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## Visual Evoked Potentials in Diabetic Patients

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**Abstract:** Currently there are conflicting results regarding optic neuropathy in diabetes mellitus. Therefore, the aim of the present study was to evaluate optic neuropathy in diabetic patients. We studied visual evoked potentials (VEPs) in 20 diabetic patients (6 insulin dependent, 14 noninsulin dependent; 8 women, 12 men; mean age:  $49.70 \pm 18.22$  years; mean duration of diabetes:  $9.33 \pm 5.75$  years) and 20 age-, and sex-matched healthy subjects (7 women, 13 men; mean age:  $52.40 \pm 16.02$  years) as a control group. Nine of 20 diabetic patients had sensorimotor neuropathy, and 5 diabetic patients had both sensorimotor neuropathy and autonomic neuropathy, as well as 3 diabetic patients had diabetic retinopathy. P<sub>100</sub> wave

latency was significantly longer in diabetic patients than those of the control group ( $p < 0.0001$ ). Forty-five percent of diabetic patients (9 patients) had P<sub>100</sub> wave latencies above the normal range. There was no correlation between P<sub>100</sub> wave latency and age, sex, degree of metabolic control or presence of degenerative complications. However, there was a significant positive correlation between P<sub>100</sub> wave latency and the duration of diabetes mellitus ( $r = 0.79$ ,  $p < 0.05$ ). Our results abnormalities are dependent upon the duration of diabetes.

**Key Words:** Diabetes Mellitus, Visual Evoked Potentials

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### Introduction

Previous studies have shown the peripheral nervous system involvement in diabetes mellitus. However, little is known about the central nervous system involvement in diabetes. Evoked potentials is a convenient and non-invasive tool for the evaluation of central nervous system. Visual evoked potentials (VEPs) could be used to evaluate disturbances in the central visual pathways (1-3). VEPs is also helpful in determining subclinical lesions in the optic nerve, spinal cord and the brain stem; therefore, it is a convenient tool in the diagnosis and follow-up of neurologic disorders (4-6).

In diabetes mellitus, visual deficit appears to result from both vascular disease and metabolic abnormalities, which can affect the retina, optic nerve and visual pathways. Optic neuropathy is considered to be most uncommon in diabetes mellitus. There are conflicting results regarding optic neuropathy in diabetic patients. Tests for optic neuropathy have been performed in children and adults on a comparatively small scale (1). Therefore, the aim of the present

study was to evaluate optic neuropathy in diabetic patients. This study established the prevalence of VEPs abnormalities in diabetic of both sexes in comparison with a control population.

### Materials and Methods

Twenty diabetic patients (6 insulin dependent, 14 noninsulin dependent; 8 women, 12 men) were enrolled in the study. Their ages ranged from 18 to 80 years (mean age  $\pm$  SD:  $49.70 \pm 18.22$  years). The duration of diabetes ranged from 2 to 21 years (mean duration of diabetes  $\pm$  SD:  $9.33 \pm 5.75$  years). Nine of 20 diabetic patients had clinical and electromyographic evidence of sensorimotor neuropathy, and 5 diabetic patients had both sensorimotor neuropathy and autonomic neuropathy. All patients underwent dilated fundoscopic examination and fluorescein angiography. Exclusion criteria were proliferative retinopathy, maculopathy, glaucoma or opacification, or visual acuity  $< 6/18$  with corrective lenses. Three of 20 diabetic patients had background diabetic retinopathy. We studied 20 sex-, and age-matched healthy subjects

(7 women, 13 men; mean age  $\pm$  SD: 52.40  $\pm$  16.02 years) as a control group. Clinical and metabolic characteristics of the groups of study subjects are shown in Table 1.

Table 1. Clinical and metabolic characteristics of the groups of study subjects.

	Diabetic Patients	Control Subjects
n(F/M)	20 (8/12)	20 (7/13)
Age (years)	49.70 $\pm$ 18.22	52.40 $\pm$ 16.02
BMI (kg/m <sup>2</sup> )	23.97 $\pm$ 3.26	24.87 $\pm$ 3.03
Type of diabetes (IDDM/NIDDM)	6/14	
Duration of diabetes (years)	9.33 $\pm$ 5.75	
FPG (mg/dl)	226.75 $\pm$ 86.33*	96.55 $\pm$ 9.11
HbA <sub>1C</sub>	9.41 $\pm$ 1.07*	5.47 $\pm$ 0.44

Values are means  $\pm$  SD. F, female; M, male; BMI, body mass index; FPG, fasting plasma glucose; IDDM, insulin dependent diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; HbA<sub>1C</sub>, glycosylated hemoglobin.

