methods: Visual evoked potentials (VEPs) were assessed under basal conditions and after photostress in normal control subjects and in newly diagnosed diabetic patients free of any fluorescein angiography signs of retinopathy. ● Results: In basal conditions VEP P100 latency was significantly increased in the diabetic patients compared to controls ($P<0.01$), while N75-P100 amplitude was similar in both groups. After photostress N75-P100 amplitude (mean percentage decrement) was significantly higher in diabetic patients ($P<0.01$), while P100 latency (mean increment) and recovery time (time at which VEPs were superimposable on basal condition) were similar in the two groups. ● Conclusions: The impaired basal VEPs suggest an early involvement of conduction in the optic nerve. In contrast, the preserved recovery time after photostress indicates that a short duration of disease does not induce physiopathological changes in macular function.

Introduction

Visual evoked potentials (VEPs) recorded in basal conditions and after photostress, have been widely used to assess the visual function in diabetic patients [1–10].

These tests reveal several deficits in patients with long duration of disease, but some alterations have been observed after only 2 years of disease [11]. However, to our knowledge, visual function in newly diagnosed type 1 diabetes patients has not yet been investigated. Therefore the aim of our study was to assess whether electrophysiological abnormalities in visual function exist in newly diagnosed diabetic patients.

Materials and methods

10 control subjects (mean age 27.8±2.44 years) and 10 age-matched insulin-dependent diabetes patients (mean 25.20±6.78 years) with a duration of the disease under 1 year were entered in the study. The following criteria had to be satisfied by the control

Table 1 Clinical characteristics (*IDDM* insulin-dependent diabetes mellitus, *Hb* hemoglobin)

	Age (years)	Duration of disease (months)	Hb A_{1c} (%)	Gender (M/F)
Controls	27.8±2.4	–		6/4
IDDM patients	25.2±6.7	5.3±3.5	7.5±1.17	5/5

subjects: normal intraocular pressure (<21 mmHg), normal visual acuity, normal visual field (Goldmann perimetry), no ocular or other clinically relevant neurological problems.

The criteria that had to be met by diabetic patients were: normal intraocular pressure (<21 mmHg) best corrected visual acuity 10/10, and absence of retinopathy on fluorescein angiography (Klein level 1) [12].

The clinical characteristics of the patients are shown in Table 1.

Visual evoked potential recording

The subjects were seated in a semi-dark acoustically isolated room. Prior to the experiment each subject was adapted to the ambient room light level for 10 min until pupil diameter was about 3 mm. The display was surrounded by a uniform field of luminance 5 cd/m^2.

VEPs were recorded according to a previously described method [10].

The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 110 cd/m^2) generated on a television monitor and reversed in contrast at the rate of two reversals per second. At the viewing distance of 114 cm the individual check size subtended 15 min of visual arc and the screen of the monitor subtended 25 deg. The stimulation was monocular, after occlusion of the other eye. The test was performed in the right eye of all patients.

Cup-shaped electrodes of silver–silver chloride were fixed with collodion at Oz (active electrode), and Fpz (reference electrode), with the ground in the left arm. The interelectrode resistance was kept below 3 kohm. The bioelectric signal was amplified (gain 20000), filtered (band-pass 1–100 Hz) and averaged, with automatic rejection of the artifacts, over a number of stimulus periods using a Cadwell 7400 (Pollman, Bologna, Italy).

The recording session began with a preliminary experiment in which at least two VEPs were recorded, averaging over 100 stimulus periods and excluding artifacts. The analysis time was 500 ms.

The transient response was characterized by several waves with three peaks, which in normal subjects appeared after 75, 100 and 145 ms. These peaks had negative (N75), positive (P100) and negative (N145) polarity, respectively.

Visual evoked potentials after photostress

After a preliminary trial, a control VEP was recorded, reducing the averages to 40 events per trial (with no more than two sweeps discarded because of artifacts). This VEP record was defined as "basal" and it was kept on display on the computer monitor. Photostress was then induced for 30 s by means of a circular diffusing surface (the bulb of a 200-W lamp) that was centrally fixated by the subject from a distance of 20 cm and produced a central scotoma of 6° diameter. The pupil diameter decreased to about 2 mm.