\*p<0.0001, diabetic vs. control subjects.

Visual evoked potentials were recorded with a DISA equipment. Refraction defects were corrected. Both eyes were stimulated separately by checkerboard pattern reversal at 1 Hz. The screen was placed one meter from the nasion. The response was recorded by surface electrodes that were placed at the occipital region, the active ones being placed at Oz, and the reference at Fz. Two series of 128 responses were averaged (band-width, 0.5-200 Hz). The first major positive peak (P<sub>100</sub>) was measured after stimulation of each eye.

Blood glucose levels were measured at the beginning of the VEP recording sessions, and no patient showed clinical or biological signs of hypoglycemia during the study (mean blood glucose levels: 226.75  $\pm$  86.33 mg/dl, range: 120-441 mg/dl). Glycosylated hemoglobin (HbA<sub>1C</sub>) was determined according to a microcolumn method (normal range: 4.3-6.5%).

The results were expressed as means  $\pm$  SD. Comparisons between groups were carried out with Student's t test for unpaired series, and correlations between parameters were computed with linear regression analysis. Values of P<0.05 were considered significant.

## Results

For both control and diabetic groups, we did not find significant differences in P<sub>100</sub> latency between the right and left eyes (Table 2). Regarding additional results, we only took into account the mean values for both eyes. P<sub>100</sub> wave latencies were significantly longer in diabetic patients than those of the control group (116.62  $\pm$  8.43 vs. 104.40  $\pm$  7.30 ms, P<0.0001; Table 2 and Figure 1). Forty-five percent of diabetic patients (9 patients) had P<sub>100</sub> wave latencies above the normal range. In diabetic patients, there was no correlation between P<sub>100</sub> wave latency and age, sex, degree of metabolic control or presence of degenerative complications. We found significant positive correlation between P<sub>100</sub> wave latency and duration of diabetes mellitus (r=0.79, P<0.05; Figure 2).

Table 2. P<sub>100</sub> wave latency in diabetic patients and control subjects.

	Diabetic Patients	Control Subjects
n	20	20
Right eye	117.0 $\pm$ 10.47 (104-146)*	104.30 $\pm$ 7.34 (93-114)
Left eye	116.15 $\pm$ 7.46 (103-130)*	104.50 $\pm$ 7.32 (91-115)
Mean both of eyes	116.2 $\pm$ 8.43 (104-134)*	104.40 $\pm$ 7.30 (92-114.5)

Values (in milliseconds) are means  $\pm$  SD (ranges in parantheses).

\*P<0.0001, diabetic vs. control subjects.

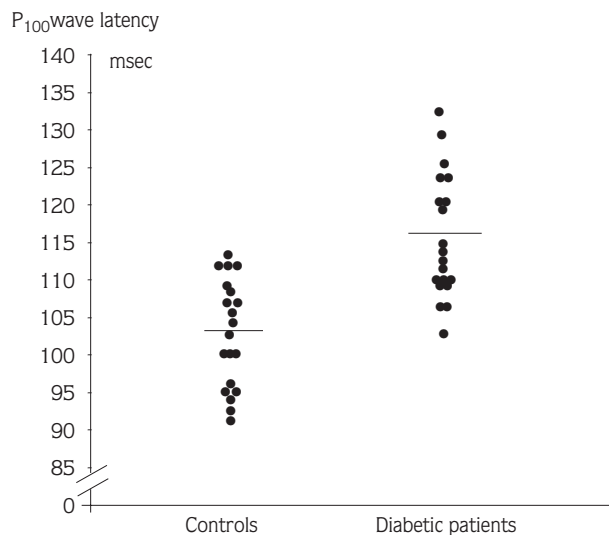


Figure 1. P<sub>100</sub> wave latency in diabetic patients and control subjects.