Immediately after the end of photostress, fixation was shifted to the pattern stimulus and recording of VEPs started. Recordings were taken for successive 20-s periods (averaging 40 stimuli every 20 s) and displayed successively on the monitor until the VEP obtained was superimposable on the basal recording. The time taken for VEP to become superimposable was considered as the recovery time after photostress (RT).

For all VEPs the peak latency and the peak amplitude of each of the waves were measured directly from the displayed recordings with a pair of cursors. The amplitudes were measured in absolute values directly by Cadwell 7400. Our method did not allow us to record the pattern ERG or the focal ERG in the same averaging run as the VEP. These two ERG recordings require a longer time to obtain a reliable record than the preestablished recording time required by our experimental procedure.

Statistics

Results are expressed as mean±standard error (SE). If not otherwise indicated, *n* refers to the number of eyes. Differences between groups were statistically evaluated with a one-way analysis of variance for repeated measures (ANOVA) and with linear regression and were considered significant with $P<0.05$.

Results

Basal visual evoked potentials

The mean data for all groups of patients are shown in Figs. 1 and 2.

In control eyes, the VEP parameters (P100 latency and N75-P100 amplitude) were within our normal limits [13], expressed as mean value ±1 SD for N75-P100 amplitude (9.23±2.18 μV) and mean ±3 SD for P100 latency (93.15±3.43 ms).

P100 latency was significantly higher in all diabetic patients than in control eyes. N75-P100 amplitude values were similar in both groups.

Visual evoked potentials after photostress: control eyes

The mean results of P100 latency and N75-P100 amplitude are presented in Table 2 and in Figs. 1 and 2.

At 20 s after photostress, we observed an increase in P100 latency and a decrease in N75-P100 amplitude. At 40 and 60 s after photostress the P100 latencies were shorter than the 20 s value, but still longer than the basal latency. The N75-P100 amplitude increased from the

Table 2 Visual evoked potentials after photostress in control subjects (*C*) 15 and patients with insulin-dependent diabetes mellitus (*IDDM*)

	N75-P100 amplitude (mean % decrement)	P100 latency (mean increment, ms)	Recovery time (s)
C (n=10)	14.08±1.25	9.10±0.92	73.0±6.1
IDDM (n=10)	27.24±2.28*	9.41±1.04	73.6±1.18

* $P<0.01$

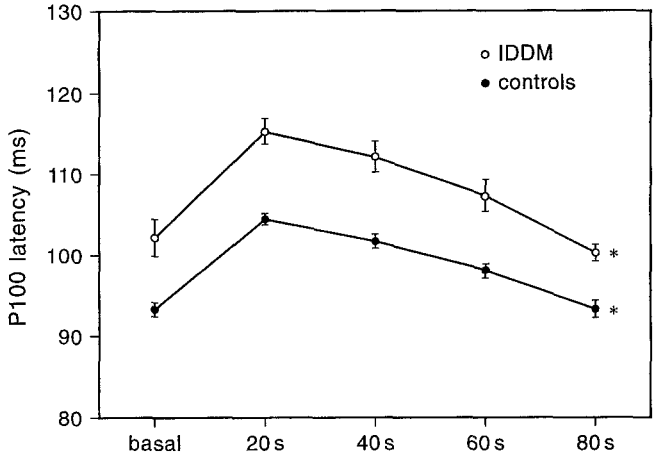

Fig. 1 Graphic representation of mean values of latency P100 under the basal condition and 20, 40, 60, 80, 100 and 120 s after photostress. *Error bars* represent one standard error of the mean. * Recovery time after photostress (see Table 2 for mean values)

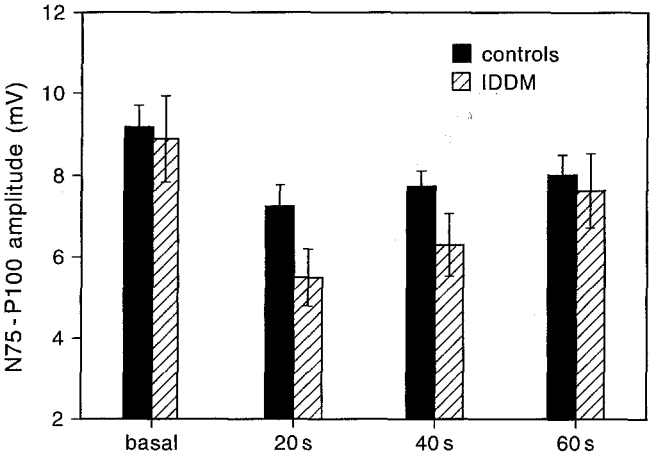

Fig. 2 Histograms of mean values of VEP amplitude under the basal condition and 20, 40 and 60 s after photostress. The *vertical lines* represent one standard error

value observed at 20 s, but without reaching the basal value. The RT was 73.0±2.21 s.

Examples of recordings from a normal subject are shown in Fig. 3.

Visual evoked potentials after photostress in IDDM patients

The mean results are presented in Table 2 and Figs. 1 and 2. In IDDM patients the response to photostress followed a pattern similar to that described for control subjects.

The mean percentage decrement of N75-P100 amplitude observed at 20, 40 and 60 s after photostress were higher in diabetic patients than in control eyes. The mean

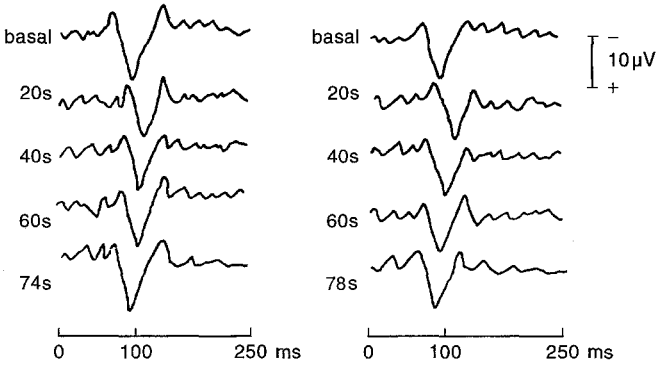

Fig. 3 VEP layout of a control subject (*left*) and of a diabetic patient (*right*) under basal conditions and 20, 40 and 60 s after photostress. After photostress there was an increase in latency and a decrease in amplitude. The VEPs are superimposable on the basal waveform at 74 s in the control subjects and at 78 s in the diabetic patients

increments in P100 latency observed at 20, 40 and 60 s after photostress and the RT were similar in the two groups. Examples of recordings from a diabetic patient are shown in Fig. 3.

Discussion

In the newly diagnosed IDDM patients we found in the basal VEP an impaired P100 latency compared to controls, while N75-P100 amplitude was equivalent.

A delay in VEP P100 latency has already been observed in diabetic patients with longer duration of disease and has been ascribed to a reduced velocity of nervous conduction in the optic nerve, as further supported by studies with pattern ERG [14–20], and with measurement of retino-cortical time [8, 19].

Since a delay of the VEP can also be ascribed to macular involvement [21], we performed the VEP after photostress test in order to assess the contribution of the macular function on the longer P100 latency of VEPs observed in newly diagnosed type 1 diabetic patients. This test is an objective method of evaluating the macular function [22–25], since patients with macular involvement show a longer RT [23]. The RT, which represents the overall activity of the macula [21, 23], is unchanged in newly diagnosed type 1 diabetes patients, suggesting a preserved macular function.

However, using the focal ERG, another method for studying macular function, Ghirlanda et al. [26] have found in IDDM patients with a short duration of disease (3.8±3.5 years) that early diabetes causes selective neurosensory deficits of the inner retinal layers, whereas the photoreceptors appear unaffected.

Our data might appear in contrast with those of Ghirlanda et al. [26], but the shorter duration of disease in our

patients may explain the different results; in fact, in our previous studies we found impaired macular function in diabetic patients without retinopathy after 2 years of disease [10, 11].

In conclusion, the impaired basal VEPs suggest early involvement in IDDM of conduction in the optic nerve. In contrast, the normal RT indicates that a short duration of disease does not induce physiopathological changes on macular function.

A role of metabolic control in the pathogenesis of these alterations may be suggested by the fact that our patients, although in stable metabolic control, had unsatisfactory control of glycemia, with a hemoglobin A_{1c} level of 7.5±1.1%.

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