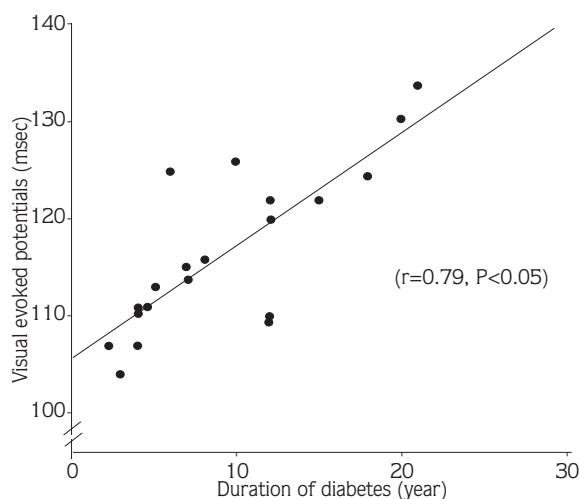


Figure 2. Correlation between duration of diabetes and visual evoked potential

## Discussion

Evoked potentials are a simple, sensitive and objective technique for evaluating impulse conduction along the central nervous pathways. Evoked potential abnormalities have been described in diabetes mellitus, but the proportion of patients with increased latencies of visual  $P_{100}$  is very variable, ranging 9% to 77% (1,2,7-10). Such high variability could be explained by several factors, such as the criteria of ascertainment inclusion or diagnosis, the presence of retinopathy or peripheral polyneuropathy and differences in stimulus recording conditions. Algan et al. (1) found prolongation of  $P_{100}$  latencies in 50 DM patients which 6 of them had diabetic retinopathy. Mariani et al. (7) found prolongation of  $P_{100}$  latencies in their 35 diabetic patients, but they did not have retinopathy. Ponte et al. (8) reported prolongation of VEPs latencies in 50 asymptomatic insulin dependent diabetic patients without retinopathy. Puvanendran et al. (2), Cirillo et al. (9) and Anastazi et al. (10) also reported VEPs abnormalities in diabetic patients. Although Collier et al. (11) found VEP abnormalities in diabetic patients with retinopathy, they did not find any abnormalities in other diabetic patients which did not have retinopathy. In this study, number of cases is significantly less. Yaltkaya et al. (12) found prolongation of  $N_{140}$  latencies and  $N_{90}-N_{140}$  interpeak latencies as well as  $P_{100}$  latencies and they explained it with the existence of retrochiasmal involvement. Millinger et al. (13) reported similar findings. Bortec et

al. (14) found 77 % VEP abnormalities in diabetic patients and reported that these abnormalities did not correlate with retinopathy. Sima et al. (15) have recently shown that the diabetic BB rat develops a central sensory neuropathy, in which there are prolonged latencies of the VEPs, related with an axonopathy of optic nerve fibers.

Evoked potential abnormalities have correlated with hyperglycemia in some studies (2) but not in others. Martinelli et al. (16) showed that abnormal VEPs tend to be persistent and that these abnormalities are apparently not reversible, but the influence of metabolic control was not the end point of these studies. Although several studies have assessed the visual pathway function by VEP recordings and observed a delay in latency in patients with long-standing diabetes (1,2,9). In the newly-diagnosed IDDM patients, Uccioli et al. (17) found an impaired  $P_{100}$  latency in basal VEP compared to control subjects.

Some researchers found correlation between recent metabolic control and  $P_{100}$  wave latencies in diabetic patients, however, others did not so. In fact a recent study report has shown that short-term strict metabolic control is able to improve VEP latencies in patients with poorly-controlled diabetes (18). Uccioli et al. (17) reported that metabolic control plays a role in the pathogenesis of VEP alterations by showing that their patients, although in stable metabolic control, were in unsatisfactory glycaemic control with a mean  $HbA_{1c}$  of  $7.5 \pm 1.1$  %.

We have previously shown that  $P_{100}$  wave latencies are significantly longer in patients with new onset non insulin dependent diabetes mellitus (NIDDM) when compared with healthy controls. Thus, our results indicate that optic nerve involvement may be developed in patients with NIDDM prior to the onset of symptoms (19).

In this study, we found significantly longer  $P_{100}$  wave latencies in diabetic patients when compared with 20 control subjects. Abnormal latencies were found in 45 % of diabetic patients (9 of 20 diabetic patients). Most previous studies did not find significantly different latencies in groups of diabetic patients and control subjects. Other researchers found delayed latencies in 15% (20), 20% (21) and 62.5% (2) of diabetic patients. Harrad et al. (22) have shown that  $P_{100}$  wave latency was significantly lengthened during hypoglycemic episodes. None of the patients in our study had clinical or biological evidence of hypo-

glycemia during the VEP session.

Some researchers found correlation between recent metabolic control and P<sub>100</sub> wave latencies in diabetic patients. However, others did not find a correlation between recent metabolic control and P<sub>100</sub> wave latencies. We could not find a relationship be-

tween recent metabolic control and P<sub>100</sub> wave latencies in diabetic patients. There were conflicting reports regarding correlations between duration of diabetes and P<sub>100</sub> wave latencies. We found significant correlation between duration of diabetes and P<sub>100</sub> wave latencies.

Our results suggest that impaired visual evoked potentials exist in diabetic patients and these ab-

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